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IMPACT OF MICROGRAVITY ON ENDOTHELIAL FUNCTION: MEASUREMENT OF FLOW-MEDIATED DILATION (FMD) IN ASTRONAUTS ON SUBORBITAL AND ORBITAL FLIGHTS

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Introduction: Microgravity induces changes in the cardiovascular system, which undergoes significant adaptations to cope with changes in pressure and fluid flow in the body in space. Among these are the redistribution of liquids (one of the most immediate effects), reduction in plasma volume, decreased cardiac workload leading to cardiac atrophy, and potential endothelial dysfunction. The vascular endothelium is the main regulator of vascular homeostasis, as it maintains vascular tone by balancing vasoconstriction and vasodilation, which in turn activates and inhibits further mechanisms involved in the genesis and progression of atherosclerosis (primarily platelet aggregation). The endothelium can be affected by the space environment, with potential implications for astronaut health during and after prolonged missions. The technique used to study endothelial function is "flow-mediated dilation" (FMD), performed at the level of the brachial artery and involving the ultrasound measurement of the vessel diameter increase, induced by increased arterial flow and, consequently, increased shear stress, following the induction of ischemia in the distal forearm segment.
Study Objective: To assess changes in endothelial function, using FMD, in astronauts subjected to missions in microgravity, both suborbital (Virtute-01 mission) and orbital (Ax-3 mission).
Materials and Methods: Five astronauts were included: 3 from the suborbital Virtute-01 mission (exposure to microgravity ≈4 minutes) and 2 from the orbital Ax-3 mission (18 days on the International Space Station). All subjects had no cardiovascular risk factors and all potentially vasoactive substances were temporarily suspended. FMD of the brachial artery was measured by ultrasound according to international standards, before and after the flight (for Virtute-01), and at multiple pre- and post-flight time points and in orbit (for Ax-3). The data were analyzed using paired t-tests, with significance set at $p<0.05$.
Results: In the Virtute-01 group, no statistically significant differences were found in FMD% values pre- and post-flight ($p=0.1062$), despite a trend towards a slight post-flight reduction. In the Ax-3 group, FMD% values were significantly reduced in orbit compared to pre-flight values ($p=0.048$) and compared to the return day ($p=0.015$) and 30 days after landing ($p=0.003$), with progressive recovery to baseline values at 60 days post-landing. Furthermore, the comparison between FMD% values measured 30 days before departure and 30 days after return showed no significant variations. To sum up, the data suggest that the value measured in orbit is lower compared to what was observed up to 30 days after the flight.
Conclusions: Microgravity seems to induce temporary endothelial dysfunction during prolonged exposure, followed by recovery after returning to Earth. Although the sample size is limited (due to the special conditions and the study population), the results suggest that echocolor-Doppler and FMD may represent a useful, non-invasive, low-cost, and easily applicable technique even in orbit, allowing the detection and, potentially, prevention of subclinical vascular damage. Further studies, with larger samples and possible inclusion of endothelial biomarkers, could clarify in more detail the impact of microgravity on endothelial function.

LIPOPROTEIN(A) AND CORONARY PLAQUE VULNERABILITY: EXPLORING THE CONNECTION WITH OPTICAL COHERENCE TOMOGRAPHY IN PATIENTS WITH ACUTE CORONARY SYNDROME

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Background: Atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of morbidity and mortality in Western countries. This is primarily due to the presence of vulnerable atherosclerotic plaques, which carry a higher risk of rupture and subsequent acute cardiovascular events. Recent advances in intravascular imaging technologies have enabled detailed plaque characterisation, allowing for the identification and assessment of plaque vulnerability in vivo. Among the many factors contributing to ASCVD, lipoprotein(a) [Lp(a)] has emerged as an important independent risk factor. Lp(a) is an LDL-like particle in which apolipoprotein(a) [apo(a)] is covalently linked to the apolipoprotein B-100 component of LDL via a single disulfide bridge. A growing body of epidemiological, genome-wide association, and Mendelian randomization studies has demonstrated that elevated plasma Lp(a) levels are causally associated with ASCVD, particularly coronary artery disease and ischemic stroke. It is important to note that Lp(a) contributes to cardiovascular events even when plasma LDL cholesterol (LDL-C) levels are optimally controlled, thus representing a significant component of residual cardiovascular risk. Plasma Lp(a) concentrations are largely genetically determined by variations in the LPA gene and remain stable throughout life, minimally influenced by environmental factors. Individuals with elevated Lp(a) levels are exposed to a lifelong increased risk of plaque formation and progression. While the overall association of Lp(a) with ASCVD is well established, the specific impact of Lp(a) on plaque vulnerability and the propensity for plaque rupture remains unclear and warrants further investigation.
Aim: This study aims to determine if serum Lp(a) levels influence plaque vulnerability using intracoronary imaging techniques with the highest in vivo resolution to detect the atherosclerotic plaque microarchitecture, specifically intravascular optical coherence tomography (OCT).
Methods: This ongoing multicenter study is being conducted at the Lipid Clinic, Department of Translational and Precision Medicine, Sapienza University of Rome, in collaboration with the Departments of Interventional Cardiology at San Giovanni-Addolorata Hospital, Rome, Italy. Patients with prior acute coronary syndrome (ACS) and previous OCT imaging of non-culprit plaques were referred for lipidology consultation. Those who consecutively consented were enrolled in the LIPIGEN study for plasma Lp(a) measurement and genetic analysis. The previously collected OCT imaging data are being retrospectively analyzed to assess plaque vulnerability features (thin-cap fibroatheroma [TCFA] with cap thickness <75 μm, minimum lumen area, lipid arc extension, macrophage infiltration, neovascularization, healed plaques, and intraplaque hemorrhage) in relation to Lp(a) levels.
Results: To date, 32 participants have been enrolled (mean age 62.6 ± 8.2 years; 6.25% female). All patients were treated with lipid-lowering therapy at the maximum tolerated dose, achieving guideline-recommended LDL-C levels. The median Lp(a) concentration was 24.4 mg/dL, with an even distribution of patients above and below this threshold. Patients with higher Lp(a) levels (>24.4 mg/dL) were more likely to have presented with ST-segment elevation myocardial infarction ($p=0.034$), and 44% of these patients required PCI of the target vessel. There was a trend toward a greater presence of TCFA (37.5%, $p=0.446$) and macrophage infiltration (81%, $p=0.127$) in the high Lp(a) group. An inverse correlation between Lp(a) levels and TCFA prevalence was observed, suggesting a potential association between elevated Lp(a) and features of plaque vulnerability. Importantly, genetic analyses are still ongoing, and no genetic data are currently available.
Conclusions: This ongoing study aims to clarify the potential role of Lp(a) as a biomarker of coronary plaque vulnerability. While preliminary findings indicate a trend linking elevated Lp(a) levels with increased plaque vulnerability detected by OCT, these associations are not yet statistically significant. Further enrolment and analyses are required to confirm these preliminary observations and to better define the therapeutic and prognostic implications of targeting Lp(a) in ASCVD management.

THINKING OUTSIDE THE BOX: A CASE OF UNEXPLAINED ASCITES IN AN ADULT

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We here report the case of a young male patient who was referred to our uni-

versity hospital with a six-month history of persistent abdominal distension. He had previously been evaluated at another facility, where he was diagnosed with ascites, underwent a few paracentesis and initiated on diuretic therapy. The patient reported no history of liver disease, alcohol or drug abuse, and no recent travels. His medical history included obstructive hydrocephalus due to a craniopharyngioma, for which he underwent the placement of a ventriculoperitoneal (VP) shunt 10 years earlier. Clinical examination revealed no signs of chronic liver disease. Blood cell count and liver function tests were within normal limits, and viral serologies were negative. A diagnostic paracentesis was performed, yielding a serum-ascites albumin gradient (SAAG) of 1.1 g/dL, thereby excluding portal hypertension. Additional biochemical analysis of the ascitic fluid (namely bilirubin, cholesterol, triglycerides) revealed no significant abnormalities; cultures and direct testing for Mycobacterium tuberculosis were negative. Advanced chronic liver disease was ruled out by transient elastography, which showed a liver stiffness of 7.1 kPa. Abdominal computed tomography excluded splanchnic venous thrombosis. Following the completion of our diagnostic work-up—including ascitic fluid analysis, laboratory investigations, and microbiological testing—we excluded portal hypertensive causes of ascites, as well as the most common non-portal hypertensive aetiologies, including malignancy, tuberculosis, and pancreatic disease. Consequently, attention was directed toward less frequent causes, beginning with the patient's history of obstructive hydrocephalus and prior placement of a ventriculoperitoneal shunt.

According to current literature, VP shunting remains the safest and most effective method for cerebrospinal fluid (CSF) diversion in patients with hydrocephalus. Nevertheless, the procedure is not without complications, the most common of which include shunt obstruction, disconnection, and abdominal site infection. In rare cases, however, accumulation of ascitic fluid has been reported as a complication of VP shunting. This phenomenon is exceedingly uncommon, with only 12 cases documented in the past three decades, the majority of which involved paediatric patients.

At present, diagnosis of VP shunt-related ascites remains one of exclusion, necessitating the systematic elimination of more prevalent causes of ascitic fluid accumulation and potential shunt malfunction. As such, a comprehensive diagnostic approach—including complete blood count, liver and renal function tests, viral serologies, diagnostic paracentesis with calculation of serum-ascites albumin gradient, and microbiological studies—is essential. In the absence of a non-invasive confirmatory test, the current gold standard for both diagnosis and treatment is an invasive procedure involving redirection of CSF away from the peritoneal cavity. This intervention serves a dual purpose: if resolution of ascites is observed, the VP shunt is confirmed as the underlying cause; conversely, if ascites reaccumulates, alternative aetiologies must be pursued. Importantly, VP shunt-related ascites typically does not respond to conventional management with diuretics or fluid restriction, a feature that may serve as a valuable diagnostic clue during the evaluation process. In the present case, the patient underwent elective externalization of the ventricular catheter, after which no recurrence of ascites was observed. Subsequently, the procedure was completed with the redirection of the ventricular catheter into the right atrium.

This case underscores an exceedingly rare complication of a commonly performed neurosurgical procedure. The uniqueness of this presentation is further accentuated by the patient's adult age, as most cases reported in the literature have occurred in paediatric populations. Accordingly, it is essential to maintain a high index of suspicion for this condition, particularly in patients with unexplained ascites unresponsive to standard therapies, in order to guide timely and appropriate diagnostic and therapeutic interventions while avoiding unnecessary diuretic treatment. A secondary objective of this report is to emphasize the current lack of a non-invasive diagnostic gold standard for VP shunt-related ascites. This diagnostic gap underscores the need for improved tools that could facilitate early and accurate diagnosis, thereby potentially obviating the need for invasive procedures prior to establishing a definitive diagnosis.

AN HEPATIC STORM

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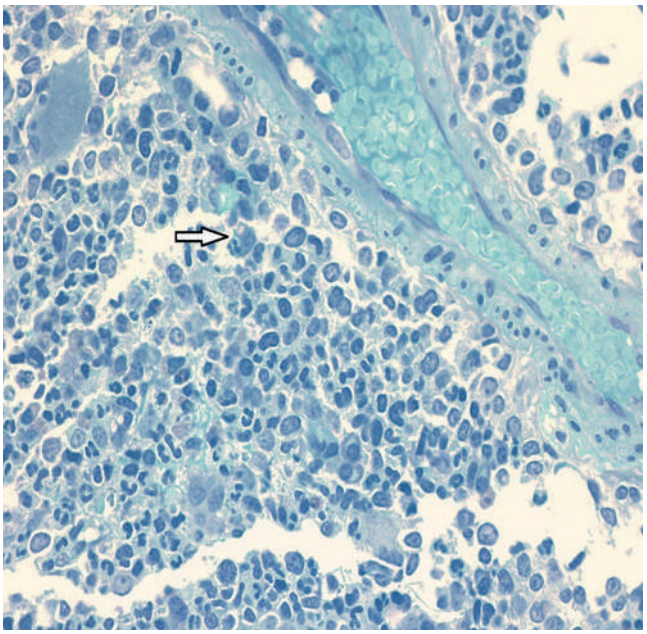
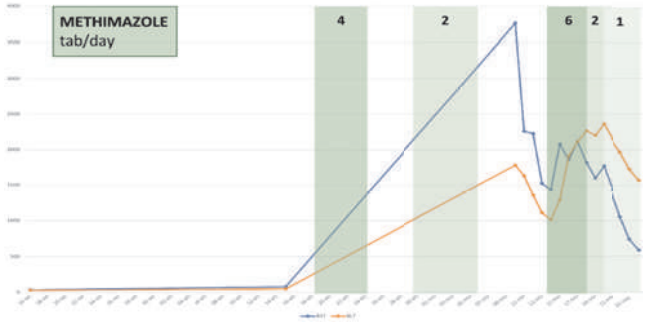
Case presentation: A 29-year-old Chinese woman was admitted to our unit due to acute cholestatic hepatitis of unknown etiology and thyrotoxicosis. She reported diarrhea, abdominal pain, jaundice, and palpitations in the last days. Her past medical history included Graves' disease with biochemical fluctuations and ophthalmopathy on treatment with levothyroxine and methimazole and a recent diagnosis of probable adult-onset Still's disease (according to Yamaguchi criteria) on treatment with anakinra. Shortly after the onset of abdominal symptoms, the patient had independently discontinued her home therapy with levothyroxine and methimazole. At admission, the patient was alert, afebrile, tachycardic, with jaundice and abdominal tenderness of the upper quadrants. Blood tests revealed acute cholestatic hepatitis (AST 3765 U/L, ALT 1780 U/L, GGT 184 U/L, ALP 344 U/L, total bilirubin 11 mg/dL, direct bilirubin 10 mg/dL), prolonged coagulation times (INR 1.64, aPTT 1.33), and thyrotoxicosis (suppressed TSH with fT4 60 ng/L). Inflammatory markers were normal such as all other screening blood tests. Abdominal ultrasound showed no biliary duct dilation or gallstones. In the suspicion of drug induced liver injury (DILI), methimazole and anakinra were kept discontinued. Given the presence of thyrotoxicosis and possible autoimmune hepatitis, therapy with propranolol and prednisone 1 mg/kg was started, resulting in a slight initial decrease in hepatic cytolysis indices. The autoimmune hepatitis antibody panel (ASMA, AMA, LKM) was negative. Serology for HIV, HBV, HCV, HAV, HEV, and HSV1/2 was negative for acute infection; EBV-DNA and CMV-DNA were also negative.

Patient management: An urgent transjugular liver biopsy was performed. Transaminase levels progressively decreased with methylprednisolone 60 mg/day and methimazole discontinuation. Subsequently, the patient developed fever with peaks up to 39 °C without specific organ recall, associated with increased inflammatory markers (WBC 22300/mm3, N 20400/mm3, CRP 9 mg/dL). Urine culture, blood cultures, nasal swab for respiratory viruses, stool cultures, stool parasite examination, and chest X-ray were negative. Chest CT was normal, while abdominal MRI with contrast showed only hepatosplenomegaly and diffuse liver edema. Empirical antibiotic therapy with gentamicin was started. At the same time thyroid tests indicated overt thyrotoxicosis. Suspecting thyrotoxicosis-induced fever and considering the low likelihood of hepatotoxicity given previous exposure to the drug, methimazole therapy was reintroduced. Elevated ferritin levels (19775 ug/L) and a relative decrease in blood count values without frank cytopenia were also noted. Given the history of adult-onset Still's disease and suspicion of macrophage activation syndrome (MAS), although not all diagnostic criteria were met, the ongoing steroid therapy was increased to methylprednisolone 1 g/day for three days. In the following days, ferritin levels increased further (30064 ug/L), and thrombocytopenia (77000/mm3) and fibrinogen consumption (73 mg/dL) developed despite ongoing steroid therapy and fever lysis. A bone marrow aspirate was performed, showing rare images of hemophagocytosis, as well as a bone marrow biopsy. Dexamethasone 8 mg twice daily was initiated. Furthermore, there was a new progressive worsening of transaminase values and anemia appeared. The liver biopsy was suggestive of DILI. The clinical picture was then interpreted as acute hepatitis due to methimazole with a hemophagocytic flare, which, however, did not appear to be the primary driver. The bone marrow biopsy showed hypoplasia of the erythroid series. The cytopenias improved with the favorable evolution of hepatitis. For the management of Graves' disease thyroid ablation with iodine-131 or total thyroidectomy were considered. However, the patient decided to self-discharge to return to China.

Discussion: Methimazole has been associated with transient, asymptomatic elevations in serum aminotransferase levels (1). However, methimazole is also capable of causing clinically apparent, idiosyncratic liver injury and the pattern of enzyme elevations is typically cholestatic or mixed (1). Recovery is usually rapid once methimazole is stopped (1). Regarding the highly elevated ferritin values, in one study ferritin level over 10,000 mg/L was 90% sensitive and 96% specific for HLH/MAS (2) but the differential diagnosis remains broad with iron overload and liver disease being the most common causes (3). In our opinion the patient had an acute hepatitis due to methimazole with a systemic hyperinflammatory syndrome due to hepatitis.





LATE NEUROLOGICAL MANIFESTATION OF MITOCHONDRIAL ENCEPHALOMYOPATHY WITH LACTIC ACIDOSIS AND STROKE-LIKE EPISODES SYNDROME (MELAS): A CASE REPORT

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Background: Mitochondrial diseases (MD) are a group of rare diseases that can present with acute neurological symptoms. Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like Episodes (MELAS) is the most common MD and should be suspected in the presence of typical clinical, radiological, and anamnestic features.
Case Report: V.N., a 66-year-old male, presented to the emergency department (ED) in December 2024 due to the onset of postural instability, muscle weakness, and sphincter release. His medical history included type 2 diabetes mellitus with retinopathy and nephropathy, mixed dyslipidemia, right mononeuritis, and severe sensorineural hearing loss.
At admission, the patient was alert but confused, with neurological findings including anisocoria, generalized muscle atrophy, and weak deep tendon reflexes. Although the onset of symptoms could not be clearly determined, a general worsening had been reported starting at least 24 hours before. Arterial blood gas analysis showed a lactic acidosis, while an acute pneumonia of the lower right lobe was diagnosed at chest X-ray. A head CT scan was performed, consistent with a large subacute ischemic stroke in the temporo-parietal region. The neurological evaluation in the ED already suspected a a possible mitochondrial disorder (MD) on the maternal side due to the concomitant presence of hearing loss, short stature and DM2, and the presence of similar features also in the patient's sister.
The patient was then transferred to the Internal Medicine department, where antibiotic therapy with ceftriaxone and azytromicin and antiplatelet treatment were started. As supplementary neurological imaging, a carotid ultrasound evaluation, an MRI, angiography and spectroscopy brain scan were performed. Moreover, as instrumental workup, an electroneuromyography was done, consistent with sensory-motor neuropathic involvement, and an EEG showed non-specific slow activity bilaterally in the fronto-temporal regions. A cardiac evaluation was conducted, revealing concentric hypertrophy of the left ventricle at ultrasound, initially suggestive of amyloidosis, but later diagnosed as hypertrophic cardiomyopathy by cardiac MRI. Serum pyruvate levels and urine sediment analysis were obtained. All the above findings were consistent with MELAS mitochondrial encephalopathy, with the hallmark of the disease being the lack of flow alterations on MRI angiography and the lactate peak observed on MRI spectroscopy in the areas of abnormal signal on previous CT and MRI (figure 1 and figure 2).
The diagnosis of MELAS was confirmed in the Neurology department by genetic testing, which demonstrated the presence of the m.3243A>G variant in the MT-TL1 gene (tRNA Leucine1) in the mitochondrial DNA. Levetiracetam was started to prevent further stroke-like episodes, and the patient was discharged with recommendations for a low-lipid, low-carbohydrate diet, endocrinology and cardiology follow-up visits, and genetic counseling for the sister.
Discussion: MELAS is a mitochondrial disorder typically manifesting before the age of 40. The mutation in mitochondrial DNA, specifically in the MT-TL1 gene encoding tRNA, leads to multi-organ involvement, including stroke-like episodes, encephalopathy, myopathy, lactic acidosis, epileptic seizures, type 2 diabetes, cardiomyopathy, and sensorineural hearing loss. Although the diagnosis of MELAS is usually reached at younger age, the occurence in older patients of an ischemic stroke in an atypical area, such as the temporo-parietal region, without clear correlation between the vascular territory and the localization of the lesion, should raise suspicion for MELAS, especially in the presence of typical comorbidities such as diabetes, muscolar weakness, hearing loss and short stature, involving the patient and other family members.
References: *Metabolic Brain Disease, et al. BMC Neurol*

RECURRENT NON-INFECTIOUS ENDOCARDITIS IN ATYPICAL ADULT-ONSET STILL'S DISEASE EFFECTIVELY TREATED WITH ANAKINRA: A CASE REPORT

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Introduction: Adult-onset Still's disease (AOSD) is a systemic inflammatory disorder usually affecting young adults. The most common clinical features are spiking fever, arthralgia/arthritis and salmon-pink erythema, but patients can develop other manifestations like sore throat, hepatomegaly, splenomegaly, lymphadenopathy and serositis. Cardiac involvement is quite frequent in AOSD (up to 29% of patients) and pericarditis is the most frequent form followed by myocarditis, while non-infectious endocarditis is a very rare manifestation with few cases reported in literature (1).
Case report: We report about a 33 years-old man with a history of recurrent endocarditis since July 2022, complicated by aortic valve insufficiency in the absence of microbiological findings, necessitating biological valve replacement. In November 2023 the patient developed aortic valve stenosis and periprosthetic fluid collection requiring new valve replacement surgery with mechanical aortic valve, closure of sub-valvular pseudoaneurysm and simultaneously mitral plastic surgery for mitral insufficiency. In January 2024, he underwent a new aortic valve replacement with homograft prosthesis and mitral valve replacement with mechanical prosthesis due to recurrence of

endocarditis; he also presented intermittent fever and increased inflammatory markers (CRP, ERS) despite appropriate antibiotic therapy due to the positivity at 16S test for Cutibacterium acnes on valve material. Given the persistence of intermittent high fever despite antimicrobic therapy, he was re-admitted to intensive cardiologic care unit department. Laboratory findings were significant for anaemia (Hb 8,7 g/dL, nv 12-16 g/dL), increase in CRP (184 mg/L, nv<5 mg/L), serum amyloid A (SAA, 1173 mg/L, nv <5 mg/L) and ferritin (1043 ng/mL, nv 25-330 ng/mL), while procalcitonin tested negative. Complete blood count confirmed a moderate neutropenia, already extensively investigated in the past for primary immunodeficiency and hematologic causes.
Considering recurrency of fever and endocarditis associated with inflammatory arthralgias, and splenomegaly on CT scan, together with inflammatory markers increase, a complete immunological evaluation was performed, consisting of ANA, anti-ENA, anti-dsDNA, ANCA, anti-phospholipid and rheumatoid factor, which all tested negative.
Based on the clinical and laboratory data, a diagnosis of AOSD was made, despite the incomplete typical features (absence of lymphadenopathy, skin rash, leucocytosis, predominant valvular involvement). Anakinra at the daily dose of 100 mg was started, with close clinical and laboratory monitoring, associated with an empiric antibiotic therapy. Within a week, the patient achieved a complete resolution of fever and arthralgias, with a consequent reduction in inflammatory markers (CRP 6 mg/L, ferritin 597 ng/mL, SAA 35 mg/L) at 1 month. However, the clinical course was complicated by acute kidney failure requiring continuous-replacement renal therapy due to cardiogenic shock in progressive valvular degeneration detected by repeated ultrasound-echocardiography and polymicrobial sepsis due to nosocomial pathogens with need of anakinra discontinuation and filgrastim administration for worsening neutropenia. After 2 months of hospitalization (May 2024), he underwent new cardiac surgery, with mechanical Bentall surgery, hemiarch and mitral valve replacement with mechanical prosthesis. Given the persistence of intermittent fever and increased inflammatory markers, without further evidence of microbial infection, therapy with anakinra 100 mg/day was reintroduced, with marked clinical improvement and substantial regression of inflammatory markers. The patient fully recovered after 30 days from surgery and was discharged on daily subcutaneous anakinra. At the last 6-months follow-up the patient still presented excellent general conditions with no clinical, laboratoristic and imaging signs of endocarditis recurrency.
Conclusion: We observed an atypical case of AOSD in a young man displaying recurrent endocarditis with need of repeated cardiac surgery. In the absence of infections demonstration, it should be noted that inflammatory causes must be ruled out in these cases. The overall clinical, laboratory and imaging findings were suggestive for an inflammatory form of endocarditis requiring anakinra treatment, after a careful risk-benefit evaluation in a critically ill patient. Despite in this case report we observed a consistent response with anakinra, further research is needed to investigate the real effectiveness and safety of anakinra for endocarditis treatment in AOSD and in idiopathic inflammatory endocarditis.
References:
1) Bodard Q. et al, Cardiac involvement in adult-onset Still's disease: Manifestations, treatments and outcomes in a retrospective study of 28 patients. J Autoimmun. 2021 Jan;116:102541.

SUCCESSFUL SUSPENSION OF ELTROMBOPAG AND SUSTAINED RESPONSE OFF TREATMENT FOLLOWING TREATMENT INITIATION FOR BREAST CANCER: A CASE REPORT

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Background: Secondary immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by a low platelet count, which occurs in association with a condition known to cause immune-mediated thrombocytopenia. Causes of secondary ITP include systemic autoimmune diseases, chronic infections, drugs and malignancies. Whereas the association of ITP with lymphoproliferative malignancies is established in scientific literature, its occurrence in patients with non-hematologic solid tumors is less well documented.1,2
Case presentation: A 67-year-old woman with a history of breast cancer radically treated in 2003 and a subsequent negative follow-up presented to our center in 2022 with spontaneous bleeding and severe thrombocytopenia. Based on the negative results of the initial diagnostic work-up, which included a bone marrow biopsy, a diagnosis of primary ITP was made. Corticosteroid therapy was initially effective but was followed by frequent relapses, prompting the introduction of the thrombopoietin receptor agonist (TPO-RA) eltrombopag in November 2022. During treatment with eltrombopag, the patient required several dose adjustments due to fluctuations of the platelet count, alternating between thrombocytopenia and thrombocytosis. At the beginning of 2024 the patient was diagnosed with a recurrence of luminal B breast cancer and was started on treatment with letrozole and ribociclib in March 2025. Following the initiation of treatment for breast cancer, we noticed a steady improvement in the platelet count, with fewer fluctuations, which allowed a gradual tapering of eltrombopag. In the process of staging the recurrence of breast cancer, the patient was incidentally diagnosed with a marginal zone lymphoma. Given the low proliferation index of the lymphoma, treatment options – including a watch-and-wait strategy, radiotherapy and systemic treatment – were discussed. After careful consideration, the patient opted for rituximab monotherapy (375 mg/m2 for four weeks), which was started in the second half of May 2024. In light of the successful tapering of eltrombopag and of the stability of the platelet counts since March 2024, we attempted discontinuing eltrombopag in June 2024. The choice was made after carefully evaluating the balance between the risk of drug-induced thrombocytopenia posed by ribociclib and the thrombotic risk posed by the active malignancy and continued treatment with a TPO-RA. Over the following months, blood tests showed safe platelet counts with no need for resumption of ITP-specific therapy nor for the discontinuation of ribociclib due to incident thrombocytopenia. At the most recent follow-up in March 2025, more than six months after the discontinuation of eltrombopag, the patient exhibits a sustained response off-treatment (SROT), with platelet counts stably above 100.000/mmc.
Discussion: We presented the case of a patient whose ITP diagnosis preceded by 2 years the recurrence of breast cancer, which had been radically treated approximately 20 years before. The unexpected discovery of a low-grade lymphoproliferative disorder further complicates the interpretation of this clinical scenario. This case description highlights the possible paraneoplastic nature of ITP associated with solid tumors. Although less frequently reported than the association with lymphoproliferative disorders, there have been descriptions of ITP secondary to solid tumors. In this setting, ITP can accompany, precede or follow the diagnosis of the concomitant malignancy.1,2,3,4 In the case of our patient, the start of the treatment for breast cancer was followed by a significant improvement in the patient's platelet counts, allowing for the first time to consider the discontinuation of eltrombopag. This possibility was evident even before administering rituximab, which is known to be an effective treatment for some patients with ITP. The management of breast cancer, which started temporally before the treatment of the indolent lymphoma, seems to have facilitated the suspension of the TPO-RA, suggesting that the effective control of the solid malignancy may have played a more significant role in ITP management than the treatment of the accompanying indolent lymphoma.
References:
[1] doi:10.1080/09537104.2020.1822521
[2] doi:10.1182/blood-2009-01-129155
[3] doi:10.1016/j.critrevonc.2011.02.004
[4] doi:10.1002/ccr3.1939

UNVEILING THE COLD TRUTH: TRACING THE VASCULAR PUZZLE OF A SYSTEMIC DISEASE

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A 63-year-old woman, with a prior diagnosis of seropositive rheumatoid arthritis (RA) with mild clinical activity (2022), presented with acral ischemia and progressive distal digital necrosis. Her past medical history included osteoporosis, degenerative joint disease (, and a suspected B-cell lymphoproliferative disorder identified in late 2024 due to persistent lymphocytosis and splenomegaly. Imaging had shown erosive arthropathy and vascular irregularities.
She was an ex-smoker, with no known allergies or substance use.
In May 2024, she developed intermittent painful ulcers on the lower extremities, sometimes post-traumatic, and cyanosis involving toes I, IV, V of the left foot and the dorsum. The symptoms partially regressed. Vascular evaluation diagnosed peripheral arterial occlusive disease with critical ischemia of the left foot, for which antiplatelet therapy (ASA 100 mg/day) was started.

Imaging revealed posterior tibial artery occlusion and diffuse narrowing of anterior tibial and peroneal arteries.
Concomitantly, rheumatologic assessment raised suspicion for thromboangiitis obliterans (Buerger's disease). IV prostanoids and tiopronin were trialed without benefit. Laboratory testing indicated elevated inflammation (CRP 78.76 mg/dL, fibrinogen 641 mg/dL), high rheumatoid factor (136 IU/mL), normal ANA/ENA panels, and D-dimer of 1.47 µg/mL.
In November 2024, hematology follow-up for worsening lymphocytosis (15,320/mm^3) confirmed a clonal B-cell population via flow cytometry. Imaging revealed hepatosplenomegaly and gallbladder lithiasis. Serologies showed past HBV exposure (anti-HBc positive, HBsAg negative).
In March 2025, she developed dark discoloration and progressive necrosis of digits II–IV (right hand) and II–III (left hand), with hypoesthesia and weakness. Doppler of the upper limbs showed diffuse intimal thickening without hemodynamic obstruction.
She presented to the emergency department with worsening digital necrosis. Labs showed leukocytosis (WBC 36,870/µL, lymphocytes 47%), normocytic anemia (Hb 10 g/dL), thrombocytosis (466,000/mm^3), hyponatremia (130 mmol/L), and elevated inflammatory markers (CRP 72.1 mg/dL, fibrinogen 965 mg/dL). Dry gangrene was confirmed on digits II and III of the right hand and ischemia on the left. Lower extremity pulses were diminished. CT angiography was unremarkable; chest CT showed nonspecific micronodules and reactive lymphadenopathy.
Initially admitted to surgery, she was later transferred to internal medicine. On admission, physical exam showed bilateral lower limb ulcers and injection site hematomas. No cardiac abnormalities were noted. Doppler confirmed stenosis in palmar metacarpal arteries without signs of Buerger's disease. Echocardiography and ECG excluded cardioembolic causes.
Autoimmune workup showed ANA 1:640, high rheumatoid factor, and strongly positive anti-CCP antibodies (4254 CU). Skin biopsy of a lower limb lesion excluded overt vasculitis. Given rapid clinical progression, she was started on high-dose steroids, prostanoids, and calcium channel blockers, without improvement. Necrosis progressed to the second digit of the left hand with cyanosis of the third.
Due to the clinical context, HBV history, and suspicion of cryoglobulinemia related to a lymphoproliferative process, serum cryoglobulins and viral serologies were requested. Anti-HBc was positive with negative anti-HBs, suggesting past or occult HBV. Lamivudine prophylaxis was initiated prior to immunosuppression. Cryoglobulins were detected and classified as type I. Given ischemic progression, urgent consultation led to indication for plasma exchange. However, during the first session, the patient developed rash and hypotension, consistent with an allergic reaction to human albumin. Plasma exchange was permanently contraindicated.
Further evaluation included lymphocyte typing confirming clonal B-cell proliferation and bone marrow biopsy. Pending pathology, rituximab therapy was initiated (two infusions: 01/04 and 14/04) under HBV antiviral cover.
On 02/04/2025, surgical amputation was performed of digits II–IV (right hand) and II (left hand). The procedure was uneventful. A biopsy of the ulnar neurovascular bundle of the second digit was obtained and remains under analysis. Final histology from bone marrow showed marginal zone B-cell differentiation, suggestive of splenic marginal zone lymphoma (SMZL), a B-cell malignancy known to associate with chronic HBV infection and monoclonal cryoglobulinemia.
This likely underlies the patient's type I cryoglobulin production and resultant vascular damage via hyperviscosity and cold-precipitating immune complex deposition. PET-CT excluded large vessel vasculitis but showed mild pulmonary uptake requiring follow-up. This case exemplifies the complex intersection of autoimmune disease, hematologic malignancy, and vasculopathy. The patient's rapidly progressive ischemia was likely driven by SMZL-associated monoclonal cryoglobulins, with RA potentially contributing to endothelial dysfunction. Diagnostic challenges included overlap with Buerger's disease and autoimmune vasculitis, highlighting the importance of early cryoglobulin testing and multidisciplinary care.

SYSTEMIC INFLAMMATION WITH CARTILAGINOUS INVOLVEMENT IN A CASE OF FUO: DIAGNOSTIC CHALLENGES AND UNEXPECTED FINDINGS

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Background: Fever of Unknown Origin (FUO) is one of the most challenging scenarios in clinical practice, often requiring a comprehensive and multidisciplinary approach to reach a definitive diagnosis. While the causes of FUO are various, ranging from infections to autoimmune disorders and malignancies, the process of identifying the underlying etiology can be complex. Here, we present the case of a 69-year-old Caucasian woman whose persistent symptoms and lack of initial organ-specific involvement complicated the diagnostic process, ultimately revealing a rare underlying condition.
Discussion: The patient, with a history of hypertension and active smoking, presented to the emergency department with progressive asthenia and intermittent low-grade fever lasting three weeks. Accompanying symptoms included mild unintentional weight loss (3 kg in one month) with preserved appetite. Notably, the patient reported a prior episode of transient nasal and periorbital edema associated with erythema and pain, which had resolved spontaneously and was absent at admission. Laboratory findings revealed neutrophilic leukocytosis, mild normocytic anemia, mild thrombocytosis, and markedly elevated inflammatory markers (C-reactive protein, erythrocyte sedimentation rate and ferritin), with procalcitonin levels within the normal range. Empirical antibiotic therapy with amoxicillin/clavulanic acid was initiated after performing blood and urine cultures, which subsequently tested negative.
Further diagnostic investigations aimed at excluding infectious, neoplastic, and autoimmune causes were conducted. Extensive infectious serologies (Human Immunodeficiency Viruses, syphilis, Borrelia, Coxiella, Brucella, Citomegalovirus, Toxoplasma, Hepatitis C Virus, Hepatitis B Virus, Mycoplasma, and Chlamydia) and blood cultures for Mycobacterium tuberculosis gave negative results. Contrast-enhanced whole-body CT excluded occult malignancies, while transthoracic echocardiography showed no evidence of endocarditis but revealed a minimal pericardial effusion without hemodynamic compromise. As the infectious disease workup remained inconclusive, the empirical antibiotic therapy was discontinued.
A PET-CT scan revealed increased FDG uptake in the walls of the aortic arch, suggestive of inflammatory activity. These findings were confirmed by an angio-CT imaging of the aorta, raising suspicion of a vasculitic process (*Figure 1*).

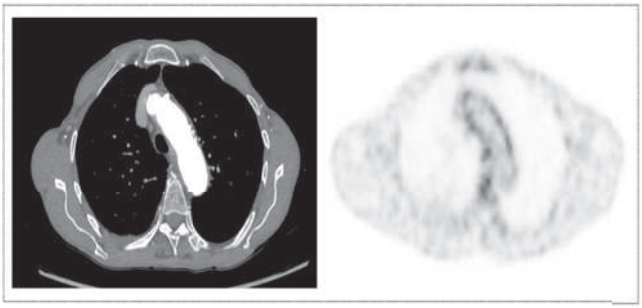

Figure 1. Autoimmune panel results showed positivity for Antinuclear Antibody (ANA) with a titre of 1:640, homogeneous pattern, and perinuclear Antineutrophil Cytoplasmic Antibody (pANCA), while other markers were negative. Temporal artery ultrasound ruled out giant cell arteritis. Empirical steroid therapy (prednisone 25 mg/day) was initiated, leading to initial improvement in fever.
During hospitalization, the patient developed sudden auricular edema and erythema of the right ear, consistent with perichondritis (*Figure 2*).

Figure 2. Retrospective analysis of her symptoms, including the prior nasal and periorbital edema episodes, auricular involvement, and the inflammatory process affecting the aortic arch, pointed toward relapsing polychondritis as the unifying diagnosis. Steroid therapy was intensified to 1 mg/kg/day, resulting in resolution of auricular inflammation and fever. The patient was

discharged on a tapering steroid regimen with the addition of methotrexate for long-term steroid-sparing management. Close outpatient follow-up was arranged to monitor clinical progress and prevent disease flares.
After five months, the patient remains clinically stable, with no recurrence of fever or perichondritis episodes. Laboratory tests have normalized, and she continues tapering prednisone (currently at 5 mg) alongside methotrexate therapy. Due to glucocorticoid-induced osteoporosis, bisphosphonate treatment was initiated. A follow-up PET scan was performed (*Figure 3*), showing a marked regression of the previously described diffuse radiotracer uptake in the aortic arch walls.

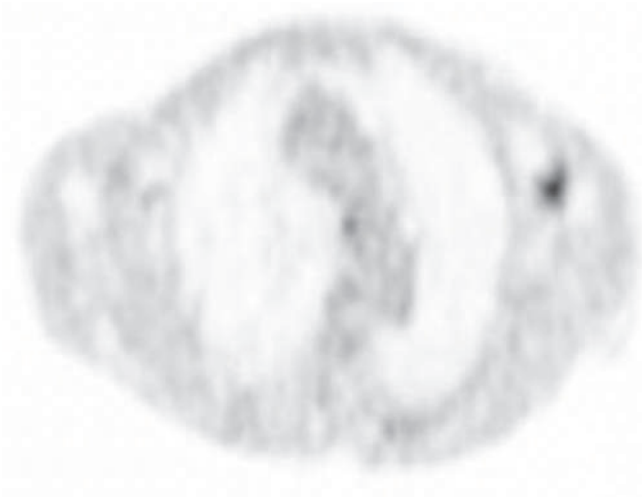

Figure 3. Follow-up PET scan performed after five months, showing a marked regression of the previously described diffuse radiotracer uptake in the aortic arch walls, with only mild residual segmental heterogeneity in distribution.

Conclusion: Relapsing polychondritis should be considered in patients presenting with unexplained fever, systemic inflammatory markers, and recurrent cartilaginous inflammation. In this case, the recognition of perichondritis during hospitalization was crucial in achieving a timely diagnosis, highlighting the importance of detailed symptom analysis and multidisciplinary collaboration in managing FUO.

PERSISTENT NEUROLOGICAL IMPAIRMENT AND HYPERNATREMIA IN LITHIUM INTOXICATION: A CLINICAL CHALLENGE

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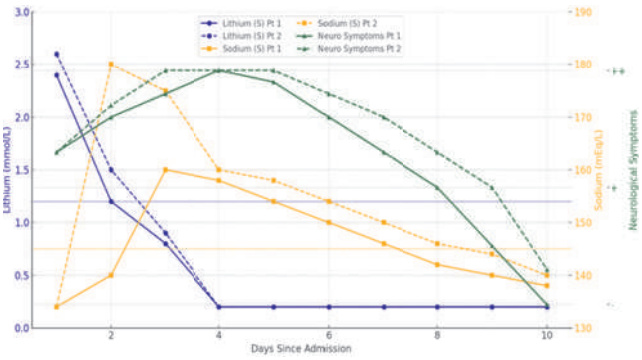
Lithium intoxication poses a diagnostic and therapeutic challenge, as clinical manifestations may persist despite normalization of serum lithium levels. We describe two clinical cases of women admitted with neurological symptoms and hypernatremia in the context of lithium therapy. Both cases developed nephrogenic diabetes insipidus (NDI), unmasked by limited water intake during hospitalization. Diagnosis was guided by persistent euvolemic hypernatremia and neurological impairment. Management required hydration support and discontinuation of lithium.
Case Presentation: We present the case of a 69-year-old woman who arrived at our Emergency Department complaining of severe asthenia associated with disorientation, mental confusion, and language disturbances that had gradually developed over the past month. Her past medical history included bipolar disorder treated with lithium carbonate (Carbolithium) with a recent dose increase, a previous ischemic stroke, and a recent percutaneous closure of a sinus venosus-type atrial septal defect with right-to-left shunt. On initial evaluation, the patient was alert but poorly oriented, mildly slowed down, and exhibited some speech incoherence. A brain CT scan ruled out ischemic or hemorrhagic lesions. Blood tests, including serum lithium, revealed toxic serum lithium levels (2.4 mmol/L, n.v. <1.2 mmol/L) and altered liver function indices. Following neurological and psychiatric consultation, the symptoms were attributed to lithium intoxication. Hydration therapy was initiated with close observation. The following day, the patient's neurological status worsened (GCS 4) despite normalized serum lithium levels, with onset of a mild fever associated with increased inflammatory markers. A meningoencephalitic process was suspected; a lumbar puncture and a repeat brain CT were negative. Urine culture was positive for Citrobacter koseri, and intravenous ceftriaxone 2 g daily was started. The body temperature and inflammatory markers normalized within 24 hours, but the neurological symptoms (alternating sopor and psychomotor agitation) persisted for more than a week. During hospitalization, the patient developed euvolemic hypernatremia (Na+ up to 160 mEq/L), suggestive of NDI unmasked by the restricted water access. A nasogastric tube was placed for free water administration and enteral feeding, leading to gradual normalization of sodium levels. About 10 days after serum lithium normalization and discontinuation of Carbolithium, cognitive function began to recover. The patient was able to resume oral intake.
An additional case of particular interest involved a 60-year-old woman who presented to the Emergency Department with neurological symptoms similar to the previous case. Her laboratory tests revealed an elevated serum lithium level (2.6 mmol/L). As in the first case, neurological symptoms persisted for several days, and clinical improvement occurred with delay, despite the normalization of serum lithium levels. Also the second patient developed marked hypernatremia (Na+ up to 180 mEq/L) secondary to NDI induced by lithium toxicity. Prior to hospitalization, the condition had been masked by excessive oral fluid intake, which had compensated for the underlying renal concentrating defect.
Discussion: Lithium intoxication represents a complex diagnostic and therapeutic challenge, in which serum lithium levels often do not correlate well with clinical symptoms [Figure 1]. This is due to the slow intracellular penetration and compartmentalization of lithium, especially in the central nervous system, where it may persist and exert toxic effects even after serum levels have normalized. This dissociation between biochemical parameters and clinical presentation is well described in the literature and highlights the need for a clinical over laboratory-based approach in the management of lithium intoxication [1-2]. NDI is one of the most common renal adverse effects of lithium therapy, reported in up to 20 to 40% of long-term users, and is often underrecognized in its early stages [3]. It is caused by a concentrating defect in the kidneys, resulting in the excretion of dilute urine [4]. Normally, the resulting thirst and increased intake of free water compensate for these fluid losses. However, hypernatremia can become clinically manifest when access to water is limited because of the onset of neurological symptoms of lithium toxicity or in the context of concurrent acute illnesses and/or hospitalization [5].
These cases underscore the importance of integrating clinical evaluation with laboratory findings, and of promptly recognizing NDI in lithium-treated patients. Notably, the persistence of neurological symptoms despite normalized lithium levels highlights the long-lasting intracellular effects of lithium, with significant implications for patient management.



1NOT ALWAYS INFECTIVE: STERILE BRAIN ABSCESS DUE TO ATYPICAL BEHÇET'S DISEASE - A CASE REPORT

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Background: The diagnostic work-up of brain abscesses is ample and in-

cludes exclusion of mimics, such as primary or metastatic tumours, pyogenic meningitis, acute focal necrotizing encephalitis, mycotic aneurysms, septic emboli with infarction, septic sural sinus thrombosis, and epi/subdural empyema.
Case report: Here we present the case of a 31-year-old man, a smoker, suffering from psychosis on clozapine therapy, who came to our attention in 2021, hospitalized for fever and visual loss of the right eye with evidence of panuveitis and retinal vasculitis. During diagnostic work-up, he developed left lower limb paresis; brain MRI showed a necrocytic right cortico-subcortical lesion with an edematous edge, suggestive of an abscess. Therapy with ceftazidime, metronidazole, vancomycin and acyclovir was implemented. Direct and indirect microbiologic work-up on blood and liquor (direct microscopy including mycobacterial, Nocardial and fungal stains, cultures, and molecular test for mycobacteria, cysticercosis, toxoplasma, and serology for herpes, syphilis, HIV, toxoplasma, and cysticercosis) were unrevealing. Similarly, blood biochemistry, total antibody and complement levels, autoantibody profile were negative or within normal limits except for systemic inflammation (CRP 63 mg/l). A whole body-CT scan was unrevealing. Clinical and serological picture did not improve after three days of antibiotic therapy: upon investigation, the patient reported few episodes of oral and genital aphthosis and acne during his past life. A diagnosis of Behçet's disease was made and the possibility of a sterile brain abscess was formulated: prednisone 50 mg was added to anti-microbial therapy, with clinical and radiological improvement. Before discharge, mycophenolate mofetil and steroid tapering was begun. After 9 months, brain MRI revealed the re-appearance of peri-lesional edema, consistent with the hypothesis of an immune rather than infectious nature of the abscess. Biologic therapy with adalimumab was begun, with resolution of the inflammatory findings at MRI. However, after further eleven months, the patient experienced a generalized seizure. Brain MRI showed increased dimension of the lesion with re-appearance of edema. Steroids were up-titrated transiently, and adalimumab was shifted to IV infliximab. Over the next two years, the patient remained in clinical and MRI remission on prednisone 5 mg, mycophenolate mofetil 1.5 g die and infliximab 6 mg/kg every six weeks.
Discussion and conclusions: Behçet's disease is an idiopathic systemic vasculitis that affects venous and arterial vessels of different size, characterized by recurrent oral and genital aphthae and inflammation in the skin, gastrointestinal tract, eyes, joints or central nervous system (CNS). Skin involvement may be characterized by excessive inflammation as a results of sterile or microbial stimuli, resulting in manifestations such as pathergy, folliculitis and acne. CNS involvement occurs in 5-10% of patients and is charachterized by an unfavourable prognosis; it may be due to cranial vasculitis, cerebral venous thrombosis, meningeal inflammation and parenchymal inflammatory lesions, sometimes with a pseudo-tumoral appearance. Here we present an atypical case of Behçet's disease causing a sterile brain abscess that required the combination of steroids, mycophenolate mofetil and infliximab. The possibility of sterile abscess should therefore be considered in the case of unrevealing microbiology testing together with poor response to antimicrobial therapy and concomitant features suggestive of systemic idiopathic inflammatory diseases such as Behçet's.

CEREBRAL AMYLOID ANGIOPATHY: THE MEDICAL MYSTERY BEHIND AN UNUSUAL BEHAVIOR

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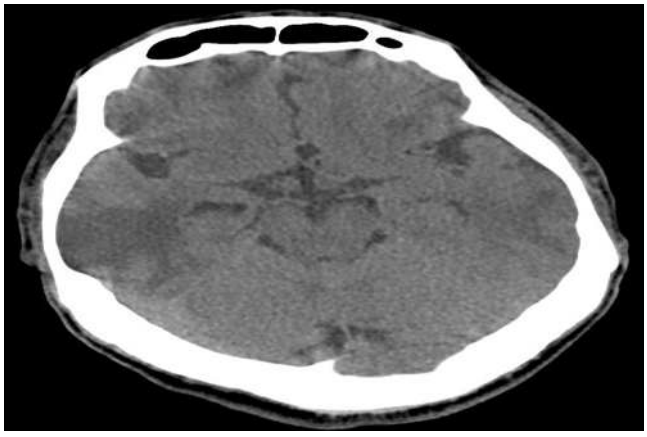
Background: Cerebral Amyloid Angiopathy (CAA) is a neuropathological condition characterized by the extracellular deposition of amyloid proteins, predominantly β-amyloid, within the walls of small to medium-sized cerebral blood vessels. This vascular accumulation contributes to increased susceptibility to cerebral hemorrhages and has been implicated in the pathogenesis of cognitive impairment and various forms of dementia.
Clinical Presentation :A 67-year-old man presented to the emergency department with confusion and bradyphrenia. While awaiting evaluation, he experienced a generalized tonic-clonic seizure. His medical history included major depressive disorder, arterial hypertension and dyslipidemia. In the past, he had two acute myocardial infarctions and an abdominal aortic aneurism, treated with endovascular repair. EEG revealed bilateral diffuse slowing. An initial non-contrast brain CT excluded acute events, but showed new bilateral hypodense lesions in the temporal regions—absent in previous imaging—as well as progression of chronic small vessel disease affecting the white matter. Routine blood tests were unremarkable. A cerebral and neck vessel CT angiography was repeated 24 hours later. Given the stability of the clinical condition, the patient was discharged. Eight days later, the patient was brought back to the emergency department after being found unconscious in the bathroom, with associated sphincter release. A repeat brain CT scan showed findings similar to the previous one. Due to elevated D-dimer levels, a chest CT angiography was performed, which ruled out PE.
Differential Diagnosis: The patient was admitted to our Department. Given the suspicion of chronic ischemic lesions, the patient's relatives were asked about any previous symptoms suggestive of stroke in the preceding months. In the meantime, the patient exhibited a rapid cognitive decline, with progressive temporal-spatial disorientation and loss of autonomy in self-care. Behavioral disturbances were managed with Quetiapine. A contrast-enhanced brain CT scan revealed additional bilateral, recurrent lesions with partial contrast enhancement and surrounding edema, suggestive of metastases. However, tumor markers were negative. A contrast-enhanced total body CT scan and colonoscopy were performed to search for a primary tumor, both of which were negative. Due to elevated CRP levels, a work-up for infectious diseases, including blood and urine cultures, was conducted, yielding negative results.
Results: Subsequently, a contrast-enhanced brain MRI was performed, revealing innumerable bilateral micro-hemorrhagic sequelae within the white matter, predominantly in the temporal regions, along with multiple gliotic foci and malacic changes, involving both cerebral and cerebellar hemispheres. These findings were consistent with cerebral amyloidosis. Primary, familial, and secondary causes of amyloidosis were ruled out. Based on the Boston criteria, a diagnosis of probable Cerebral Amyloid Angiopathy (CAA) was established.
Pathophysiology: In CAA, amyloid deposits are found exclusively in the meningo-cortical vessels, and the pathology is not associated with other forms of amyloidosis. These amyloid deposits predispose the blood vessels to rupture, increasing the risk of cerebral hemorrhages, which can range from microhemorrhages to larger, more extensive bleeds. Due to the accumulation of β-amyloid, these patients have a higher likelihood of developing Alzheimer's disease. For in vivo diagnosis of the condition, the Boston criteria are used, which allow for diagnosis in patients over 55 years of age, with cerebral hemorrhages (the distinction between single and multiple hemorrhages allows for a diagnosis of possible or probable CAA), and the exclusion of other causes of hemorrhage. Furthermore, the diagnosis of CAA can be supported by histopathological analysis of samples obtained through brain biopsy or hematoma evacuation. A definitive diagnosis is only possible through post-mortem histological examination. The clinical symptoms depend on the type of cerebral hemorrhage. In our case, where hemorrhages predominated, the patient developed cognitive deficits in the absence of motor deficits.
Discussion And Conclusion: This clinical case illustrates the complexity of approaching a non-elderly patient with cognitive disturbances in the absence of well-defined cerebral lesions. In clinical practice, we often limit ourselves to searching for ischemic or hemorrhagic lesions, systemic infections with cognitive dysfunction, or, in patients with hypertension, we attribute the symptoms to chronic cerebral vasculopathy. This report highlights the utility, in cases of diagnostic uncertainty, of contrast-enhanced brain MRI as the first-line diagnostic tool for the diagnosis of CAA.



PERCUTANEOUS ENDOSCOPIC NECROSECTOMY (PEN) IN THE MANAGEMENT OF INFECTED WALLED-OFF NECROSIS

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Background: Acute necrotizing pancreatitis (NP) represents a severe form of acute pancreatitis, frequentlycomplicated by local collections such as acute necrotic collections (within the first 4 weeks) and,after four weeks, walled-off necrosis (WON) [1]. Infected pancreatic necrosis (IPN) significantlyincreases mortality and requires a step-up therapeutic approach including antibiotics,percutaneous or endoscopic transmural drainage, endoscopic necrosectomy, and, when needed,minimally invasive surgery or open surgery [2]. Historically, surgical necrosectomy was the onlyoption for patients with infected WON when endoscopic drainage and necrosectomy were notfeasible or failed to achieve clinical resolution, despite being associated with high morbidity andmortality [3]. In this context, percutaneous endoscopic necrosectomy (PEN) has emerged as apromising minimally invasive alternative [4]. This technique uses an existing percutaneous tract,dilated and stabilized with a self-expanding esophageal metal stent, to allow access for a flexibleendoscope and direct debridement of necrotic material. PEN has been described in several casereports and case series and has demonstrated encouraging outcomes in terms of safety,feasibility, and clinical efficacy; reported complications include pancreatic-cutaneous fistula,bleeding, peritonitis, and pneumoperitoneum [4].
Case Presentation: A 66-year-old male was hospitalized for recurrent acute necrotizing pancreatitis, complicated byrespiratory failure, bilateral pleural effusion, anemia, and multiple abdominal acute necroticcollections. MRI excluded biliary etiology; metabolic and autoimmune causes were ruled out. Thepatient was discharged but later re-hospitalized due to persistent elevated inflammatory markers,worsening asthenia and poor oral food intake.Follow-up contrast-enhanced CT demonstrated progressive encapsulation of the previouslyknown necrotic collections, consistent with evolution to walled-off necrosis (WON), along with asignificant increase in size. The main collection, located between the stomach and spleen,measured 10×9 cm and caused compression of adjacent structures; another major collection waslocated anterior to the right iliac muscle.Given the absence of clinical improvement after initiation of empirical antibiotic therapy,percutaneous drains were placed in the two major collections, yielding brownish fluid. Culturesrevealed S. sanguinis, VRE E. faecium, and Candida albicans; accordingly, antibiotic therapy wasadjusted to daptomycin, piperacillin/tazobactam, and caspofungin. Despite targeted treatmentand drainage, the patient showed no significant response, either clinically or radiologically.EUS-guided drainage was then attempted but deemed unfeasible due to several findings: markeddeformity and displacement of the antropyloric region, inaccessibility of the duodenal bulb, andabsence of targetable fluid cavities on transgastric EUS scans. Endoscopy revealed a tight,substenotic and rigid segment of the duodenal sweep (approximately 6 cm in length) and extrinsiccompression from a solid necrotic mass not amenable to drainage.A multidisciplinary team opted for bilateral PEN. A self-expanding metal stent was placed in thetwo percutaneous tracts, allowing repeated access with a diagnostic gastroscope. Multiplenecrosectomy sessions were performed with clinical and laboratory improvement. The onlycomplication observed was a mild anemia due to self-limited bleeding, which resolvedspontaneously without the need for intervention.
Discussion: PEN provides an effective solution when traditional endoscopic access to infected WON is not feasible or fails to achieve clinical resolution. This approach allows direct endoscopicdebridement through a percutaneous route, significantly reducing invasiveness compared tosurgery; literature supports its safety and efficacy, with low complication rates. In the past,surgical necrosectomy was the only viable intervention for such patients and was associated withhigh rates of major complications and mortality. The case described highlights how PEN canrepresent a valuable and well-tolerated therapeutic option in IPN where standard techniques fail,offering a safer and increasingly accessible alternative to surgery.
References: 1. Banks PA et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification anddefinitions by international consensus. Gut. 2013;62:102–1112. Arvanitakis M et al. Endoscopic management of acute necrotizing pancreatitis: European Society ofGastrointestinal Endoscopy (ESGE) evidence-based multidisciplinary guidelines. Endoscopy.2018;50(5):524-5463. van Santvoort HC et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. NEngl J Med. 2010 Apr 22;362(16):1491-502.4. Gjeorgjievski M et al. Percutaneous endoscopic necrosectomy (PEN) for treatment of necrotizingpancreatitis: a systematic review and meta-analysis. Endosc Int Open. 2023;11(3):E258-E267

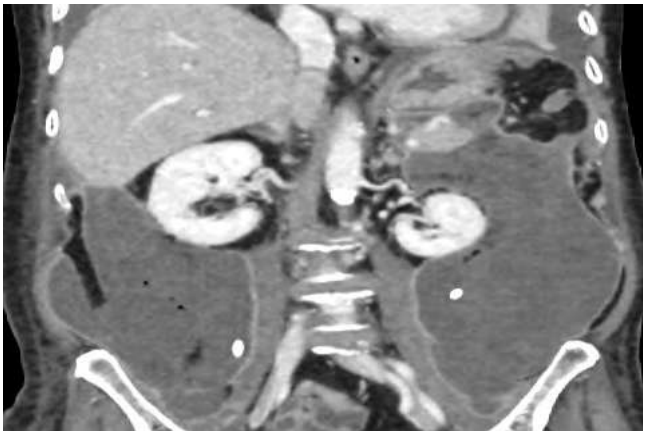

Fig. 1. Abdomen CT coronal scan showing the two major necrotic collections

BACTEREMIA FROM ELIZABETHKINGIA ANOPHELIS: A CASE REPORT

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Background: Bacteremia from *Elizabethkingia anophelis*, a gram-negative, aerobic, non-motile bacillus, is a rare clinical entity. However, this microorganism has recently emerged as an opportunistic human pathogen, causing neonatal meningitis and sepsis, as well as nosocomial outbreaks with various clinical presentations, including pneumonia and bacteremia, in adults with underlying clinically significant comorbidities. First isolated in 2011 from the midgut of the *Anopheles gambiae* mosquito, it remains poorly understood, with unclear epidemiology, transmission route and pathogenicity. Nevertheless, it is associated with significant morbidity and mortality in hospitalized patients according to literature, so a prompt diagnosis, antimicrobial stewardship and treatment are crucial to improve clinical outcomes.
Case presentation: A 66-year-old patient was admitted for traumatic head injury after alcohol abuse, with subsequent subarachnoid hemorrhage, cerebral contusion and intraventricular hemorrhage, which required surgical treatment, ICU admission, mechanical ventilation and tracheostomy. He was then transferred to our ward for the management of respiratory insufficiency due to Ventilator-Associated Pneumonia (VAP) from *P. aeruginosa* and carbapenem-resistant *A. baumanii*. During his long hospital admission, he developed multiple infections, including Catheter-related-Blood Stream infection (CR-BSI) from *coagulase-negative Staphylococci*, for which he underwent multiple antibiotic lines, with complete clinical response. After 1 month from admission and 7 days of antibiotic wash-out, we observed a sudden development of fever (up to 38.4 °C), desaturation and respiratory distress, increase in blood lactates and acute worsening of the neurological status. Laboratory tests showed an increase of C-Reactive Protein (up to 10 mg/dL) and Procalcitonin (up to 13.7 µg/L). Blood and urine cultures were taken and a chest X-Ray showed parenchymal consolidations and left pleural effusion. An empiric antibiotic treatment with Cefiderocol and Fosfomycin was started in the suspicion of VAP recurrency.The day after, blood cultures resulted positive for *E. anophelis*. The antibiogram indicated resistance to most antibiotics, including Cefepime, Ceftazidime, Ciprofloxacin, Imipenem, Meropenem, Piperacillin/Tazobactam, Cefiderocol, Gentamicin and Amikacin, while susceptibility to Levofloxacin (*MIC <2*). Add-on treatment with Levofloxacin (750 mg/die IV) was implemented for a total of 17 days, with a rapid clearance of *E. anophelis* in the following blood cultures, together with a gradual improvement in the clinical conditions and laboratory parameters of the patient.
Discussion: *E. anophelis* is a ubiquitous bacterium, found in soil and water worldwide, considered now an emerging pathogen, as there has been an increased incidence among hospitalized patients, and hospital outbreaks are rising worldwide. Although its transmission is still unclear, evidence suggests that it contaminates health care setting, and can be found in hospital tap water, as well as on commonly used devices' surfaces, so further research is needed to implement outbreak control strategies. The route of transmission

was not identified in our case, but it was likely acquired during the prolonged hospital stay. Even if it rarely causes infections in healthy people, clinical manifestations, especially lower respiratory tract infections and bacteremia, are more common among immunocompromised patients with comorbidities. Our patient had many risk factors, including prior ICU stay, mechanical ventilation, tracheostomy tube, and several courses of antibiotics. Although *Elizabethkingia* species are generally resistant to all beta-lactams and carbapenems, according to literature, they seem more susceptible to Minocycline, Rifampicin and Levofloxacin, as in our case. So, antimicrobial susceptibility testing and immediate antibiotic treatment are crucial in cases of bacteremia and sepsis from *E. anophelis*, to contrast the associated high morbidity and mortality.
Conclusion: Although a limited number of cases have been reported worldwide, *E. anophelis* is an emerging opportunistic pathogen, especially in hospital settings. It often leads to a high mortality rate in immunocompromised patients and patients with underlying comorbidities because of its intrinsic antibiotic resistance. Therefore, bacteremia from *E. anophelis* should be considered clinically significant, and antimicrobial stewardship combined with timely treatment should be implemented to improve patients' clinical outcomes and prognosis.

ACUTE RESPIRATORY DISTRESS SYNDROME ASSOCIATED WITH EPSTEIN-BARR VIRUS INFECTION: A RARE CLINICAL MANIFESTATION IN A PATIENT WITH CLASSIC INFECTIOUS MONONUCLEOSIS SYMPTOMS

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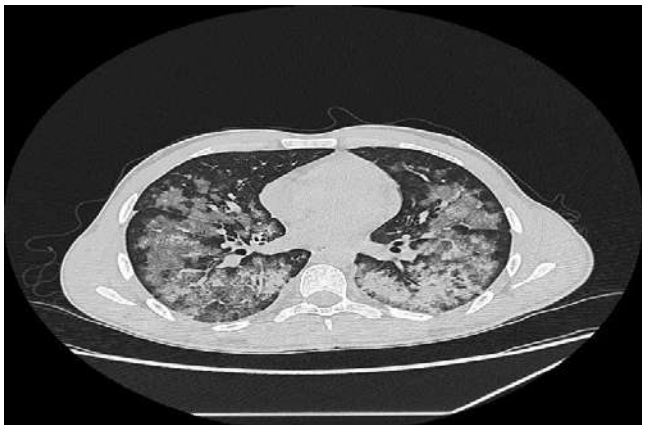
Infectious mononucleosis (IM) is the most common acute clinical manifestation of Epstein-Barr virus (EBV) infection. However, EBV has the potential to affect virtually any organ system, and has been associated with such diverse disease manifestations as pneumonia, myocarditis, pancreatitis, mesenteric adenitis, myositis, glomerulonephritis, and genital ulceration.This case report focuses on the rare and potentially life-threatening complication of pulmonary involvement in the setting of acute EBV infection.
A 17-year-old previously healthy male presented with a two-week history of sore throat, fever, and cervical lymphadenopathy. Additional symptoms included persistent dry cough, nausea, anorexia, and progressive asthenia. He had been empirically treated at home with clarithromycin, which was discontinued due to the onset of a cutaneous rash.
Serological testing revealed elevated EBV VCA IgM antibodies (>160), confirming an acute EBV infection. Abdominal ultrasonography showed mild hepatosplenomegaly. Upon hospital admission, the patient developed progressive hypoxemia. Chest X-ray (Figure 2) demonstrated bilateral confluent parenchymal opacities suggestive of an inflammatory process. High-resolution chest computed tomography (Figure 1) revealed findings consistent with acute interstitial pneumonia and acute respiratory distress syndrome (ARDS). Initial management included oxygen supplementation and empirical intravenous levofloxacin (750 mg q24h). Due to worsening respiratory function, the patient was transferred to the intensive care unit, where he received non-invasive ventilation and systemic corticosteroid therapy with methylprednisolone at 1 mg/kg/day. This treatment led to a marked clinical improvement, with gradual resolution of respiratory failure.The patient was subsequently transferred to the infectious diseases department, where addictional infectious etiologies were ruled out. Corticosteroids were gradually tapered during hospitalization.The patient's clinical condition significantly improved with timely and targeted therapy. He was discharged in good general condition, without evidence of permanent organ damage or need for ongoing treatment. A follow-up chest X-ray performed three weeks after the acute episode (Figure 3) showed near-complete resolution of pulmonary infiltrates.
This case underscores a rare but severe complication of EBV infection: ARDS secondary to pulmonary involvement. Early recognition and multidisciplinary management, including respiratory support and corticosteroid therapy, were critical in achieving a favorable outcome. Clinicians should maintain a high index of suspicion for atypical manifestations of EBV, especially in patients presenting with respiratory symptoms and systemic involvement.



BEYOND THE SKIN

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Introduction: Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), also known as Drug-Induced Hypersensitivity Syndrome (DIHS), is a rare but potentially life-threatening adverse drug reaction. It typically manifests with a constellation of features including fever, widespread cutaneous eruption, hematologic abnormalities such as eosinophilia or atypical lymphocytosis, and internal organ involvement, most commonly affecting the liver, kidneys, and lungs. DRESS is often associated with aromatic anticonvulsants, such as carbamazepine, and reactivation of herpesviruses. Diagnosis is frequently delayed, particularly in elderly patients, due to atypical presentations, the presence of multiple comorbidities and overlapping symptoms from concomitant medications. Early recognition and prompt initiation of appropriate treatment are critical to improve patient outcomes.
Case Presentation: We present the case of a 77-year-old male with a complex medical history including supra-aortic trunks atherosclerosis, arterial hypertension, hypercholesterolemia, benign prostatic hyperplasia and a prior severe cutaneous adverse drug reaction, presumed to be acetylsalicylic acid-induced Stevens-Johnson Syndrome. The patient was started on carbamazepine to manage new-onset right-sided facial paresthesias. After approximately three weeks of therapy, he developed neurological symptoms including sensory disturbances and instability, leading to discontinuation of the medication. Within days, a diffuse, itchy, erythematous rash involving more than 75% of the body surface area emerged, sparing mucosal membranes. Systemic symptoms followed, including high-grade fever, significant weight loss, insomnia, progressive sensory neuropathy and acute kidney injury. Neurological examination revealed sensory ataxia and a positive Romberg sign. Laboratory analysis on admission demonstrated hyponatremia, neutrophilic leukocytosis with monocytosis, elevated liver transaminases and pancreatic enzymes and a marked rise in serum creatinine (6.18 mg/dL), consistent with acute kidney injury. Peripheral blood smear identified atypical lymphocytes and flow cytometry confirmed a reactive immunophenotype. Serological testing excluded active bacterial, viral, and parasitic infections; however, low CMV DNA levels were detected (499 copies/mL), without evidence of active disease. Autoimmune screening was negative. Electromyography showed sensory neuropathy and mild neurogenic muscle

involvement (L5–S1). No evidence of demyelinating disease was seen on neuroimaging. A renal biopsy was performed, revealing acute granulomatous tubulointerstitial nephritis with a pattern strongly suggestive of drug-induced injury. An echocardiogram showed left ventricular hypertrophy with moderate dynamic outflow obstruction. The diagnosis of DRESS/DIHS was considered based on clinical chronology, characteristic multiorgan involvement, and supportive histopathological findings, despite the absence of peripheral eosinophilia,highlighting the variability of the syndrome's presentation in elderly patients. The patient was promptly treated with high-dose intravenous methylprednisolone (500 mg/day for 3 days), followed by a tapering course of oral prednisone at an initial dose of 0.5 mg/kg/day. Supportive care included intravenous fluid resuscitation and topical corticosteroids for cutaneous symptoms. Broad-spectrum antibiotics initiated empirically were withdrawn after exclusion of infectious causes. The patient showed progressive clinical and laboratory improvement: defervescence occurred within days, the rash gradually resolved, hepatic and pancreatic enzyme levels normalized and renal function improved significantly (creatinine decreased to 1.54 mg/dL). Neurological symptoms partially improved, though some distal paresthesias persisted. He was discharged in stable condition on a tapering regimen of corticosteroids and scheduled for follow-up with nephrology, neurology, and dermatology.
Discussion and Conclusion: This case underscores the diagnostic complexity of DRESS/DIHS in the elderly, particularly in the presence of prior drug hypersensitivity and multiple comorbid conditions. Notably, eosinophilia, a hallmark of the syndrome,was absent in this patient, reinforcing that its absence does not rule out the diagnosis when other key clinical and histopathological features are present. The renal biopsy played a pivotal role in confirming the etiology of the kidney injury and directing appropriate immunosuppressive therapy. Timely intervention led to favorable clinical recovery. Long-term follow-up remains essential to monitor for potential relapses and manage persistent or delayed sequelae, including chronic kidney disease or residual neuropathy. This case highlights the importance of considering DRESS/DIHS in the differential diagnosis of acute systemic illness in elderly patients recently exposed to high-risk medications such as carbamazepine.

PARANEOPLASTIC HYPOGLYCEMIA IN PLEURAL SOLITARY FIBROUS TUMOR. CASE REPORT

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Introduction: Paraneoplastic hypoglycemia, or non-islet cell tumor hypoglycemia (NICTH), is a rare cause of hypoglycemia due to secretion of insulin-like growth factor type 2 (IGF-2) and its precursor by benign and malignant non-pancreatic tumors. Association of NICTH and solitary fibrous tumor (SFT) configures the Doege–Potter Syndrome (DPS). SFTs are uncommon tumors of mesenchymal origin that make up 2% of soft tissue tumors. In more than 80% of the cases, SFTs are slow-growing, indolent neoplasms with low malignant potential. Pleura is the most involved site, and intrathoracic tumors account for approximately 30% of cases. Possible extraperitoneal sites are intraabdominal, including peritoneum, retroperitoneal soft tissue, liver and pelvis. We report a case of presumptive DPS secondary to recurrent and extensive pleural solitary fibrous tumor (SFTP).
Clinical case: 84-year-old woman was admitted to our department because of confusion and altered consciousness. Recurrent hypoglycemic events, confirmed by finger stick test, characterized by sweating, tremors and weakness were reported in previous 2 months. Past medical history of the patient was remarkable for type 2 diabetes mellitus, adequately controlled by linagliptin, arterial hypertension and solitary fibrous pleural tumor of right hemithorax, diagnosed according to WHO criteria and surgically treated 4 years previously. On admission, the patient presented severe hypoglycemia (40 mg/dl) associated with confusion and lethargy. Patient's vital signs were normal. In first instance, cerebrovascular event was ruled out by computed tomography (CT) of brain and Color-Doppler test of neck vessels that highlighted no relevant findings. Intravenous (IV) correction of hypoglycemia by 10% dextrose infusion resulted in full symptom reversal and recovery of consciousness, without neurological sequelae. Linagliptin treatment was discontinued and, because of persistent and recurrent hypoglycemia, the patient was kept on continuous dextrose iv infusion. Physical examination was unremarkable, except for decreased breath sound in right middle and upper lung fields. Laboratory tests showed low plasma levels of both C-peptide (0.04 ng/ml) and insulin (<0.5 mIU/ml); these results allowed us to exclude insulinoma, ectopic insulin production or exogenous insulin administration. Renal and hepatic function, basal 8am serum cortisol and adrenocorticotropic hormone were normal and no insulin antibodies were detected; glycosylated hemoglobin was normal. Chest X-ray showed space-occupying lesion in right hemithorax; because of this alteration, chest and abdomen contrast-enhanced CT was performed. CT images revealed large noninvasive heterogeneous enhancing mass measuring 13 x 9 cm on right upper lung and analogous 13 x 10 cm lesion on middle lobe, causing pressure on adjacent lung and cardio-mediastinal structures. NICTH diagnosis was strongly suspected, and further work-up revealed low insulin-like growth factor 1 (IGF-1) plasma levels (18 ng/mL); IGF-2 was not tested due to unavailability. Although we were unable to assess IGF-2 plasma levels, DPS diagnosis was established based on presumptive SFTP recurrence associated with hypoinsulinemic hypoglycemia alongside low C-peptide, insulin and IGF-1 levels, in conjunction with significant tumor burden. The patient was not surgical candidate because of disease extent. During hospitalization hypoglycemia was effectively prevented by fractionated glucose-enriched diet.
Discussion: SFTP is rare subset of pleural tumors that causes less than 5% of primary pleural tumors. In most cases SFTP has indolent and benign course, although patients may recur and occasionally metastasize. Hypoglycemia associated with this tumor, known as DPS, is infrequent, accounting for less than 5% all cases. DPS patients are difficult to identify since this syndrome is rarely considered while making a differential diagnosis of hypoglycemia. Few case reports and reviews make up the majority of the literature on DPS. In this syndrome, hypoglycemia is due to tumoral overproduction of incompletely processed IGF-2, also known as big IGF-2, resulting in the stimulation of insulin receptors and subsequent insulin-like effects responsible for hypoglycemia by inhibiting gluconeogenesis, glycogenolysis, and ketogenesis. In addition, increased activity of IGF-2 suppresses insulin, growth hormone, and IGF-1 secretion. We acknowledge that IGF-2 was not measured; this laboratory result could have supported and further confirmed our diagnosis. However, in this case, measurement of insulin, C-peptide and IGF-1, performed at the time of the hypoglycemia, revealed low hormone levels, and these results allowed to exclude hyperinsulinism as potential cause of hypoglycemia and to retain diagnosis of paraneoplastic hypoglycemia, given the presence of SFTP.
Conclusion: Our experience might be useful to clinicians by raising awareness of DPS and enhancing early detection and effective patient management. High level of suspicion regarding NICTH diagnosis is warranted, especially in patients with large solid tumors which exhibit recurrent fasting hypoglycemia.

MULTIPLE ISCHEMIC STROKES AS INITIAL PRESENTATION OF OCCULT UTERIN CANCER: A CASE REPORT

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Background: Venous thromboembolism (VTE) is a frequent and often underestimated paraneoplastic syndrome, and in some cases it can represent the first clinical sign of an occult malignancy. Among the potential complications of VTE, paradoxical embolism through a patent foramen ovale (PFO) may result in cerebral ischemia, particularly in the setting of elevated right-sided cardiac pressures induced by pulmonary embolism (PE). The early recognition of this mechanism is crucial for appropriate etiologic treatment and oncologic evaluation.
Clinical Presentation: A 56-year-old woman, menopausal for approximately one year, with no prior relevant medical history and no pharmacologic treatments, presented to our unit in March 2025 for vomiting followed by syncope. Upon admission, she was alert but showed mildly slowed speech. Neurological examination revealed no motor, sensory, or cranial nerve deficits, and cerebellar tests were normal. She complained of mild deep tenderness on palpation of the lower abdominal quadrants. Vital signs were stable. ECG showed sinus tachycardia; arterial blood gas analysis revealed mild hypoxemia with hypocapnia. Blood tests indicated a modest increase in D-dimer and troponin levels.
Results: An initial non-contrast brain CT was negative. A chest CT angiography revealed bilateral pulmonary embolism. A second brain CT performed 24 hours later showed multiple ischemic lesions in the posterior cerebral artery territory, consistent with embolic stroke. A new ECG demonstrated T wave inversions in anterolateral leads. Despite the ECG changes, a serial troponin curve was negative. Transthoracic echocardiography

showed preserved left ventricular ejection fraction and mild interatrial septal bulging. A transesophageal echocardiogram (TEE) confirmed the presence of a patent foramen ovale (PFO) with a left-to-right shunt that reversed to a right-to-left flow during the Valsalva maneuver, indicating transient right atrial pressure overload due to PE and a pathway for paradoxical embolism. Given the absence of inherited thrombophilia and the negativity for antiphospholipid antibodies, a paraneoplastic process was suspected. A total-body CT scan revealed a uterine mass consistent with a neoplastic lesion. The patient was started on anticoagulant therapy with fondaparinux and transferred to the Gynecology Unit for surgical management of the uterine neoplasm.
Discussion: This case is emblematic of the complex interplay between malignancy and thromboembolism. While the link between VTE and cancer is well established, thromboembolic complications such as PE and paradoxical embolism may be the first and only manifestations of an occult neoplasm. In this patient, the pulmonary embolism triggered an acute rise in pulmonary arterial pressure, leading to right-to-left shunting through a PFO and subsequent cerebral ischemic events. This mechanism highlights the importance of considering cardioembolic and paraneoplastic origins in cases of cryptogenic stroke, especially when associated with signs of systemic embolism or unprovoked VTE. Epidemiologic studies report that up to 20% of patients with unprovoked deep vein thrombosis or pulmonary embolism have an underlying malignancy, and 10% of those with idiopathic VTE will develop cancer within 12 to 18 months. Furthermore, PFOs are present in nearly 25% of the general population, and their clinical significance becomes particularly relevant in contexts of transiently elevated right-sided pressures. The combination of cerebral and pulmonary embolic events in an otherwise healthy patient should raise suspicion for a right-to-left shunt and prompt an active search for cancer. This case also emphasizes the importance of multidisciplinary diagnostic strategies, including neurologic, cardiologic, hematologic, and oncologic assessments,typical of the internist culture and mentality, when approaching embolic events of unclear origin. The presence of a PFO alone is not sufficient to explain ischemic stroke; the presence of a venous source of emboli and an appropriate physiopathologic context must also be demonstrated.
Conclusion: In patients presenting with unprovoked pulmonary embolism and cerebral ischemia, a thorough diagnostic evaluation should include echocardiographic screening for PFO and investigation for underlying malignancy. VTE can be the first clinical manifestation of a hidden cancer, and early diagnosis may significantly alter the patient's prognosis by allowing timely oncological intervention. This case reinforces the value of an integrated and systematic approach to embolic syndromes, especially when standard risk factors are absent.

HYPOMAGNESEMIA, AN UNUSUAL CAUSE OF CEREBELLAR SYNDROME

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Introduction: Magnesium is the second most abundant intracellular cation and the fourth in the entire body. Its homeostasis is essential for a wide range of cellular function, including action potential generation, enzymatic activity, nucleic acid synthesis and neuromuscolar function. Its concentration is finely regulated by the gastrointestinal and renal systems. The main causes of hypomagnesemia include gastrointestinal losses due to diarrhea or malabsorption and chronic use of PPIs. Urinary losses—often due to uncontrolled diabetes mellitus or the use of loop and thiazide diuretics—are also common. Less frequent causes of low magnesium levels include acute pancreatitis, alcohol use disorder, certain medications such as digoxin, acquired tubular dysfunction and genetic disorders. Clinical effects of hypomagnesemia include hypokalemia, hypocalcemia and cardiovascular manifestations (arrhythmias). It can also be associated with neurological impairment (psychosis and mental status changes) or neuromuscular hyperexcitability, with tetany, muscle cramps, seizures. In a few cases, hypomagnesemia has been reported as the reversible cause of an acute cerebellar syndrome.
Case Study: A 60-year-old man presented to the ED with a 3-days course of vomiting and nausea, followed by subacute onset of gait instability and dizziness. No history of headache or fever was reported in the previous days. The patient's medical history only included ischemic heart disease. In the past months, the patient underwent 1-month hospitalization for multiple liver abscesses from E. histolytica, needing 3-weeks antibiotic cycle of meropenem and metronidazole. He was also diagnosed with acute heart failure, diabetes mellitus, sigmoid colon's diverticulosis and gastric hyperplastic polyp. After being discharged, he was admitted to the ED twice. The first ED visit was due to objective vertigo and nausea. The patient was discharged with the diagnosis of posterior circulation TIA (spontaneous restitutio ad integrum, no cerebral abnormalities in CT/ RMN). Ten days later, he was secondly admitted to the ED due to vomiting, objective vertigo and nystagmus. The patient was diagnosed with hypomagnesemia and received a magnesium supplementation with rapid symptoms resolution.
The patient had no history of smoking, alcohol and drug abuse. He denied recent travels or changes in dietary habits. Previous medications were acetylsalicylic acid, clopidogrel, atorvastatin, furosemide, spironolactone, metoprolol, pantoprazole, quetiapine and supplementation of magnesium. At the first evaluation in our ED, the patient was lucid, oriented, afebrile, presenting frequent episodes of dizziness and vomiting. The general examination showed no abnormalities. The neurological examination showed multidirectional nystagmus, mild dysarthria, bilateral intention tremors, mild adiadochokinesia, bilateral appendicular dysmetria in the finger-nose-finger test and a wide-based gait. Moreover, he also presented with delirium and hallucinations. All these symptoms were compatible with a subacute cerebellar syndrome. Urgent CT scan of the brain revealed no abnormalities. Blood examinations showed severe hypomagnesemia (Mg 0,3 - Limits 1,2 – 2,4 mg/dL), in the absence of other anomalies. The patient was therefore supplemented with magnesium i.v.. The telemetry showed a bigeminal rhythm, resolving with magnesium administration.
The patient was then admitted to the internal medicine department. I.v. magnesium therapy was continued, until laboratory tests showed normalization of the electrolyte's level. Both furosemide and pantoprazole treatments were discontinued, and the patient did not show additional episodes of diarrhea or vomiting. Magnesium levels remained stable after correction.
Neurological symptoms resolved after magnesium replacement. EEG and EMG did not reveal any abnormality. A brain MRI was performed one week after the onset of symptoms and normalization of magnesium levels, given that cerebellar edema is often temporally associated with symptom presentation. The scan revealed no abnormalities. Extensive blood tests were unremarkable, without other electrolyte imbalances. There was no evidence of toxic conditions (alcoholism, drugs' abuse) and heredo-degenerative disorders.
The improvement of neurological symptoms after magnesium replacement, along with the exclusion of other etiologies and the patient's previous similar episode, were consistent with the diagnosis of a cerebellar syndrome secondary to hypomagnesemia. Vomiting and diarrhea were identified as the main causes of magnesium loss, in addition to the patient's chronic use of furosemide and pantoprazole.
Conclusions: Hypomagnesemia should be considered in the differential diagnosis of subacute cerebellar syndromes. Low magnesium levels should be suspected in patients with history of alcohol abuse, chronic diarrhea, long term medications with PPIs and diuretics and unexplained cerebellar symptoms. Early recognition of hypomagnesemia is important, as magnesium supplementation, along with the correction of the underlying cause, allows the resolution of neurological symptoms and prevent recurrencies.

ROLE OF DYNAMIC CONTRAST-ENHANCED ULTRASOUND (D-CEUS) IN PREDICTING CLINICAL REMISSION TO ADVANCED THERAPY IN ULCERATIVE COLITIS - A MONOCENTER PROSPECTIVE PILOT STUDY

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Background: Ulcerative Colitis (UC) is a chronic inflammatory condition marked by alternating periods of relapse and remission. Although colonoscopy remains the gold standard for evaluating disease activity, its invasive nature, limited patient tolerance, and potential complications restrict its use for regular monitoring. In the context of biologic therapies, however, a "treat-to-target" strategy remains essential. Intestinal Ultrasound (IUS) has emerged as a non-invasive, cost-effective, and patient-friendly alternative for assessing therapeutic response. The recently developed Milan Ultrasound Criteria (MUC), which utilize B-mode and color Doppler imaging, provide a structured framework for evaluating UC activity. Additionally, Dynamic Contrast-Enhanced Ultrasound (D-CEUS) offers insights into tissue microvascularization through objective, quantitative metrics derived from time–intensity curve analysis, and holds promise as a novel tool for quantifying intestinal inflammation.

Aims: This prospective study aimed to evaluate the utility of Dynamic Contrast-Enhanced Ultrasound (D-CEUS) in predicting clinical remission at six months in patients receiving advanced therapies, including biologics and small molecules.
Methods: Consecutive patients with ulcerative colitis (UC) initiating a new advanced therapy in routine clinical practice were enrolled. Intestinal Ultrasound (IUS), Dynamic Contrast-Enhanced Ultrasound (D-CEUS), and clinical assessments were performed at baseline, and at weeks 8 (T1), 16 (T2), and 24 (T3) after treatment initiation. Clinical remission at T3 was defined according to STRIDE-II criteria as a partial Mayo score <3 with no subscore >1. D-CEUS time–intensity curves were quantitatively analyzed using VueBox® software. Patients who underwent surgery or required a change in therapy before T3 were classified as non-responders. Logistic regression analysis was used to assess the predictive value of D-CEUS parameters for clinical remission at T3, with statistical significance set at $p<0.05$.
Results: A total of 40 patients were enrolled (mean age 39 ± 13 years; 60% male), with 44.4% (n=18) having failed at least one prior line of advanced therapy. At week 24 (T3), 50% (n=20) achieved clinical remission. Univariate logistic regression analysis identified reductions in Peak Enhancement (PE) and Wash-in Perfusion Index (WiPI) at week 16 (T2) as significant predictors of remission at T3 (OR=0.99, p=0.032; OR=0.25, p=0.036, respectively). Additionally, percentage changes in PE and WiPI from baseline to T2 (% T2–T0) were associated with remission at six months (OR=0.19, p=0.019; OR=0.26, p=0.04). The Milan Ultrasound Criteria (MUC) at T1 and T2 also demonstrated predictive value (OR=0.62, p=0.03; OR=0.73, p=0.048, respectively).
Conclusions: D-CEUS provides early predictors of 6 months clinical remission in UC patients treated with advanced therapies.

SPATIAL IMAGING UNLOCKS THE POTENTIAL OF CHARTING MULTIPLE MYELOMA AND EXTRAMEDULLARY DISEASE

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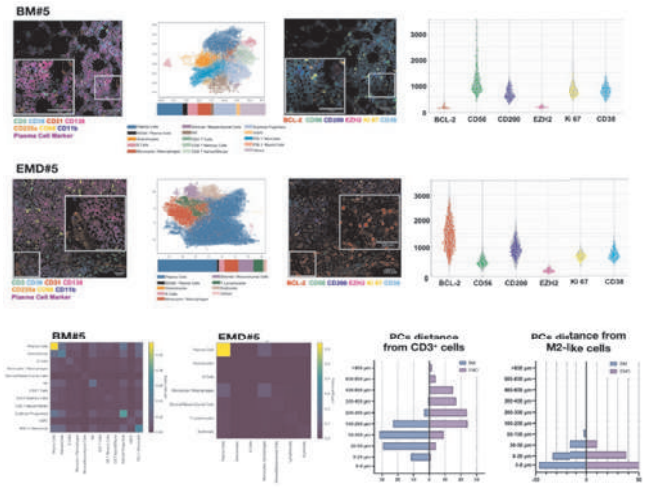
Introduction: Advanced microscopy technologies are opening new frontiers in understanding hematologic malignancies by enabling high-resolution visualization and quantifying molecular features in their native contexts. These methods reveal critical details about cellular function, tissue organization, and cell interactions, offering promise for complex diseases like multiple myeloma (MM). While survival rates for MM have improved, extramedullary disease (EMD)—where cancer spreads outside the bone marrow—remains a major therapeutic challenge. Conventional diagnostic tools rely on histopathology and bulk analyses, which fail to account for tissue spatial heterogeneity and microenvironmental interactions. Recent progress in multiplexed imaging and spatial transcriptomics offers more nuanced biological insights. This study employs MACSima™ imaging cyclic staining (MICS), a high-dimensional imaging technology, to map the spatial protein expression profiles of MM cells and their surrounding ecosystem, focusing on differences between bone marrow (BM) and EMD sites.
Methods: Using MICS, researchers stained 56 distinct markers across carefully prepared BM and EMD tissue samples from 5 newly diagnosed MM patients, totalling 10 tissue samples. Data from 231,186 cells were analysed, with 105,047 annotated as plasma cells (PCs). Computational tools processed and statistically validated the imaging data to generate spatial maps and cellular profiles. Distinct clustering patterns of plasma cells and immune infiltration profiles were identified via cell-type heatmaps and spatial distance analyses.
ResultsMICS technology enabled the identification of 14 distinct cell types in BM and 9 in EMD, showcasing the method's capacity to discern cellular diversity at a single-cell level. It revealed significant biological differences between BM and EMD environments. PCs at EMD sites exhibited higher expression of drug resistance markers like BCL-2 and EZH2, and reduced CD38 expression, confirmed by immunohistochemistry. The spatial arrangement of immune cells such as T-cells and macrophages was markedly different in EMD compared to BM. PCs were overall far distant from T-cells in EMD.
Conclusions: This study is the first to directly compare matched BM and EMD tissues using 56-marker of protein expression in MM. It demonstrates how MICS technology can serve as a valuable tool for companion diagnostics, offering detailed biomarker profiles and aiding personalized therapy strategies for MM patients, especially those with EMD. These findings provide a possible explanation for EMD's poorer response to CD38-targeting therapies and potentially even to immune-mediated treatments like CAR-T and bispecific antibodies. While larger studies are needed to validate and generalize these findings, similar insights may inform precision medicine approaches and microenvironment-based therapies that could represent a game changer for MM patients with extramedullary phenotype.
This work was supported by the "Fondo per il Programma Nazionale di Ricerca e Progetti di Rilevante Interesse Nazionale—PRIN" (project n.2022 ZKKWLW); by the Italian network of excellence for advanced diagnosis (INNOVA), Ministero della Salute (code PNC-E3-2022-23683266 PNC-HLS-DA), by a grant from "Società Italiana di Medicina Interna - SIMI" 2023 Research Award (CAMEL) and by the Italian Association for Cancer Research (AIRC) within the My First AIRC Grant 2020 (n. 24534, 2021/2025).



STROKE AT FIRST SIGHT: DIAGNOSIS AND PROGNOSIS BY A BLOOD-BASED SIGNATURE

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Background: Ischemic stroke (IS) is a leading cause of long-term disability and the second most common cause of death worldwide. Despite the clear benefits of early treatment, diagnostic delays due to limited biomarker availability and imaging constraints often hinder optimal management. In this study, we investigated the diagnostic and prognostic utility of seven blood biomarkers, namely osteopontin (OPN), platelet factor 4 (PF4), ubiquitin C-terminal hydrolase-L1 (UCHL1), interferon gamma-induced protein 10 (IP-10), soluble thrombomodulin (sCD141), glial fibrillary acidic protein (GFAP), and fatty acid-binding protein 3 (FABP3), in patients with acute IS compared with healthy controls.
Material and methods: In this case-control prospective observational study, we enrolled 116 consecutive patients with acute ischemic stroke admitted from June 2021 to January 2024 to the Internal Medicine Ward with Stroke Care at the University Hospital "Paolo Giaccone" in Palermo. Controls were consecutive patients admitted to our ward in the same recruitment period without stroke and acute or chronic inflammatory diseases, cancers, rheumatologic and hematological diseases. Venous blood samples were collected from patients and controls at admission. OPN, IP-10, sCD141, PF4, GFAP, FABP3, and UCHL1 were quantified using commercially available enzyme-linked immunosorbent assay. All statistical analyses were performed using SPSS.
Results and Discussion: Among the 116 patients enrolled with IS, 60% were

male, and the mean (±SD) age was 70.8±11.9 years. A control group of 59 individuals without a known history of cerebrovascular disease (mean age 67.7±10.7 years) was also included. Serum levels of OPN, PF4, and UCHL1 were significantly elevated in IS patients ($p<0.05$), reflecting inflammation, thrombosis, and neuronal injury, respectively. Subgroup analysis by TOAST classification revealed distinct biomarker profiles: OPN peaked in stroke of other determined etiology (TOAST 4), PF4 was highest in large-artery atherosclerosis (TOAST 1), and UCHL1 showed the greatest accuracy in small-vessel occlusion (TOAST 3). Receiver operating characteristic (ROC) analysis showed that UCHL1 had the best diagnostic performance (AUC 0.77; 92% specificity, 61% sensitivity at the optimal cutoff), followed by PF4 (AUC 0.67; 93% specificity, 45% sensitivity) and OPN (AUC 0.68). Among TOAST subtypes, PF4 and UCHL1 provided the highest discrimination in TOAST 1 (AUCs of 0.72 and 0.71, respectively), while UCHL1 alone showed high accuracy in TOAST 3 (AUC 0.88, 83% sensitivity, 85% specificity). IP-10 displayed moderate performance in TOAST 3 but did not differentiate the overall stroke population. None of the biomarkers effectively identified cardioembolic stroke (TOAST 2), underlining the complexity of its systemic pathophysiology. Multivariate logistic regression confirmed that elevated OPN, PF4, and UCHL1 were independently associated with IS. Notably, UCHL1 and PF4 remained significant predictors even after adjusting for vascular risk factors like diabetes, hypertension, and smoking. Correlation analysis showed OPN levels positively associated with stroke severity (NIHSS), C-reactive protein, erythrocyte sedimentation rate and diastolic blood pressure, supporting an inflammatory link. PF4 correlated inversely with age, dyslipidaemia and systemic inflammatory indices, while UCHL1 showed negative associations with blood pressure and metabolic risk factors, suggesting complex neuro-vascular interactions. In contrast, GFAP, FABP3, sCD141, and IP-10 did not significantly differ between stroke patients and controls, though some trends emerged. IP-10 correlated positively with age and atrial fibrillation; FABP3 was associated with markers of renal dysfunction, possibly reflecting systemic stress rather than stroke-specific injury. Patients exhibited clear neurological and functional recovery during the hospital stay, as evidenced by steadily falling NIHSS and mRS scores. Conventional vascular risk factors, advanced age, male sex, hypertension, diabetes, and dyslipidaemia, were common and remained independent predictors in multivariable analyses. Nevertheless, the biomarker panel added further diagnostic power, with UCHL1 standing out as a robust marker for early detection and subtype stratification.

Conclusion: UCHL1 was the most accurate blood marker for detecting ischemic stroke and for differentiating subtypes, especially small-vessel occlusion. PF4 showed excellent specificity, particularly in large-artery disease, making it a strong confirmatory test. OPN, though less specific, correlated with both clinical severity and systemic inflammation. The results argue for incorporating UCHL1 and PF4 into acute-stroke diagnostic workflows, provided their performance is validated in larger, multicenter studies.

THE ROLE OF EXTRACELLULAR MATRIX AND INFLAMMATION IN THE STRATIFICATION OF BLEEDING AND THROMBOTIC RISK OF ATRIAL FIBRILLATION ON ORAL ANTICOAGULANT THERAPY: INSIGHTS FROM STRAT-AF STUDY

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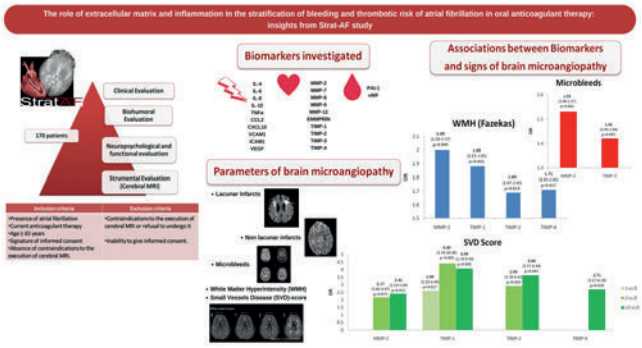
Background: In anticoagulated atrial fibrillation (AF) patients, the validity of models recommended for the stratification of the risk ratio between benefits and hemorrhage risk is limited. We hypothesize that both circulating and neuroimaging-based markers might improve the prediction of bleeding and thrombotic risk in anticoagulated AF patients.
Methods: The Strat-AF study is an observational, prospective, single-center study enrolling 170 patients with AF; recruited patients are evaluated by means of a comprehensive protocol, with clinical, cerebral magnetic resonance imaging and circulating biomarkers assessment. The main outcome is the evaluation of cerebral microangiopathy related to the levels of circulating biomarkers of inflammation and extracellular matrix (ECM) remodeling.
Results: At multivariate logistic regression analysis adjusted for age, sex, CHA2DS2-VASc, HAS-BLED and type of anticoagulant, matrix metalloproteinases (MMP)-2 levels were significantly and positively associated with the presence of cerebral microbleeds (CMBs). A significant association between MMP-2, tissue inhibitor of metalloproteinases (TIMP)-1,-2,-4 levels and white matter hyperintensity was also found. Concerning the small vessel disease (SVD) score, MMP-2 and TIMP-1,-2 levels were associated with the presence of two and three or more signs of SVD, whereas TIMP-4 levels were associated with the presence of three signs of SVD with respect to patients with no instrumental signs of SVD. As regarding the presence of enlarged perivascular spaces (EPVS), a significant association was found for high levels of interleukin (IL)-8 and TIMP 1-2-3.
Conclusions: These results demonstrate that patients with AF have evidence of impaired ECM degradation, which is an independent risk factor for thrombotic complications of AF patients on oral anticoagulant therapy. The incorporation of these markers in the prognostic schemes might improve their clinical capability in predicting stroke risk and thrombotic complications.



INTESTINAL GLUCOSE ABSORPTION IS ENHANCED IN METABOLIC DYSFUNCTION–ASSOCIATED STEATOTIC LIVER DISEASE (MASLD)

Tricò D.[1], Cimbalo N.[1], Chiriacò M.[1], Sacchetta L.[1], Nesti G.[1], Scozzaro M.T.[1], Frascerra S.[1], Gallo S.[1], Nesti L.[1], Petralli G.[1], Baldi S.[1], Fiorentino T.V.[2], Brunetto M.R.[1], Mari A.[3], Natali A.[1]
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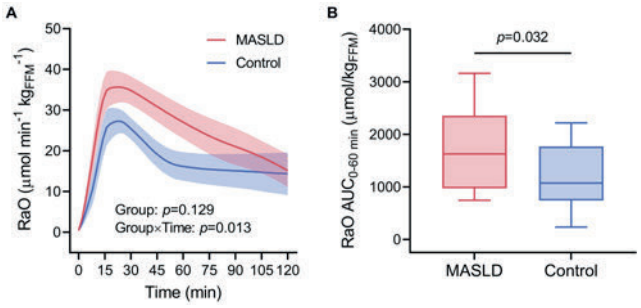
Background and aims: Oral glucose flux to the liver plays a crucial role in the development and progression of metabolic dysfunction-associated steatotic liver disease (MASLD), promoting de novo lipogenesis, inflammation, and oxidative damage. Individuals with MASLD display an augmented expression of duodenal glucose transporters, which may amplify liver exposure to hyperglycaemia by enhancing intestinal glucose absorption. However, the impact of oral glucose absorption in MASLD pathogenesis remains unexplored. This study employed stable glucose isotopes to quantify post-load glucose metabolic fluxes in individuals with MASLD.
Materials and methods: In this clinical study, 32 non-diabetic volunteers with or without MASLD (age 47.8±14.4 years, 16 [50%] women, BMI 27.5±4.8 kg/m2) underwent an oral glucose tolerance test (OGTT) with two stable glucose isotopes (oral [U-13C] glucose and intravenous [6,6-2H2] glucose) to measure glucose metabolic fluxes, including rate of appearance of oral glucose (RaO), endogenous glucose production (EGP), and glucose clearance (GCl). Insulin secretion rate (ISR) was estimated by C-peptide deconvolution.
Results: Individuals with MASLD (n=16) had higher BMI (+4.1±1.6 kg/m2, p=0.019), fasting plasma insulin (+24±9 pmol/l, p=0.015), HOMA-IR (+1.2±0.4, p=0.008), LDL cholesterol (+22±10.6 mg/dl, p=0.046), and triglycerides (+46±10 mg/dl, p=0.0002), but similar age, sex distribution, fasting glucose, HbA1c, FIB-4 score, and liver enzymes, compared to those without MASLD. During OGTT, plasma glucose at 2 hours, plasma insulin, ISR, and Matsuda index were similar between groups. The MASLD group showed higher RaO (group by time interaction: p=0.013; Figure 1A), particularly in the first hour after the oral glucose load (AUC +555±247 µmol/kg, p=0.032;

Figure 1B), along with higher 1-hour plasma glucose levels (+23±11 mg/dl, p=0.041). Group differences in RaO AUC at 1 hour remained statistically significant after adjustments for BMI (p=0.001) and for age, sex, BMI, HOMA-IR, and FIB-4 (p=0.011). EGP and GCl were not affected by MASLD, even after accounting for portal (EGP×ISR) or peripheral (GCl/Ins) insulin levels.
Conclusion: Intestinal glucose absorption is augmented in individuals with liver steatosis. This metabolic alteration, leading to post-prandial glucose overload to the liver, may be a critical driver of MASLD pathogenesis. Therapeutic strategies modulating intestinal glucose transport may complement existing treatments targeting MASLD.



SEPSIS AND LIVER CIRRHOSIS: IMMUNOMETABOLIC FEATURES

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S.C. Epatologia, Dipartimento di Scienze Mediche e Chirurgiche, Università degli Studi di Foggia

Sepsis is a systemic inflammatory syndrome triggered by a dysregulated immune response to infection. Immunometabolic reprogramming of peripheral blood mononuclear cells (PBMCs) significantly influences the progression and outcome of septic states. Although liver plays a key role in regulating immune response and metabolism in sepsis, metabolic changes when sepsis occurs in a patient suffering from liver cirrhosis are poorly understood.
The aim of this study is to understand whether and in which way the liver drives immunometabolic changes during sepsis by comparing PBMCs bioenergetic profiles from septic patients vs cirrhosis-associated septic patients. 75 patients admitted at the Liver Unit of Policlinico Riuniti of Foggia for sepsis were enrolled in this study: 63 suffering from sepsis (SEP) and 12 suffering from sepsis in the context of liver cirrhosis (SEP-CIRR), excluding individuals with malignancies. Full Blood Count, CRP, Procalcitonine, albumin levels, renal and liver function were assessed in all patients. PBMCs were collected at baseline and after antibiotic therapy response to be analyzed using Seahorse XF assays, specifically Mito Stress and Glycolysis Stress Tests, to assess mitochondrial respiration and glycolytic capacity. Additional assays included cytokine expression and the measurement of hepatokines (HGF, ANGPTL3, ANGPTL4, ANGPTL6, FGF-19, FGF-21, FGF-23). Data were compared with healthy donors. Data have shown deep immunometabolic paralysis in PBMCs from SEP patients, highlighted by significantly decreased mitochondrial respiration parameters including basal respiration, maximal respiration, spare respiratory capacity and ATP production, alongside reduced glycolytic activity. In contrast, PBMCs from SEPS-CIR patients exhibited a distinct hypermetabolic state, maintaining elevated or sustained glycolytic and mitochondrial activities. Additionally, longitudinal follow-up demonstrated that patients who clinically recovered from sepsis showed gradual normalization of their PBMC bioenergetic profiles. Both septic and cirrhotic-septic groups displayed progressive restoration of glycolytic activity and mitochondrial respiration (OCR), indicating a slow but consistent shift towards metabolic homeostasis and immune recovery. In particular, SEP-CIRR patients have shown higher levels of Il-1β and Tnf-α expression and healthy donor's PBMCs exposed to patient serum exhibited a higher expression of Il-1β and Tnf-α when the serum came from SEP-CIRR patients. Besides, SEP patients showed a very high presence of serum hepatokines such as HGF, ANGPTL3, ANGPTL4, FGF-21 and FGF-23 at the bead-based multiplex assay with Luminex® while SEP-CIRR patients displayed significant lower levels. Ultimately, significant lower levels of CRP, Albumin and Platelet were found in SEP-CIRR likely due to the typical cirrhosis complications as well as a higher mortality rate (58% vs 40%). These results show the important differences between patient suffering from sepsis and patients suffering from sepsis in the context of liver cirrhosis, underlying the crucial role played by liver as the phenomenon called "immunometabolic paralisis, possibly a rescue mechanism, does not occur in patients suffering from liver cirrhosis, where, on the contrary, a hypermetabolic state persists. This could expain why cirrhotic patients show a lower therapeutic response.
In conclusion, the liver is responsible for immunometabolic changes in sepsis, although further experiments are going to be performed in order to define underlining mechanisms at single cell level.

PRELIMINARY DATA ON EARLY DETECTION OF MINIMAL HEPATIC ENCEPHALOPATHY USING WEARABLE SENSORS

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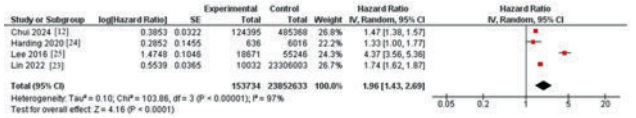
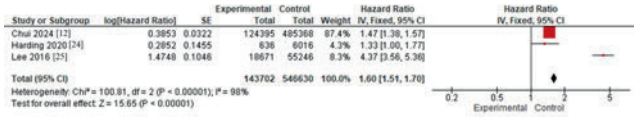
Background and Aims: Hepatic encephalopathy (HE) is a common complication of liver cirrhosis, characterized by a broad spectrum of neuropsychiatric symptoms. According to West Haven criteria, HE is classified into four grades based on severity, ranging from minimal encephalopathy (mHE) to coma (grade IV). Beyond its clinical impact, HE has significant socioeconomics consequences, as it leads to a decline in quality of life and increased mortality rates. The diagnosis of mHE, representing the subclinical phase of HE, is challenging and often overlooked due to the lack of validates tests that effectively balance ease of use, sensitivity and specificity. This study aims to introduce a novel diagnostic approach utilizing wearable sensors for the identification of mHE in cirrhotic patients without a prior diagnosis of HE.
Methods: The study design planned to enrol 120 patients with liver disease: thirty cirrhotic patients with overt hepatic encephalopathy (oHE), fifty without a previous diagnosis of hepatic encephalopathy (no-HE), and a control group of forty non-cirrhotic patients. Exclusion criteria of the study were alcohol use disorder, type two diabetes-related neuropathy, neurological disorders, muscle weakness and other forms of tremor. Demographic, anthropometric, biochemical, and clinical data – including animal naming test (ANT) and handgrip strength test – were collected for each patient in a digitalized dataset. All patients were equipped with wearable sensors to asses tremors associated with hepatic encephalopathy. The measurement setup included six inertial sensors (three per limb), positioned on the dorsum of both hands and the flexor/extensor muscles of both forearms: two configured as Inertial Measurement Units (IMUs), continuously measuring linear acceleration and angular velocity along three axes, and four configured as IMUs with additional electromyography channels. Data were recorded during arm extension with palms facing up/down (repeated twice) and during arm extension with palms extended for at least 10 seconds. The frequency domain analysed all documented signals, extracting features from each signal's power spectrum. ANOVA, Kruskal-Wallis, and Eta Squared tests were applied for feature sampling, and the Birch method was used for unsupervised clustering.
Results: Among the patients attending the Medicine and Hepatology Unit of the University Hospital of Messina from September 1st, 2024 to March 30th, 2025, 109 who met the inclusion criteria were enrolled. Study population had an average age of 67 years (range 63 – 74), 59 (54.1%) patients were male, 71 were diagnosed with liver cirrhosis (48 patients no-HE and 24 oHE), while 38 comprised the control group. Frequency analysis identified a specific range of 1 – 8 Hz associated to hepatic encephalopathy. Statistical analysis, including ANOVA and Kruskal-Wallis, selected 10 out of the 340 features extracted from the six sensors as being most relevant for distinguish patients with HE. A statistically significative difference was observed between patients with and without HE across the following features: Left-hand Amplitude Spectrum inside ratio Gyroscope Z (p=0.02), Left-hand Frequency Accelerometer Y (p=0.01), Right-hand Amplitude Spectrum inside ratio Gyroscope Y (p=0.04), Left-hand difference between power inside boundaries and outside Accelerometer Z (p=0.03), Left-hand Spectrum power outside boundaries Gyroscope Y (p=0.03), Left-hand Spectrum power Accelerometer Z (p=0.04), Right-hand Amplitude Spectrum outside ratio Accelerometer X (p=0.02), Right-hand Spectrum power Gyroscope Z (p=0.03), Right-hand maximum amplitude Accelerometer X (p=0.03) and Gyroscope Z (p=0.02). Data analysis using AI-based unsupervised clustering grouped patients into two groups:

Cluster 1 (no-HE) and Cluster 2 (oHE). Specifically, 14 of the 48 patients (29.1%) with no-HE exhibited tremors characteristic of HE, allowing for the diagnosis of mHE. Overall clustering approach correctly identified the original diagnosis in 77% of patients, demonstrating high accuracy rates.
Conclusion: Wearable IMUs represent a promising, non-invasive, objective method for the early diagnosis of minimal HE. Their implementation in daily clinical practice could help to identify patients most at increased risk of developing overt HE, allowing to timely therapeutic interventions.

Panel A



Panel B



CI, Confidence Interval; df, degree of freedom; IV, Inverse Variance; SE, Standard Error;

Panel C

Outcomes	Anticipated absolute effects* (95% CI) Risk with [comparison]	Risk with [intervention]	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
New-onset atrial fibrillation (NOAF)	42 per 1.000	**80 per 1.000** (59 to 108)	**HR 1.96** (1.43 to 2.69)	24,006,367 (4 observational studies)	⊕⊕⊕◯ Moderate[a,b]	Opioid use results in an increased risk of new-onset atrial fibrillation.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **HR:** hazard ratio

a. A moderate risk of bias for Domain 2 of study performed by Lee *et al[25].*

b. High heterogeneity among studies included.

ASSOCIATION BETWEEN OPIOID USE AND NEW-ONSET ATRIAL FIBRILLATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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[1]Department of General Surgery and Surgical Specialty Paride Stefanini, Sapienza University of Rome, Italy; [2]Department of Medical Biotechnology and Translational Medicine, Postgraduate School of Clinical Pharmacology and Toxicology, Università degli Studi di Milano, Italy; [3]Department of Oncology and Hemato-Oncology, Università degli Studi di Milano, Italy; [4]Department of Clinical Internal, Anesthesiological and Cardiovascular Sciences, Sapienza University of Rome, Italy

Introduction: The prescription of opioids is still common in clinical practice. Chronic opioids use has been associated with increased risk of adverse cardiovascular outcomes, but the association with the risk of atrial fibrillation (AF) has been less established. We evaluated the risk of new-onset atrial fibrillation (NOAF) in patients prescribed with opioids.
Methods: Systematic review and meta-analysis. MEDLINE and EMBASE databases were searched from inception to 29 January 2024 according to PRISMA guidelines. The protocol was registered at PROSPERO (CRD420 24512500). Quantitative analysis included observational studies only and results were synthetized by pooled Hazard Ratio (HR). Risk of bias was performed according to ROBINS-I Cochrane tool, and summary of evidence according to GRADE.
Results: 782 studies were retrieved and 4 met the inclusion criteria for quantitative analysis. A total of 24,006,367 patients were included, of whom 153,734 were taking opioids. Among studies, the proportion of women ranged from 13.2% to 100% and the age from 34 to 65 years. Studies reported 991,263 cases of NOAF. The pooled analysis showed a significant association between use of opioid and NOAF (HR 1.96, 95%CI 1.43-2.69 with high heterogeneity) (Figure 1, Panel A). A sensitivity analysis by removing the study with the largest cohort showed similar results of main analysis (Figure 1 Panel B). In the summary of findings, the certainty of the evidence according to GRADE was moderate (Figure 1, Panel C).
Conclusions. Chronic opioid use carries an increased risk of NOAF. Before prescribing opioids, a careful evaluation of risk factors for AF should be performed to reduce the risk of NOAF. In high-risk patients, alternative pain-relieving drugs should be considered.

EFFECTIVENESS AND SAFETY OF RISANKIZUMAB IN CROHN'S DISEASE PATIENTS FROM A LARGE ITALIAN COHORT: RESULTS FROM THE RESOLVE IGIBD STUDY

Scaldaferri F.[1], Di Vincenzo F.[1], Aloi M.[2], Ascolani M.[3], Balestrieri P.[4], Bertani L.[5], Bezzio C.[6], Bodini G.[7], Bossa F.[8], Calabrese E.[9], Cannatelli R.[10], Caprioli F.[11], Cappello M.[12], Cicala M.[13], D'Amico F.[14], Danese S.[14], De Filippo F.R.[15], Desideri F.[16], Di Paolo D.[17], Di Sario A.[18], Fantini M.C.[19], Ferracane C.L.[20], Festa S.[21], Fiorino G.[22], Gabbiadini R.[6], Geccherle A.[23], Gerardi V.[24], Giangreco E.[25], Gravina A.G.[26], Laterza L.[27], Mastronardi M.[28], Mendolaro M.[29], Merli M.[30], Mocci G.[31], Onali S.[19], Onidi F.M.[31], Pastorelli L.[32], Piagnani A.[33], Principi M.R.D.[34], Pugliese D.[35], Ribaldone D.G.[36], Rispo A.[37], Rizzello F.[38], Saibeni S.[39], Savarino E.V.[40], Spagnuolo R.[41], Tursi A.[42], Variola A.[43], Vigano C.[44], Armuzzi A.[45]
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Aims: Risankizumab has been recently approved for the treatment of moderate-to-severe Crohn's disease (CD). It is a humanized IgG1 monoclonal antibody that binds to the p19 subunit of IL-23, selectively inhibiting IL-23. Due to the limited real-world data on its effectiveness currently available, this study aims to assess the short-term effectiveness and safety of risankizumab induction treatment in a large, real-life Italian cohort of CD patients.
Methods: From September 2023 (following reimbursement of risankizumab for CD) to December 2024, all consecutive CD patients treated with risankizumab in 40 Italian centers were retrospectively enrolled. Only patients who completed the induction phase of risankizumab, with a follow-up of at least 12 weeks, were included in the final analysis. Clinical characteristics, disease activity scores, steroid use, and adverse events were collected. The primary endpoint was steroid-free clinical remission (SFCR) (Harvey Bradshaw Index [HBI] <5) at 12 weeks. Secondary endpoints included clinical response (≥3 point decrease in HBI and/or HBI <5), clinical and biochemical remission (HBI <5 and CRP ≤ 5 mg/L), changes in average daily stool frequency (SF) and average daily abdominal pain score (APS), remission of extra-intestinal manifestations (EIMs), occurrence of disease complications, and adverse events at 12 weeks.
Results: To date, 538 patients have been enrolled, with 383 completing the 12-week follow-up. The female-to-male ratio was 168:215, the mean age was 47.6 ± 17.1 years, and the mean disease duration at enrollment was 15.5 ± 10.8 years. Eleven patients (2.9%) were naive to biologics, while 283 (73.9%) had received ≥2 biologics, 204 (53.2%) had received ≥3 biologics, 220 (57,4%) were ustekinumab exposed, and 232 (60.7%) had previous intestinal resections. 106 (27.7%) were receiving concomitant steroid therapy at baseline. 233 (60.8%) patients underwent colonoscopy within the last 3 months before starting risankizumab, exhibiting a mean SES-CD of 9.5 ± 7.0 or a mean Rutgeerts score of 3.1±1.2. The rates of SFCR and clinical response at week 12 were 61.1% (234/383), and 79.1% (302/383), respectively; 37.3% (82/220) and 73.6% (162/220) in ustekinumab exposed cohort, and 35.9% (79/204) and 75.5% (154/204) in the multifailure cohort (≥3 biologics). The average daily APS and SF scores significantly decreased from 0.9 to 0.4 ($p < 0.0001$) and from 4.1 to 3.1 ($p < 0.0001$), respectively. Notably, 92.5% of patients achieved an APS score ≤1, with no worsening from baseline, while 52.7% reached a SF score ≤2.8, with no worsening from baseline. Faecal calprotectin levels significantly decreased from 742.3±1224.7 to 315.8±315.8 ($p<0.0001$), while CRP dropped from 9.8 to 5.8 ($p=0.0002$). 242 patients (63.2%) achieved normal CRP levels at week 12. The percentages of patients with active rheumatologic and dermatologic EIMs decreased from 5.0% to 2.1% ($p=0.0004$) and from 16.7% to 12.3% ($p=0.0039$), respectively. Only 9 patients developed disease complications, including 3 cases of new perianal fistula and 4 cases of stricture worsening. Nine patients discontinued treatment before week 12. Additionally, 17 patients (4.4%) experienced minor adverse events after risankizumab administration.
Conclusions: In a large cohort of refractory CD patients with multiple prior drug failures, including frequent failures to ustekinumab, nearly 60% achieved steroid-free clinical remission following risankizumab induction. Risankizumab demonstrated good effectiveness in managing dermatologic and rheumatologic EIMs. The safety profile of risankizumab was consistent with existing literature.

DIFFERENT SURVIVAL OUTCOMES OF SMALL BOWEL ADENOCARCINOMAS AND T-CELL LYMPHOMAS ASSOCIATED TO CELIAC DISEASE

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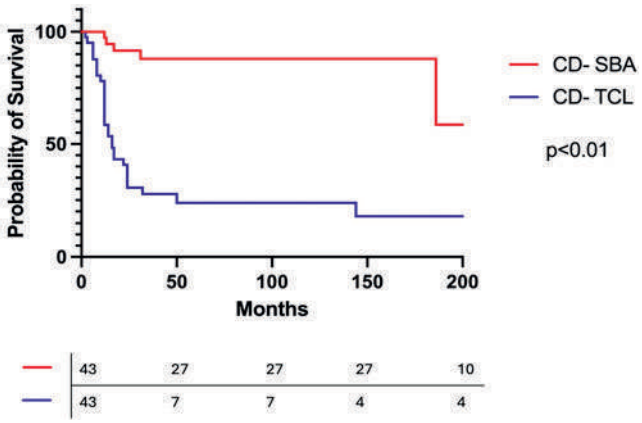
Background: Small bowel adenocarcinoma (SBA) and T-cell lymphoma (TCL) are rare but aggressive malignancies associated with coeliac disease (CD). Although individually reported, no large comparative studies have addressed their distinct clinical characteristics and survival outcomes in CD patients. Understanding these differences may improve risk stratification, monitoring, and clinical management of affected patients.
Methods: We retrospectively analysed data from 86 CD patients diagnosed with either SBA or TCL, collected from international referral centres participating in the Small Bowel Cancer Consortium. Forty-three cases of CD-associated SBA and 43 cases of CD-associated TCL were compared. Collected variables included age at CD diagnosis, sex, tumor site, refractoriness to gluten-free diet, tumor stage, and mortality. Tumor staging followed the American Joint Committee on Cancer (AJCC 8th edition) for SBA and Lugano classification for TCL. Survival data were analysed using Kaplan–Meier estimates and compared by the log-rank test.
Results: CD-associated SBA patients had a median age of 56 years (IQR 45-67) and a male-to-female ratio of 1.1:1; CD-associated TCL patients had a median age of 57 years (IQR 51-62) and a male-to-female ratio of 0.8:1. Jejunal involvement was significantly more common in SBA (67% vs 42%, $p<0.01$), whereas ileal involvement and multifocal lesions were more frequent in TCL (ileal involvement 39% vs 9%, multifocal lesions 19% vs 0%; $p<0.01$). Refractory CD was strongly associated with TCL (70% vs 2%, $p<0.01$). 60% of SBA cases presented at stage II, while 44% of TCL cases presented at stage IV ($p<0.01$). At a median follow-up of 24 months (IQR 12-61.8), mortality was significantly higher in the TCL group (76% vs 12%, $p<0.01$). Kaplan–Meier analysis confirmed a significantly better survival rate in CD-SBA patients compared to CD-TCL ($p<0.01$; see Figure 1). No significant difference in early-onset neoplasms (<50 years) was observed between groups.
Conclusion: This study represents the first large multicentre cohort comparison of CD-associated SBA and TCL, highlighting markedly different clinical behaviours and survival outcomes. CD-associated TCL is characterised by advanced stage at diagnosis, frequent multifocality, strong association with refractory CD, and significantly worse survival compared to CD-associated SBA. In contrast, CD-associated SBA patients generally present at earlier stages and have better outcomes. These findings underscore the importance of early identification and close monitoring of refractory CD patients to improve early cancer detection and outcomes. The poor prognosis of CD-associated TCL emphasises the urgent need for novel therapeutic strategies and reinforces the value of multidisciplinary management for this high-risk population.



DEVELOPMENT OF SYNTHETIC REPORTER CARDIOMYOCYTES TO MODEL TRANSCRIPTOMIC COMPLEXITY IN HUMAN HFPEF

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Introduction: HFpEF accounts for half of the cases of HF, showing phenotypic heterogeneity and association with aging, hypertension, obesity, diabetes and metabolic syndrome. HFpEF is a complex clinical syndrome, characterized by heterogeneous clinical manifestations and multiorgan systemic pathophysiology. Phenotypical heterogeneity of HFpEF is accompanied by a poor knowledge of its etiopathogenetic and pathophysiological mechanisms.
Aim: the clinical complexity of HFpEF reflects the molecular complexity of cardiomyocytes within the heart. The phenotype switch from non-failing heart to human HFpEF is characterized by changes in transcriptome profiling and transitional states of cardiomyocytes in the myocardium. Our aim was to recapitulate and break down this complexity in an in vitro cellular model.
Methods: we designed three novel HFpEF synthetic transcriptional reporter systems – termed synthetic Locus Control Regions (sLCRs) - using an ad-hoc bioinformatic pipeline (Logical design of synthetic cis-regulatory DNA - LSD), as previously described [1]. LSD integrates two inputs: (1) HFpEF signature genes (SGs) and (2) transcription factors (TFs) enriched for binding sites within these genes. SGs and TFs were derived from available human myocardial RNA-seq datasets [2,3]. LSD then predicted and ranked candidate cis-regulatory elements (CREs), which were used to construct sLCRs. Three sLCRs were designed: two (namely "Merged" and "Prior") based on LSD-guided selection of CREs using different TFs, and one (namely "Manual") via manual curation of CREs. Each sLCR was cloned into lentiviral vectors fused with sequences encoding for mCherry fluorescent protein dependent on the sLCRs promoters, and sequences conferring neomycin-resistance. AC16 cardiomyocytes were infected with these lentiviral constructs, selected with antibiotic treatment and expanded as stable reporter lines.
Results: basal mCherry expression detected by flow cytometry in reporter cells confirmed successful sLCRs integration, as compared to native uninfected AC16 cardiomyocytes. Flow cytometry analysis also revealed a significant increase in mCherry-positive cells upon inflammatory simulation with interferon-gamma (IFNγ) at 48h (Merged: p=0,0014; Manual: p=0,0005) and 72h (Merged: p<0,0001; Prior: p=0,032; Manual: p=0,0003) compared to untreated controls. This indicates the activation of the sLCRs in response to IFNγ-mediated inflammatory stimulus.
Conclusions: we developed cardiomyocyte-like reporter cell lines potentially capable of detecting transcriptomic responses relevant to HFpEF, particularly under IFN-γ-mediated inflammatory stimulus. Further inflammatory and/or metabolic conditions potentially involved in the pathophysiology of HFpEF may be investigated through the application of these models. These models lay the groundwork for exploring HFpEF-associated gene regulation and may facilitate future drug screening or mechanistic studies focused on inflammation and cardiomyocytes dysfunction in HFpEF.
References:
1. Company, C., Schmitt, M.J., Dramaretska, Y. *et al.* Logical design of synthetic *cis*-regulatory DNA for genetic tracing of cell identities and state changes. *Nat Commun* 15, 897 (2024). https://doi.org/10.1038/s41467-024-45069-6
2. Hahn, V.S., Knutsdottir, H., Luo, X. *et al.* Myocardial Gene Expression Signatures in Human Heart Failure With Preserved Ejection Fraction. *Circulation* 143(2):120-134 (2021). doi: 10.1161/CIRCULATIONAHA.120.050498
3. GeneTrail 3.2. RegulatorTrail. https://genetrail.bioinf.uni-sb.de/

LOCAL AND SYSTEMIC ENDOTHELIAL DAMAGE IN PATIENTS WITH CEAP C2 CHRONIC VENOUS INSUFFICIENCY: ROLE OF MESOGLYCAN

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Background: Chronic venous disease (CVD) is a prevalent vascular condition marked by structural and functional alterations of the venous system. The presence of varicose veins defines a C2 score in the clinical-etiological–anatomical–pathological (CEAP) classification. Endothelial damage, driven by inflammation and endothelial cell (EC) activation, underlies CVD pathogenesis. This inflammatory microenvironment is characterized by elevated cytokines, pro-angiogenic factors, matrix metalloproteinases (MMPs), and their inhibitors (TIMPs), leading to vessel wall and venous valve remodeling. A key player in this process is the endothelial glycocalyx, a layer of glycosaminoglycans (GAGs) and proteins that regulate vascular tone, permeability, intercellular signaling, oxidative stress, and angiogenesis. Among glycocalyx components, syndecans (SDCs) are of particular interest for their role in vascular pathology. Glycocalyx disruption releases its components into circulation, and its restoration is crucial for preventing cardiovascular diseases. Endothelial dysfunction and glycocalyx detachment are also markers of arterial disease. Venous and arterial diseases share similar endothelial alterations, including glycocalyx damage, as highlighted by Prochaska et al. Therapeutic approaches for CVD include phlebotonic drug (e.g., diosmin, hesperidin), and GAG-based treatments effective across disease stages. Mesoglycan, a GAG mixture including heparan sulfate, dermatan sulfate, chondroitin sulfate, and slow-mobility heparin, targets the endothelium and glycocalyx, promoting membrane integrity and extracellular fluid balance. The objectives of our study are (1) to confirm the presence of inflammatory changes in patients with CVD, regarding the role of the SDCs in the assessment of glycocalyx damage both locally and systemically, and (2) to assess the effect of mesoglycan administration on the local and systemic inflammatory states.
Methods: This monocentric, prospective, interventional study was conducted at the Angiology and Non-invasive Vascular Diagnostics Service of the A. Gemelli IRCCS Polyclinic (Rome, Italy), enrolling consecutive patients who presented spontaneously for angiological or ultrasonographic evaluation between January 1, 2023, and June 1, 2024. CVD was assessed through physical examination and high-resolution ultrasonography. In patients that met the inclusion criteria (age ≥ 18, either sex, CEAP C2 CVD), paired blood samples with an enzyme-linked immunosorbent assay (ELISA) tube were collected from an antecubital and a varicose vein in the standing position from the same patient. Serum was obtained at baseline (T0) and after a 90-day oral mesoglycan regimen (50 mg every 12 h, T1) to measure levels of ICAM-1, VCAM-1, IL-6, IL-8, TGF-β, MMP-2, MMP-9, TIMP-2, SCD-1, and SCD-4. Patient with chronic inflammatory or active infectious diseases (systemic or localized to the lower limbs), diabetes, cancer, BMI > 35 kg/m^2, ongoing or recent use of statins, phlebotonics, corticosteroids, or NSAIDs, and a history of venous thromboembolism were excluded.
Results: Out of 187 patients assessed, 23 patients were recruited. At baseline (T0), serum analysis revealed significantly higher levels of VCAM-1, MMP-2, MMP-9, SCD-1, IL-6, IL-8, ICAM-1, TGF-β, and SDC-4 in blood samples from varicose veins compared to systemic circulation. In contrast, TIMP-2 levels were slightly lower in varicose vein samples. These findings reflect a localized pro-inflammatory profile in the affected venous segments at T0. At T1, there was a significant decrease in serum levels of VCAM-1, IL-6, IL-8, MMP-2, MMP-9, SCD-1, and SDC-4 ($p < 0.05$ for all comparisons) in varicose veins compared to T0. A significant increase in TIMP-2 levels was also

observed ($p < 0.05$). At T1, comparable decreases were noted in systemic blood samples, indicating both local and systemic anti-inflammatory, endothelial-modulating effects of mesoglycan, that also promotes glycocalyx integrity restoration [Table 1]. At T1, 69.5% of patients reported improvements in signs and symptoms of CVD compared to T0.

Conclusions: This study demonstrates for the first time that short-term therapy with mesoglycan (100 mg/day) exerts significant anti-inflammatory effects both locally and systemically in patients with varicose veins. The observed reduction in circulating levels of endothelial and inflammatory biomarkers, including SDCs, suggests a potential role for mesoglycan in restoring cellular glycocalyx integrity. Within the framework of personalized medicine and in light of the increasing interest in syndecan biology, mesoglycan emerges as a promising candidate for targeted therapeutic strategies in CVD and potentially in other vascular disorders.

	Population (No. = 23)					
	Systemic Circulation T0	Systemic Circulation T1		Varicose Vein T0	Varicose Vein T1	
	Median [interquartile range]	Median [interquartile range]	P^a	Median [interquartile range]	Median [interquartile range]	P^b
VCAM-1, ng/ml	709.9 [627.4-826.0]	**650.0 [587.5-727.0]**	**0.001**	763.5 [685.7-949.1]	**660.6 [629.3-743.7]**	**0.001**
ICAM-1, ng/ml	23.18 [18.43-28.55]	24.13 [21.74-32.56]	0.38	23.72 [21.64-29.65]	25.95 [21.75-34.44]	0.89
IL-6, pg/ml	2.57 [1.67-3.77]	**1.42 [0.97-3.18]**	**0.002**	3.89 [1.95-5.20]	**2.53 [1.28-3.52]**	**0.006**
IL-8, pg/ml	8.10 [4.91-17.96]	**7.75 [4.32-13.41]**	**0.001**	9.16 [6.86-14.76]	**9.09 [6.86-13.90]**	**0.003**
TGF-β, ng/ml	29.98 [21.98-44.32]	26.01 [23.52-32.98]	0.69	31.29 [20.55-46.15]	25.33 [21.46-34.40]	0.631
MMP-2, ng/ml	43.57 [37.23-79.19]	**42.84 [39.63-65.06]**	**0.0002**	51.48 [46.94-88.39]	**46.89 [40.92-66.78]**	**0.0002**
MMP-9, ng/ml	52.91 [36.87-94.26]	**35.03 [19.88-75.61]**	**0.0003**	69.02 [39.89-96.74]	**36.22 [25.03-64.24]**	**0.003**
TIMP-2, ng/ml	129.56 [98.51-172.95]	**165.16 [122.59-197.94]**	**0.0002**	127.29 [98.14-175.98]	**172.40 [118.97-211.29]**	**0.003**
SDC-1, ng/ml	177.2 [161.7-203.2]	**148.5 [129.0-176.0]**	**0.0007**	187.4 [167.2-235.7]	**157.1 [140.5-179.4]**	**0.0005**
SDC-4, ng/ml	51.74 [38.27-62.31]	37.07 [33.41-49.26]	0.065	56.75 [46.04-71.71]	**42.22 [34.56-53.72]**	**0.0002**

Table 1: *Serum Levels of Parameters in the Systemic Circulation and in Varicose Vein at baseline (T0) and at T1. Bold characters place emphasis on statistically significant values. [a]The value of P refers to the change in parameters in the Systemic Circulation at T1 compared to T0. [b]The value of P refers to the change in parameters in the Varicose Vein at T1 compared to T0.*

LEARNING FROM POST-COVID-19 CONDITION FOR EPIDEMIC PREPAREDNESS: A VARIABLE CATALOGUE FOR FUTURE POST-ACUTE INFECTION SYNDROMES

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Scope: The emergence of post-COVID-19 condition (PCC) after SARS-CoV-2 infection underscores the critical need for preparedness in addressing future post-acute infection syndromes (PAIS), particularly those linked to epidemic outbreaks. The lack of standardized clinical and epidemiological data during the COVID-19 pandemic has significantly hindered timely diagnosis and effective treatment of PCC, highlighting the necessity of pre-emptively standardizing data collection in clinical studies to better define and manage future PAIS. In response, the Cohort Coordination Board, a consortium of European-funded COVID-19 research projects, has reviewed data from PCC studies conducted by its members. This paper leverages the Cohort Coordination Board's expertise to propose a standardized catalogue of variables, informed by the lessons learned during the pandemic, intended for immediate use in the design of future observational studies and clinical trials for emerging infections of epidemic potential.

Recommendations: The early implementation of standardized data collection, facilitated by the PAIS data catalogue, is essential for accelerating the identification and management of PAIS in future epidemics. This approach will enable more precise syndrome definitions, expedite diagnostic processes, and optimize treatment strategies, while also supporting long-term follow-up of affected individuals. The availability of harmonized data collection protocols will enhance preparedness across European and international cohort studies, and trials enabling a prompt and coordinated response, as well as more efficient resource allocation, in the event of emerging infections and associated PAIS.

CATEGORY	SETTING			STANDARD					RESULTING VARIABLES
	Pre-infection	Infection	Post-infection	SNOMED CT	LOINC	ATC/DDD	ICD	NCit	
Demographics & Lifestyle habits	x			x	x				19
Genomics and metagenomics	x	x		x	x			x	36
Quality of life & PROMS	x	x	x		x				27
Comorbidities	x	x	x	x			x		105
Vaccination	x		x	x					31
Exposure	x			x	x				8
Physical examination		x	x	x	x				65
Presentation & symptoms		x	x	x	x				109
Vital signs	x	x	x	x					27
Laboratory tests		x	x	x	x				140
Imaging		x	x	x	x				34
Hospitalisation and complications		x	x	x	x				79
Treatment		x	x	x		x			63
Immune response	x	x	x	x	x				143
Functional tests		x	x	x	x				35

DYSREGULATED IRON METABOLISM, ANEMIA OF INFLAMMATION, AND ALTERED MYELOPOIESIS AT ONSET AND 3 AND 6 MONTHS AFTER DISCHARGE IN A COHORT OF PATIENTS HOSPITALIZED FOR SEPSIS

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Background/Aims: Anemia prevalence is very high in patients affected by sepsis. Inflammation-induced hypoferremia and inflammatory cytokines suppress erythropoiesis and could lead to anemia of inflammation (AI), although the pathophysiologic pathways are not fully understood. Increasing interest has grown in iron metabolism dysregulation during acute infections. However, little evidence is available about the prognostic role of iron-related biomarkers, such as hepcidin, in this setting. Altered myelopoiesis has been described during the initial phases of sepsis. Its imprinting could persist after infection resolution and drive chronic disruption of immune homeostasis, causing persistent low-grade inflammation and immunosuppression. We aimed to study iron metabolism, AI, and circulating myeloid precursor characteristics in patients hospitalized for sepsis at disease onset, during hospitalization, and at 3- and 6-months post-discharge.

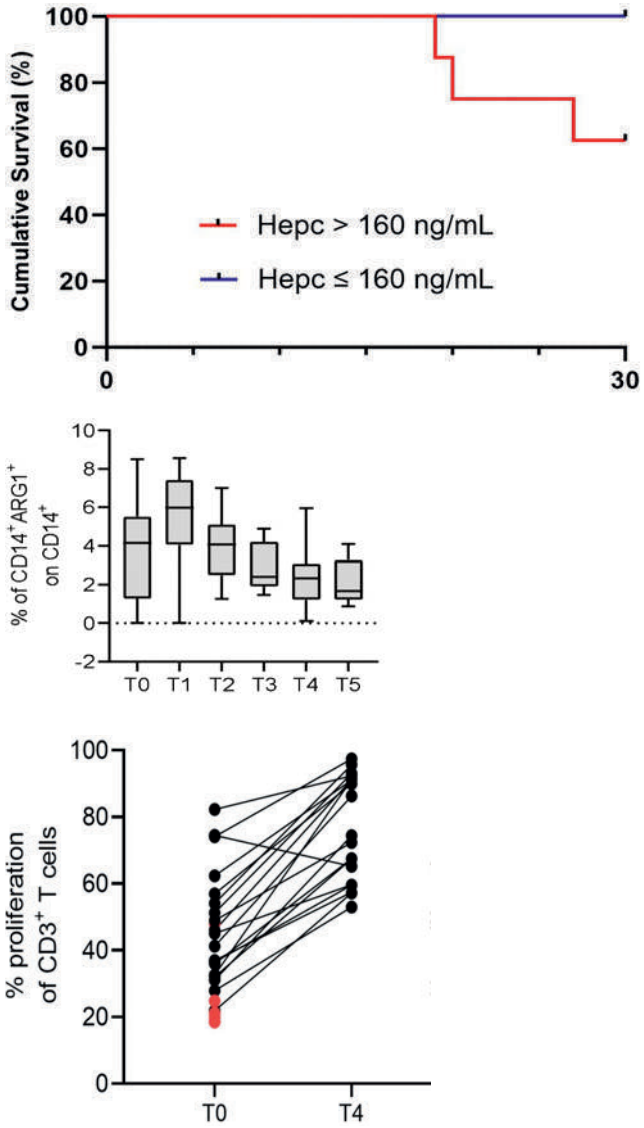
Materials And Methods: 60 newly diagnosed septic patients were enrolled at Verona University Hospital, aged 18-79 years. Septic shock at presentation and severe pre-existing conditions were excluding criteria. Data and serum were collected at disease onset (T0), after 5 (T1) and 10 (T2) days, at discharge (T3), and at 3- and 6-month follow-up (T4 and T5 respectively).

Results: At diagnosis, anemia prevalence was high (76.7%) and all nonsurvivors (n=6) were anemic. Iron metabolism was markedly dysregulated because of acute inflammation, showing low transferrin saturation, serum iron, erythroferrone, soluble transferrin receptor/log ferritin (sTfR index), and high ferritin and hepcidin. Compared to survivors, deceased patients were more frequently affected by comorbidities and had a lower P/F ratio and higher SOFA score and RDW. Nonsurvivors had significantly lower sTfR index values compared to survivors, suggesting inflammation rather than iron deficiency as the main culprit mechanism for anemia. Figure 1 shows that basal hepcidin >160 ng/dL was associated significantly with 30-day mortality (log-rank 4.154, p=0.042). At follow-up, iron biomarkers generally returned to normal values. In particular, sTfR index significantly increased, although anemia prevalence was still relevant at T4 (33.3%) and T5 (40.0%). Circulating arginase-positive myeloid precursors (CD14+ARG1+), usually undetectable in healthy donors, have been isolated in patients' plasma at every time point and were still present in survivors at follow-up despite clinical sepsis resolution (Figure 2). Deceased patients had higher circulating myeloid precursor counts, which showed an immunosuppressive effect on T lymphocytes (Figure 3).

Discussion and Conclusion: Hepcidin could be an important prognostic

marker of worse outcomes in patients with sepsis. The persistence of circulating myeloid precursors after clinical sepsis resolution suggests post-septic never-reached immune homeostasis. Further research aimed to better define the possible role of sTfR index in the differential diagnosis of anemia's causes in acute infections is needed.

Keywords: sepsis, iron metabolism, hepcidin, myeloid precursors



CANDIDA TROPICALIS ENDOCARDITIS ON TRICUSPID AND AORTIC VALVE: A PARADIGMATIC CASE

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Case Presentation: A 67-year-old Caucasian man was transferred to our Unit for *C. tropicalis* infective endocarditis on native tricuspid valve complicated by pulmonary embolism with multiple pulmonary inflammatory foci, partly excavated.

Past medical history included T2 diabetes mellitus, COPD, alcoholic liver cirrhosis (Child-Pugh B7), moderately differentiated esophageal adenocarcinoma that 8 months before underwent esophagectomy with stomach tubulization after neoadjuvant chemotherapy administered via peripherally inserted central catheter (PICC). The anatomic-pathological examination of the surgical specimen showed the absence of residual neoplasia. In the following two months, the patient received parenteral nutrition via PICC, then removed in suspicion of a catheter-related infection. In the early post-operative period, he underwent an abdominal CT scan that was significant for two perisplenic-localized fluid collections.

Diagnostic And Therapeutic Management:

Physical examination:

Haematochemicals:

At admission to the first hospital, **3 sets of blood cultures** were collected and all resulted positive for *C. tropicalis*. Then, a **transthoracic echocardiography** showed a large hyperechoic mobile mass on tricuspid valve (maximum size of 36x26 mm) attached to the anterior tricuspid leaflet and prolapsing in the right atrium with the result of a severe insufficiency. Moreover, multiple echodense images have been identified on a tricuspid native aortic valve characterized by mild aortic regurgitation**.** So, the patient received 4 weeks of antifungal therapy with caspofungin 150 mg/day and then he was transferred to our department.

At the arrival in our Unit, it was decided to switch antifungal therapy to anidulafungin 100 mg/day, after loading, and fluconazole 400 mg/day, given the poor clinical-laboratory response and the evidence at the **chest CT scan** of signs of septic embolization at the level of the right main branch of the pulmonary artery with tri-lobar extension.

Furthermore, after 6 weeks of antimicrobial treatment and 3 consecutive sets of blood cultures tested negative, the patient underwent **open heart aortic and tricuspid valve replacement with bioprosthesis**. Despite persistently negative blood cultures even after surgery, culture of the valves explanted during cardiac surgery were positive for *C. tropicalis* and, considering high inflammation indices, the patient was switched from anidulafungin plus fluconazole to amphotericin liposomal B at the dosage of 5 mg/kg/day i.v.

Upon improvement of the clinical picture, the patient was discharged with the indication to continue antifungal therapy with weekly administration of rezafungin (400 mg first dose, then 200 mg/week for the following 4 weeks), in association with long-term fluconazole 400 mg/day orally. The patient is currently monitored as out-patient and remains in stable clinical condition, to date, with CRP and BDG values decreasing but not negative after two months since the discharge.

Discussion and Conclusions: Candidemia is currently considered one of the main causes of bloodstream infections associated with healthcare practices, with a substantial mortality rate reaching up to 47%; therefore, early initiation of effective antifungal therapy and source control are critical for therapeutic success. The main risk factors for Candida endocarditis are represented by antineoplastic chemotherapy and prolonged use of central venous catheter. The overall sensitivity of blood cultures for the diagnosis of candidemia is 50%; in fact, false negative results are possible in the case of low load candidemia or invasive candidiasis that persists after resolution of the bloodstream involvement. In these cases, BDG may offer a diagnostic advantage. The best therapeutic option for Candida endocarditis on native or prosthetic valves is the combination of surgical source control with valve replacement and prolonged antifungal therapy with a still unknown optimal duration of therapy. Echinocandins are recommended as initial therapy for candidemia; in case of resistance, the use of liposomal Amphotericin B, which is very active on biofilm, is recommended. Rezafungin is an echinocandin with a long half-life and duration of action. It is characterized by a reduced excretion rate so it can be administered once weekly, reducing costs and duration of hospitalization. In conclusion, no clinical trial on antifungal treatment has been conducted in this setting, being fungal endocarditis an extremely rare condition; however, clinical experience suggests the need for a case-by-case approach based on the global patient response to treatment. BDG monitoring may be proposed as a tool for monitoring treatment but, given the high rate of false positive results, further studies are needed on this topic.

ROLE OF EXTRACELLULAR VESICLES AS KEY MEDIATORS OF PATHOGENESIS IN ANDERSON-FABRY DISEASE

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Background: Anderson-Fabry disease (AFD) is an X-linked lysosomal storage disorder caused by mutations in the GLA gene, resulting in a deficiency of α-galactosidase A enzyme activity and progressive accumulation of globotriaosylceramide (Gb3).
Despite significant progress in understanding the genetic basis of lysosomal storage diseases, the systemic mechanisms linking lysosomal defects in specific cells to widespread organ damage remain unclear, particularly in AFD. This project proposes an innovative perspective, investigating the role of extracellular vesicles as mediators of intercellular communication and as possible contributors to the spread of disease in AFD
Objective: To explore the mechanisms of extracellular vesicles-mediated renal cell damage in the progression of AFD.
Methods: Urinary extracellular vesicles (EVs) from adult AFD patients and healthy controls were isolated and characterized by ultracentrifugation and flow cytometry.
Renal cells (HEK293) were incubated with the same amount of EVs for 24, 48 and 72 hours, and then the autophagic flux was assessed, measuring the expression of Beclin 1, the LC3-II/LC3-I ratio and the p62 protein.
Gb3 accumulation in HEK293 cells was analyzed by confocal microscopy.
Results: After 24 hours of incubation of HEK293 with EVs isolated from AFD patients (males: 4; females: 3), the cells showed an accumulation of Gb3, similar to that observed in urinary epithelial cells of AFD patients.
Subsequently, after 48 h, an increase in Beclin-1 was observed (arbitrary units [AU] at 24h: 0.00 ± 0.00; at 48h: 0.07 ± 0.00, $p<0.05$) and, after 72 h, an increase in the LC3-II/LC3-I ratio (AU at 48h: 0.68 ± 0.19; at 72h: 1.14 ± 0.42, $p<0.05$).
However, the absence of degradation of p62 — a functional autophagic flux marker (AU at 48h: 0.07 ± 0.03; at 72h: 0.05 ± 0.04, $p>0.05$) — suggested a blockade of autophagic flux.
In contrast, incubation of HEK293 with EVs derived from healthy volunteers (males: 3; females: 2) resulted in only a transient increase in Beclin-1 expression (UA at 24h: 0.00 ± 0.00; at 48h: 0.08 ± 0.02, $p<0.05$), without accumulation of Gb3 or alterations in autophagy markers.
In particular, the LC3-II/LC3-I ratio remained stable (UA at 48h: 1 ± 0.23; at 72h: 1 ± 0.38, $p>0.05$), as well as p62 levels (UA at 48h: 0.05 ± 0.03; at 72h: 0.04 ± 0.02, $p>0.05$).
Discussion: This study provides new insights into the potential role of EVs in the progression of AFD, suggesting that systemic manifestations of the disease may result, at least in part, from the dissemination of toxic metabolites and signaling molecules via EVs.
Challenging the traditional view of AFD as a predominantly localized genetic disease characterized by the accumulation of substrates confined to cells expressing the altered enzyme, this work introduces a new pathophysiological perspective, particularly relevant in female patients.

THE SWEET ROLLERCOASTER: A CASE OF MYSTERIOUS GLYCEMIC SWINGS

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A 33-year-old woman from Sri Lanka presented to the Emergency Department with recurrent episodes of documented symptomatic hypoglycemia (45–65 mg/dL), primarily occurring postprandially. These episodes were accompanied by adrenergic and neuroglycopenic symptoms and resolved promptly following carbohydrate intake, consistent with Whipple's triad. Home glucose monitoring revealed marked glycemic fluctuations within the same day, alternating between postprandial hyperglycemia (140–150 mg/dL) and symptomatic hypoglycemia.
She was not on chronic medications but reported recent intake of a dietary supplement containing alpha-lipoic acid, prescribed for menstrual irregularities in known polycystic ovary syndrome. She subsequently discontinued the supplement following the development of a cutaneous rash and urticaria.
On admission, the patient presented with a headache and blurred vision. Moreover, she complained of fatigue and a sensation of chest discomfort associated with diaphoresis. Her blood glucose level was 47 mg/dL, which improved rapidly after a 10% dextrose infusion. Due to the recurrent spontaneous hypoglycemia, the patient was admitted for further evaluation.
In-hospital glucose monitoring confirmed wide glycemic excursions (36–270 mg/dL), with postprandial hypoglycemia predominating. Common causes of hypoglycemia - including hypoglycemic agents, alcohol abuse, thyroid or adrenal dysfunction (hormonal profile within normal limits), malabsorption (with negative celiac disease antibodies), hepatic and renal impairment -were excluded. A critical blood sample taken during a symptomatic episode (glucose 36 mg/dL) revealed marked hyperinsulinemia (>1000 mIU/L) and elevated C-peptide (14.3 mcg/L), consistent with endogenous hyperinsulinism. Differential diagnosis focused on autoimmune versus neoplastic etiologies. Anti-insulin autoantibodies (IAA) were significantly elevated (>100 U/mL), while 68Gallium PET imaging showed no lesions suggestive of insulinoma or beta-cell hyperplasia (nesidioblastosis).
Based on clinical, biochemical, and imaging findings, the final diagnosis was insulin autoimmune syndrome (IAS), also known as Hirata's disease.
IAS is a rare cause of spontaneous hypoglycemia, characterized by recurrent episodes associated with high titers of IAA in patients without prior exposure

to exogenous insulin. The most frequently implicated triggers are drugs containing sulfhydryl (-SH) groups, such as methimazole and alpha-lipoic acid. These compounds can disrupt insulin disulfide bonds, rendering the hormone immunogenic and promoting autoantibody production. IAA typically exhibits high binding capacity and low affinity, leading to the formation of large insulin-antibody complexes. Initially, these complexes sequester circulating insulin postprandially, inhibiting its action and causing early hyperglycemia, often associated with elevated HbA1c values (although in our case, it remained within normal limits – 35 mmol/mol). Subsequently, delayed spontaneous dissociation of the complexes results in a surge of free insulin, triggering late-onset hypoglycemia. This biphasic mechanism underlies the typical glycemic variability seen in IAS.

A genetic predisposition has been identified, particularly involving the HLA-DR4 haplotype, notably DRB1*04:06, which may explain the higher prevalence of IAS in East Asian countries, where it is the third leading cause of spontaneous hypoglycemia. In this case, the patient's Sri Lankan origin suggests a possible genetic susceptibility, further supported by her recent exposure to alpha-lipoic acid. To explore this further, HLA genotyping revealed DRB*104 and the DQ8 heterodimer, a combination that has been associated with insulin autoimmune syndrome, especially in the context of the DR4 haplotype.

IAS often follows a self-limiting course, with spontaneous regression typically occurring within 3 to 6 months after diagnosis. Management involves immediate discontinuation of the suspected agent and dietary modifications, emphasizing small, frequent meals with low simple carbohydrate content to reduce insulin stimulation and glycemic variability. In some cases, alpha-glucosidase inhibitors such as acarbose may be used to blunt postprandial glucose peaks and prevent subsequent reactive hypoglycemia. In this patient, the introduction of acarbose contributed to stabilization of glucose profiles, with a gradual decrease in hypoglycemic episodes and normalization of laboratory values after 3 months of therapy (insulin 101 mIU/L, C-peptide 3 mcg/L, IAA 20 U/mL).

For patients unresponsive to dietary measures alone, corticosteroids at immunosuppressive doses may be employed to reduce autoantibody production and the frequency of hypoglycemic episodes. In refractory or relapsing cases, additional immunosuppressive strategies or plasmapheresis may be required for rapid clearance of circulating antibodies.

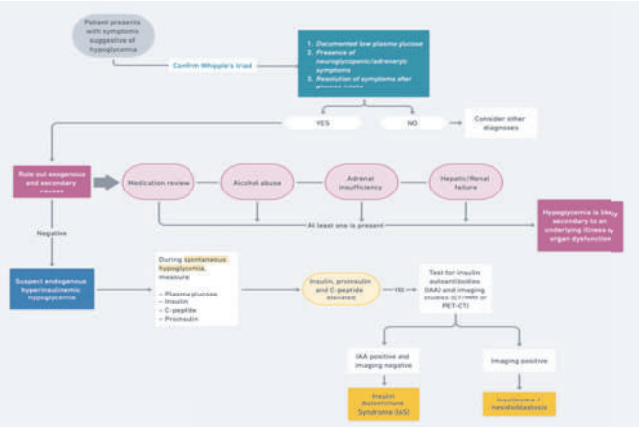

Figure 1. Diagnostic algorithm for the evaluation of spontaneous hypoglycemia

MITOCHONDRIAL FATTY ACID BETA-OXIDATION DISORDERS (FAODS) IN ADULT AGE: LONG-TERM MANAGEMENT AND METABOLIC OUTCOMES OF A SINGLE-CENTRE COHORT

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Background and rationale: Mitochondrial fatty acid oxidation disorders (FAODs) are inherited metabolic disease (IMD) caused by defects in the enzymatic pathway responsible for the breakdown of fatty acids, that impair energy production, particularly during fasting or stress. The clinical presentation is highly variable, ranging from asymptomatic individuals to those experiencing acute metabolic decompensation, with hypoketotic hypoglycaemia, metabolic acidosis, rhabdomyolysis, cardiomyopathy or sudden death. Disease onset and severity depend on the specific enzymatic defect and environmental triggers (such as fasting, infections, life-style or concomitant medications). Late-onset FAODs are increasingly recognized and may present in adulthood with acute or chronic symptoms.

Aim of the study: to report clinical data of a monocentric adult cohort of patients affected by FAODs.

Materials and Methods: We retrospectively collected data of a monocentric cohort of patients affected by FAODs and currently followed at the Adult Metabolic Diseases Clinic of Careggi University Hospital in Florence, as part of the Transition Project between the IRCCS Meyer and Careggi University Hospital. For each patient, demographic, clinical, and laboratory data were collected.

Results: The study cohort consists of 9 patients diagnosed with four different FAOD subtypes, namely very-long-chain acyl-CoA dehydrogenase (VLCAD) deficiency (n=3), carnitine palmitoyltransferase II (CPTII) deficiency (n=2), multiple acyl-CoA dehydrogenase (MAD) deficiency (n=2), and long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency (n=2). Six patients were diagnosed in adulthood (mean age 33 ± 18 years). Patients with LCHAD deficiency were diagnosed in early infancy following episodes of acute metabolic decompensation. One patient with MAD deficiency was diagnosed at the age of 10 years after a muscle biopsy-performed for chronic fatigue and muscle symptoms-revealed lipid storage myopathy. Despite delayed diagnosis, clinical symptoms invariably began in childhood or adolescence and were predominantly muscular. The most frequent manifestation was acute rhabdomyolysis, typically triggered by prolonged exercise or fasting and requiring hospitalization, which was the presenting symptom in patients with CPTII and VLCAD deficiency. One patient with MAD deficiency was diagnosed at age 47 following an episode of severe metabolic acidosis precipitated by reduced food intake. Molecular analysis was performed in all patients. The majority (n = 7) were found to be compound heterozygous, with no predominance of any specific pathogenic allele. In two cases, a novel pathogenic variants were identified: c.354C>A (p.Asn118Lys) in the *ETFDH* gene associated with MAD deficiency, and c.98delA (p.Gln33Argfs*40) in the *CPT2* gene. One patient with LCHAD deficiency was homozygous for the missense mutation G1528C. In the second LCHAD case, genetic analysis was inconclusive and, the diagnosis was confirmed biochemically by demonstrating reduced mitochondrial trifunctional protein (MTP) activity in cultured fibroblasts. Patients were treated with personalized dietary regimens aimed at preventing catabolic stress which included shortened fasting intervals (from 4–6 hours during the day and no more than 8–12 hours overnight), restriction of total fat intake (ranging from 9–35% of total energy), supplementation with medium-chain triglyceride (MCT) oil, and caloric supplementation with maltodextrin before exercise. Patients with MAD deficiency additionally received pharmacological treatment with riboflavin and carnitine. At last visit, five patients reported symptoms exclusively after physical exertion, while the others were completely asymptomatic. Two patients experienced episodes of acute rhabdomyolysis within the past year, triggered by intense exercise combined to poor adherence to dietary recommendations. Mean creatine phosphokinase (CK) level at rest was 188 U/L (±141) and did not differ significantly between subgroups. Fasting acylcarnitine profile at last visit was abnormal in all patients consistently with the metabolic disorder. Patients with CPTII deficiency had high levels of long-chain acylcarnitines with (C16+C18:1)/C2=0.39±0.1. Patients with MAD deficiency had high levels of all acylcarnitines. Patients with LCHAD deficiency had high levels of long-chain acylcarnitines (C14OH, C16OH, C18OH, C18:1OH). Patients with VLCAD deficiency had high levels of long-chain acylcarnitine and C14:1=2.15±1.36 umol/L.

Conclusions: FAODs are rare IMD that may present in adulthood with

chronic muscular symptoms or acute rhabdomyolysis requiring emergency care. Due to their nonspecific presentation, symptoms are frequently underrecognized. Management relies on strict dietary measures, including lipid restriction and pre-exercise carbohydrate supplementation to ensure energy balance. MAD deficiency shows a favourable response to carnitine and riboflavin therapy. Early diagnosis is crucial to initiate appropriate therapy and prevent metabolic decompensation and long-term complications.

COMPARISON OF FOUR NON-INVASIVE TOOLS FOR PREDICTING SEPSIS AND SEPTIC SHOCK MORTALITY: A PROSPECTIVE COHORT STUDY

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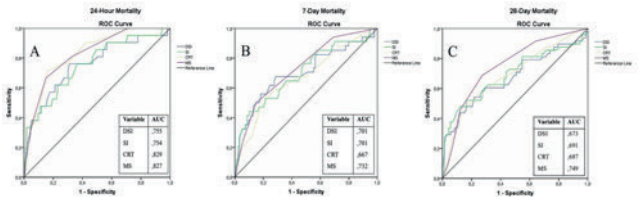
Objective: Sepsis, a life-threatening organ dysfunction, remains a major global health concern. Early detection remains challenging due to nonspecific symptoms. Non-invasive tools such as the Shock Index (SI), Diastolic Shock Index (DSI), Capillary Refill Time (CRT), and Mottling Score (MS) may help assess hemodynamic status and predict mortality, but a comprehensive comparison of their prognostic value is lacking. This study compares the performance of these tools in predicting mortality at 24 hours, 7 days, and 28 days in septic patients.
Methods: A monocentric, prospective observational study was conducted from January to September 2024 at St. Anna University Hospital, Ferrara, Italy. Adult patients (≥18 years) with suspected infection and a National Early Warning Score-2 ≥5 were enrolled. Demographic data, vital signs, CRT, MS, and mortality outcomes were recorded at 24 hours, 7 days, and 28 days.
Results: A total of 135 patients were included (median age 85 years, IQR 79–90; 44.4% female). Mortality rates were 15.7% at 24 hours, 26.6% at 7 days, and 39.7% at 28 days. CRT showed the highest predictive value for 24-hour mortality (AUC: 0.829, p<0.01), while MS had the best performance at 7 days (AUC: 0.732, p<0.01) and 28 days (AUC: 0.749, p<0.01). No significant differences emerged in pairwise comparisons.
Conclusion: While no tool was found to significantly outperform others, CRT and MS provide valuable, non-invasive mortality prediction in sepsis. Indeed, CRT is most effective for early risk stratification, while MS correlates with mid- and long-term outcomes, supporting their integration into clinical assessment.

Figure 2. Comparison of ROC curves of DSI, SI, CRT and MS to assess 24-hour (Panel A), 7-day (Panel B) and 28-day mortality (Panel C) for sepsis and septic shock.



Note: AUC: Area Under the Curve; CRT: Capillary Refill Time; DSI: Diastolic Shock Index; MS: Mottling Score; ROC: Receiver operating characteristic; SI: Shock Index.

PROGRESSIVE DIFFERENCES IN ADIPOSITY AND ECTOPIC FAT SURROGATES ACROSS FOUR PROGRESSIVE GLYCAEMIA STATUS GROUPS REINFORCES WEIGHT /ECTOPIC FAT REDUCTION AS THE MAJOR TARGET FOR PREVENTION

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Background and aims: There is growing evidence that obesity and ectopic liver fat are major modifiable risk factors for type 2 diabetes (T2D). However, less is known about changes in weight and ectopic fat distribution as individuals progress from normoglycemia to prediabetes and eventually to T2D. Understanding these transitions could help better emphasize the role of obesity in the development and progression of prediabetes. This cross-sectional study examined differences in adiposity measures and commonly measured surrogate markers of ectopic fat across the glycaemia lifecourse.
Materials and methods: UK Biobank white participants without baseline cardiovascular disease or known T2D (n = 287,987) were classified into four groups based on HbA1c: Normal (<42 mmol/mol), Prediabetes 1 (42–44.9 mmol/mol), Prediabetes 2 (45–47.9 mmol/mol), and Undiagnosed T2D (48–75 mmol/mol, without prior T2D diagnosis) We limited to upper end of the undiagnosed T2D group to 75mmol/mol limit unintentional weight loss. Ordered logistic regression and linear regression were used to test associations between HbA1c groups and differences in BMI, waist-to-height ratio (WHtR), alanine aminotransferase (ALT; a surrogate of liver fat), and triglycerides (circulating fat), after adjusting for age, sex, deprivation status, and statin use (as statins are known to influence HbA1c levels). The hypothesis was that a stepwise increase in these markers would occur with worsening glycemic status.
Results: With increasing baseline HbA1c levels across the four groups, there was evidence of higher BMI, WHtR, ALT, and triglycerides. In particular, after adjustment, BMI exhibited a stepwise increase, with the prediabetes1, prediabetes2, and undiagnosed T2D groups having 2.73, 3.56, and 3.83 kg/m² higher BMI, respectively compared to the normal HbA1c group, with each step being significant. Notably, such BMIs differences are broadly equivalent to average weight differentials of ~8 to 11kg in progressing from normoglycemia to prediabetes to T2D. WHtR followed a similar trend, rising by 0.044, 0.058, and 0.061 across the same groups.
Notably, ALT and triglyceride levels also increased progressively. ALT was 3.81, 5.64, and 9.89 U/L higher, while triglycerides were 0.39, 0.46, and 0.63 mmol/L higher in the prediabetes1, prediabetes2, and undiagnosed T2D groups, respectively, compared to the normal group, again with each step being significantly different to preceding group.
Conclusion: A clear stepwise relationship emerged between worsening glycemic status and higher levels of adiposity and in circulating and hepatic ectopic fat markers. These findings reinforce weight intervention programs as a primary intervention target for preventing the progression from normoglycemia to pre-diabetes to frank T2D.

HEALTH PROFESSIONALS' PERCEPTIONS OF "MISSED CARE": A QUALITATIVE STUDY

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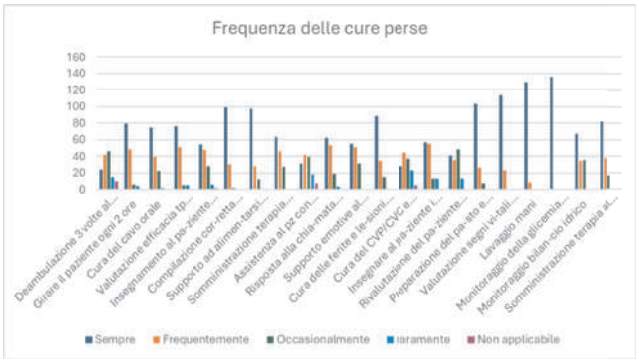
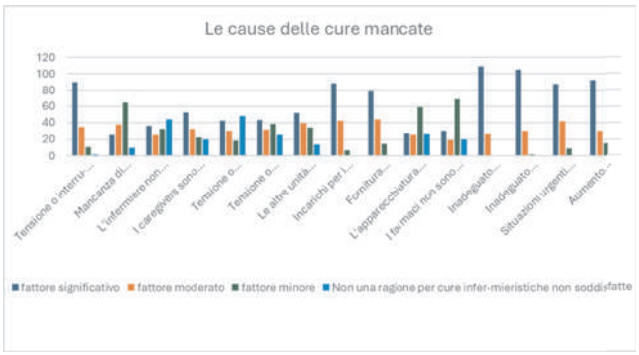
Background: In recent years, the global financial crisis and policies to curb health care spending have led to a significant reduction in the health care workforce, increasing the workload.In Italy, the nurse-to-patient ratio is significantly lower than in other European countries, negatively impacting the quality of care. This phenomenon is known as Missed Nursing Care, or the total or partial omission of essential care for the cared-for. As this problem threatens the quality of care, it becomes critical to develop measurement tools and preventive strategies to reduceits incidence and improve patientsafety. This studyaims to analyze health care providers' perceptions of "Missed Care" and the reasons that lead to such omissions.
The study was carried out from January 2023 to April 2023 by administering an anonymous online questionnaire (the ISSCARE Survey), administered through socialchannels, which is useful for investigatingthe perceptions of health care providers to sidentify the most omittedcare and assesswhat are the main causes of this issue. The questionnaire consists of a first part of 21 items on a Likert scale (1-5), which investigates what are the most or least frequent "missed care," and a second part consisting of 15 items on a Likert scale (1-4), which investigates the causes of these omissions. The questionnaire was administered to 162 caregivers, nurses and OSSs; only 137 caregivers were included in the study, excluding the emergency- ungency, mental health and resuscitation settings.
The results show that some care activities are not performed regularly. Among the most frequently omitted care by nurses are the management of CVPs and CVCs (for 27 % occasionally, for 20.4 % rarely or not applicable), the timeliness of assisting the pt with need for elimination within 5 minutes(for 28.5 % occasionally, for 18.2 % rarely or not applicable), and patient ambulation (for 33.6 % occasionally, for 18.2 % rarely or not applicable). Failure to performthese interventions often turns out to be related to staffshortages and the need to work in teams, which is not always possiblewith limited resources. Other care, such as re-evaluation of the patient at each shift, emotional support and patient education are also frequently omitted,

with percentages ranging from 28% to 53%. Among the main causes of omitted care, nurses point to staff shortages (defined as significant by 79.5 % of providers), limited resources (significant for 57.7 %), communication problems withinthe team (65.7 %), and the occurrence of sudden events such as ward emergencies (67.2 %).
The study conducted highlights the prevalence of the phenomenon of omitted nursing care, mainly attributed to staff shortages, sudden worsening of patient conditions and scarcity of resources. Current healthcare policies, geared toward cost containment and turnover freeze, have increased the workload of healthcare workers, necessitating better planning of activities and more effective decision-making to manage care priorities. In addition, the normalization of these omissions may lead to a reduction in care quality and justification. The limitations of this study are a limited sample and data that may be over- or underestimated due to the subjectivity of perceptions.
Bibliografia: *L'infermiere 56*





EFFECTS OF NOCTURNAL CONTINUOUS POSITIVE AIRWAY PRESSURE ON RENAL FUNCTION DECLINE IN A COHORT OF ELDERLY PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Background: Obstructive sleep apnea syndrome (OSA) could play a key role in the pathogenesis of rapid decline in renal function (RDRF). Intermittent hypoxia, oxidative stress, inflammation and endothelial dysfunction lead to structural and functional damage of kidney and consequently to chronic kidney disease (CKD) Treating OSA, continuous positive air pressure (CPAP) may prevent this downstream effects that are potentially deleterious to kidney function.
Porpuse: The Aim of this study was to evaluate, the possible impact of CPAP therapy on the RDRF, defined as GFR annual loss ≥5 ml/min/1.73 m 2, in a cohort of elderly patients affected by moderate to severe OSA and several comorbidities.
Methods: In this prospective single-center observational study were enrolled 469 elderly patients, including 327 men (69.7%) and 142 women (30.3%). Mean age was 74.4 ± 5.3 years. After a seven days' period of CPAP titration, 210 patients showed good adherence to therapy (>4h/night) and good tolerability to CPAP, so chose to continue CPAP therapy, whereas the remaining 259 patients received best support care only. A log-rank test was performed to compare the hazard function estimates of the two groups in renal events observed during follow-up. Subsequently, the variables that significantly correlated with the occurrence of RDRF were included in a multivariate Cox regression model was build to determinate the independent predictors RDRF occurrence.
Result: After 20.7±5.5 months follow up, we observed 129 (27.5%) total renal events, 8.33 events/100patient/year in CPAP group versus 18.20 events/100patient/year in untreated group (p<0.0001). the difference in the incidence of RDRF is statistically significant between the two groups at all times of follow-up (2 log-rank test p<0.0001). The multivariate stepwise Cox regression analyses indicate that the use of CPAP is associated with a reduced risk of RDRF (HR 0.27; CI95° 0.18-0.41; p<0.0001).Therapy with SGTL2i is also associated with a reduced risk of eGFR decline (HR 0.24; CI95° 0.14-0.41; p<0.0001). Instead, TIA/STROKE (HR 1.76; CI95° 1.17–2.64; p=0.006), dyslipidemia (HR 1.68; CI 95° 1.04-2.71; p=0.034), age (10 years increase) (HR 1.61; CI95° 1.16-2.25; p=0.005), loop diuretics (HR 1.61; CI 95° 1.09 – 2.38; p = 0.017), T2DM (HR 1.57; CI95° 1.03-2.38; p=0.036), are all associated with an increased risk of RDRF.
Conclusion: Our results confirm the positive impact of CPAP therapy in slowing the progression of renal damage, as demonstrated by the lower incidence of RDRF in patients treated with CPAP compared to untreated ones; in a cohort of elderly patient suffered from OSAS with several comorbidities.

RISK FACTORS FOR SELF-REMOVAL OF VASCULAR ACCESS DEVICES IN NON-INTENSIVE CARE UNIT DEPARTMENTS: A MONOCENTRIC RETROSPECTIVE OBSERVATIONAL STUDY

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Background: Vascular access devices (VADs) are essential for managing critically ill patients, and knowledge regarding indications for placement is continually expanding. The rate of inadvertent VAD removal serves as a marker of quality of care in the Intensive Care Unit (ICU). To our knowledge, no study has analyzed this phenomenon in medical and surgical non-intensive departments worldwide. The age of patients admitted to these departments is increasing and is associated with greater fragility and multimorbidity. The primary aim of this observational, retrospective study was to evaluate the rate and identify risk factors related to VAD self-removal in ten medical and surgical non-intensive care units. As a secondary outcome, a subgroup analysis of patients with and without cognitive impairment and delirium was performed.
Materials and methods: This study was conducted at Luigi Sacco Hospital, Milan, Italy, between January 2021 and March 2023. The VADs evaluated included long peripheral catheters, midline catheters, peripherally inserted central catheters (PICC), and femoral-inserted central catheters. A time-to-event cumulative incidence analysis was performed using Cox proportional hazards models to assess the risk over time. This analysis was used to identify risk factors for VAD removal. Potential risk factors were first analyzed using univariate Cox models. Variables with a p-value of less than 0.2 in the univariate analysis were subsequently included in three separate multivariate models:
1. The whole population.
2. Patients with a diagnosis of cognitive impairment or delirium.
3. The remaining patients without a diagnosis of cognitive impairment or delirium.
Results from the Cox proportional hazards models were expressed as Odds Ratios (OR) with 95% confidence intervals (CI) and corresponding p-values. A p-value of less than 0.05 was considered statistically significant.
Results: 1,432 VADs were positioned in 1,249 patients (mean age 78, SD 64-85), and 141 were self-removed (9.8%). Patients with VAD removal were older (77 vs 80 years, p = 0.026) and had a significantly shorter catheter dwell time (3 vs 11 days, p < 0.01). In the multivariate analysis, male sex (OR 1.789, CI 1.26-2.54, p=0.001), positioning in the lower limb instead of the upper limb (OR 2.543, CI 1.682-3.846, p<0.001), delirium (OR 1.362-5.198, p=0.004), and cognitive impairment (OR 1.87, CI 1.116-3.133, p=0.017) were identified as significant risk factors. Finally, PICC placement, compared to any other type of shorter VAD, served as a protective factor against self-re-

moval (OR 0.558, CI 0.333-0.933, p = 0.026).
1,042 VADs were positioned in 959 patients without cognitive impairment or delirium (mean age 74, IQR 60-83), and 90 were self-removed (8%). The catheter dwell time was longer in those without removal (mean 4 vs 12 days, p<0.001). In this group, male sex (p=0.011, OR 1.77, CI 1.14-2.76) and lower limb positioning (p=0.001, OR 2.23, CI 1.36-3.65) were identified as risk factors for self-removal. PICC placement was a protective factor (p<0.05, OR 0.55, CI 0.3-0.99). Conversely, 336 VADs were placed in 290 patients affected by cognitive impairment and/or delirium (mean age 83, IQR 78-87), among whom 51 were self-removed (17.1%). Catheter dwell time remained significantly lower in patients with VAD removal (mean 3 vs 10 days, p<0.01). Male sex (p=0.048, OR 1.772, CI 1.005-3.124) and lower limb placement (p=0.003, OR 3.428, CI 1.51-7.78) remained risk factors. In this population, PICC placement appeared to be no longer protective against self-removal.
Conclusions: Age, male sex, delirium, cognitive impairment, and lower limb positioning are significant risk factors for catheter self-removal. Age did not appear to be a risk factor when assessing subgroups of patients with and without cognitive impairment and/or delirium. Furthermore, in both subgroups of patients affected or not by cognitive impairment and/or delirium, male sex and lower limb placement remained risk factors. While it is easily understood that catheter self-removal is more likely from the leg than from the arm, the authors underline a potential selection bias in patients with delirium and cognitive impairment, where the procedure is often not possible on the upper limb due to limited cooperation. Finally, PICCs seemed to be a protective factor against self-removal in the general population and those without cognitive impairment and/or delirium, but not in the affected subsample. This could be attributed to selection bias: due to their low cost-effectiveness ratio, our VAD team typically minimizes PICC placement in patients at high risk of VAD removal when it is not strictly necessary for clinical reasons.
To identify a suitable solution, further prospective studies are needed to compare access placement locations in patients affected by cognitive impairment and/or delirium, while considering their fragility, tendency to self-removal, and behavior during the procedure.

DISTINCT MIRNA PROFILES IN SUBCUTANEOUS VS. VISCERAL ADIPOSE TISSUE AND THEIR ASSOCIATION WITH ADIPOSITY ASSESSED BY CT-SCAN IN PATIENTS WITH GASTROINTESTINAL CANCER

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Background: Metabolic and nutritional alterations linked to cancer frequently result in substantial adipose tissue wasting, accompanied by distinct remodeling processes in subcutaneous (SAT) and visceral (VAT) fat depots. Although microRNAs (miRNAs) are known to regulate adipose tissue function, their depot-specific expression patterns in cancer patients remain poorly understood.This study aimed to investigate and compare the expression levels of selected miRNAs—miR-26a, miR-128, miR-144, miR-155, and miR-181a—in both SAT and VAT obtained from the same gastrointestinal cancer patients undergoing surgery, in comparison to control subjects.
Methods: We conducted a cross-sectional study involving gastrointestinal cancer patients and control subjects undergoing surgery for either tumor resection or non-malignant conditions, respectively. During the procedures, adipose tissue samples from both SAT and VAT depots were collected. Expression levels of selected miRNAs were analyzed using quantitative real-time PCR (qRT-PCR). Body composition was evaluated through CT imaging at the L3 vertebral level to quantify total adipose tissue (TAT) and categorize participants according to adiposity level (high vs. low).
Results: Gastrointestinal cancer patients (n=17) compared to controls (n=5) showed higher expression of miR-128 in both SAT and VAT (p<0.05), miR-155 in VAT (p=0.018), and lower miR-181a in VAT (p<0.01). Within cancer group, miR-26a and miR-128 were lower in VAT than in SAT (p<0.001), while miR-155 levels were higher in VAT than in SAT (p<0.001). MiR-26a was consistently higher in SAT regardless of adiposity level, while miR-128 and miR-144 showed depot- and adiposity-dependent variations, with notable downregulation of miR-128 in VAT from low-adiposity patients and lower miR-144 in SAT from high-adiposity individuals. MiR-155 was elevated in VAT from low-adiposity patients, whereas miR-181a expression remained unchanged across depots and adiposity levels
Conclusions: This is the first human study to compare miRNA expression in both SAT and VAT from the same gastrointestinal cancer patients, stratified by adiposity level, showing depot-specific miRNA regulation. Given the known biological functions of certain miRNAs, our findings indicate that VAT is particularly susceptible to inflammatory and metabolic disturbances, with miR-155 emerging as a promising biomarker of visceral fat remodeling. The distinct miRNA expression profiles observed in SAT and VAT may offer new therapeutic targets to counteract adipose tissue wasting and metabolic dysfunction in cancer patients.

PRES FROM ANTI-VEGF THERAPY IN AN ONCOLOGY PATIENT: REVERSIBLE ONLY IF RECOGNIZED

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In recent years, targeted therapies and immune checkpoint inhibitors have transformed the treatment of solid tumors. While significantly improving cancer survival, they can also cause rare but severe adverse events. One of these is Posterior Reversible Encephalopathy Syndrome (PRES), also known as Reversible Posterior Leukoencephalopathy Syndrome (RPLS), a potentially life-threatening condition if not promptly recognized. PRES is primarily caused by vasogenic cerebral edema, resulting from dysfunction of the blood–brain barrier, which underlies its characteristic neurological symptoms.PRES is typically a diagnosis of exclusion, based on clinical presentation, medical history, and risk factors such as hypertension, preeclampsia, renal disease, sepsis, autoimmune disorders, and the use of immunosuppressive drugs and antineoplastic agents. Among these, lenvatinib, a VEGF inhibitor, may impair the blood–brain barrier and promote vasogenic edema. Early identification is essential, especially in patients receiving innovative oncologic therapies, where prompt action can significantly affect prognosis. In peripheral hospitals, where access to advanced neuroimaging is limited, clinical and pharmacological reasoning plays a crucial role in diagnosing this syndrome.
A 63-year-old woman with stage IV endometrial carcinoma, treated with pembrolizumab and lenvatinib, presented after the fifth cycle with headache, seizures, confusion, and visual disturbances. Her history included mild hypertension, previously managed with ramipril, which she had discontinued independently.At admission, she exhibited a hypertensive crisis (190/130 mmHg),Brain CT and CT angiography showed no acute lesions. MRI was unavailable. Lumbar puncture revealed moderate protein elevation without pleocytosis. Infectious screening (PCR, CSF/blood/urine cultures), combined with clinical and imaging data, excluded sepsis, autoimmune/paraneoplastic encephalitis, stroke, progressive multifocal leukoencephalopathy, and metabolic/toxic encephalopathies.The concomitant use of pembrolizumab required careful exclusion of immune-related neurotoxicity, such as autoimmune encephalitis or transverse myelitis, through detailed clinical evaluation and cerebrospinal fluid analysis. This differential diagnosis was particularly relevant, as it would have warranted high-dose corticosteroid therapy—potentially inappropriate and harmful in the context of PRES, due to the risk of worsening vasogenic edema and impairing blood pressure control. Among alternative considerations, hypertensive encephalopathy was also evaluated, given the markedly elevated blood pressure values. However, it was considered less likely due to the presence of generalized seizures, which are uncommon in pure hypertensive encephalopathy and more consistent with PRES.In the absence of MRI confirmation, a diagnosis of PRES was considered highly probable, based on clinical presentation, hypertensive crisis, non-specific hyperproteinorrachia, and temporal association with lenvatinib.Lenvatinib was promptly discontinued. Levetiracetam was started for seizure control, and intravenous antihypertensive therapy (clonidine, urapidil, nitrates) was initiated, followed by oral carvedilol, amlodipine, and ramipril. These interventions aimed to rapidly lower mean arterial pressure, protect the blood–brain barrier, and reduce cerebral edema.The patient showed rapid clinical improvement, with blood pressure normalization within 48 hours, seizure resolution, and complete cognitive recovery. One month later, she remained stable with normal blood pressure without antihypertensive therapy, reinforcing the suspicion of lenvatinib-induced PRES.
Lenvatinib is a multikinase inhibitor (VEGFR, FGFR, PDGFR) that targets tumor angiogenesis and is widely used in combination regimens. Its antiangiogenic effects can disrupt the structural and functional integrity of the blood–brain barrier, favoring vasogenic cerebral edema. Although consid-

ered rare, PRES associated with VEGF inhibitors has been reported in clinical practice, with an estimated incidence below 1%, suggesting possible underrecognition. Clinical judgment is critical for differentiating PRES from other conditions, particularly in patients receiving immunotherapy. In this case, prompt drug withdrawal, blood pressure control, and anticonvulsant therapy led to full recovery.
Conclusion: Timely recognition of PRES in oncologic patients treated with VEGF inhibitors is essential to prevent irreversible neurological damage. Even without MRI, a clinical diagnosis supported by thorough pharmacologic history and differential diagnosis can guide effective intervention and improve outcomes.PRES should be suspected in patients with acute neurological symptoms undergoing anti-VEGF therapy, especially with hypertensive crises. Prompt drug discontinuation and aggressive blood pressure control are key to clinical resolution This case underscores the internist's crucial role in managing rare toxicities from novel oncologic therapies, ensuring safety—especially in peripheral settings with limited resources, promoting closer integration between internal medicine and oncology.

Differential Diagnoses	Reason for Exclusion
Sepsis	Negative cultures and PCR, no systemic inflammatory signs
Autimmuno/paraneoplastic encephalitis	Antibodies non-specific, clinical presentation not suggestive
Ischemic or hemorrhagic stroke	CT and angio-CT negative for ischemia or hemorrhage
Progressive multifocal leukoencephalopathy (PML)	No immunosuppression history, MRI unavailable but clinical sig assent
Pembrolizumab toxicity	Potentially relevant, but high-dose corticosteroid therapy deemed inappropriate and potentially harmful
Hypertensive encephalopathy	Seizures more consistent with PRES, rapid response to BP control

IMPACT OF CLINICAL AND SOCIAL RISK FACTORS ON METABOLIC DYSFUNCTION–ASSOCIATED STEATOTIC LIVER DISEASE (MASLD): COMPARISON BETWEEN TWO GROUPS OF NATIVE AND MIGRANT PATIENTS

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Introduction: Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD) is a multifaceted disease associated with obesity, insulin resistance (IR), type 2 diabetes mellitus (T2DM), in a word the metabolic syndrome (MetS). Its burden is increasing at an alarming rate, with a projected global prevalence of 55% by 2040. MASLD new definition has replaced NAFLD (Non-Alcoholic Fatty Liver Disease) incorporating cardiometabolic risk factors (CMRF) and alcohol consumption, but except for some recent publications relating to the US population, there are few data on the burden and severity of SLD subtypes and especially on the impact of risk factors such as social determinants of health (SDOH).
The aim of our study was to estimate the weight of clinical and SDOH in a population of adults with SLD attending the Migration Medicine clinic, comparing them with those of a native population with the purpose to analyse differences in the prevalence of metabolic and cardiovascular comorbidities between the two groups and to examine the role of SDOH in modulating disease risk.
Methods: 90 and 32 subjects with MASLD were consecutively enrolled at the Liver Diseases Outpatient Clinic and the Migration Medicine Outpatient Clinic respectively, of the Internal Medicine Unit of the "Paolo Giaccone" University Hospital in Palermo, from June 2022 to December 2024. At the visit, we collected the clinical history, anthropometric data, the main laboratory tests, scores such as the Fibrosis-4 (Fib-4) and the non-alcoholic fatty liver disease fibrosis score (NFS), as well as the pharmacological anamnesis. At the same time an ultrasound (US) study of the upper abdomen was performed.
Results: A statistically significant difference in mean age was observed between the two groups (p<0.0001). Native patients had a significantly higher mean age (60.2±9.1 years) than migrant patients (47.4±16.9 years). In relation to the main metabolic and cardiovascular risk factors, natives had a high prevalence of hypertension (91.1%), than migrants (54.4%) (p<0.0001). T2DM was significantly more frequent in natives (84.4%) than in migrants (37.5%) (p<0.0001). On the contrary migrants showed significantly higher mean values of total cholesterol (191.5±46.9 mg/dl) than natives (160.5±43.5 mg/dl, p<0.001) and also LDL (117.8±38.9 mg/dl) than natives (86.1±41.0 mg/dl, p<0.0001), suggesting a possible predisposition to a different alteration of lipid metabolism.
The analysis of the main haematological and biochemical parameters between native and migrant patients, showed that migrants had significantly lower haemoglobin values (13.2±2.1 g/dl, p<0.01) compared to natives (14.2±1.7 g/dl), while γ-GT levels were significantly higher in migrants (29.5 U/l (19.5-89) in migrants vs. 21 U/l (14.7-28) in natives, p<0.01).
FIB-4 [1 (0.7-1.4) vs 0.9 (0.5-1.7)] as well as NFS [-0.1 (-0.2/-0.09) vs -1.3 (-3.7/-0.2)] values were not statistically different in the two populations and also steatosis was present with different severity in both groups, without statistically significant differences.
When we analysed some cardiovascular risk conditions but above all the manifestations of organ damage, we found that atherosclerosis was significantly more common in migrants (40.6%) than in natives (15.6%) (p<0.01), hypertensive heart disease was significantly more frequent in migrants (28.1%) than in natives (4.4%) (p<0.001), and heart failure was significantly more frequent in migrants (21.9%) than in natives (1.1%) (p<0.0001).
The analysis of the most commonly used drugs also highlighted significant differences in the use of some drugs between the two groups, in particular, the angiotensin II receptor antagonists (ARBs) were significantly more used in natives (36.6%) than in migrants (12.5%) (p<0.05), as well as Metformin more used in natives (71.1%) than in migrants (28.1%) (p<0.0001), Incretins (GLP-1 agonists) more used in natives (37.8%) than in migrants (9.4%) (p<0.003) and Gliflozins (SGLT2 inhibitors) used in 40% of natives and 15.6% of migrants (p<0.01).
Conclusions: The analysis of our data highlighted that, although no significant differences emerged in the characteristics of liver involvement in MASLD between the two populations examined, migrants present a significantly higher burden of cardiovascular diseases compared to natives. This difference could reflect:
• Lower diagnosis and early management of cardiovascular diseases in migrants, with a risk of progression to more severe forms.
• Differential burden of SDOH, including socioeconomic difficulties, language and cultural barriers and limited access to health services, which could negatively influence the prevention and treatment of chronic diseases.
• Potential genetic or environmental differences that predispose migrants to a higher cardiovascular risk.
These findings underline the need to adopt a multidisciplinary approach to promote health education, screening and facilitated access to care, to ensure effective management of metabolic and cardiovascular diseases in this specific population setting, possibly also intercepted by the presence of MASLD.

ATRIOVENTRICULAR CONDUCTION IN CHRONIC INFLAMMATORY ARTHRITIS: ENHANCED ASSESSMENT BY NEW ELECTROCARDIOGRAPHIC PARAMETERS

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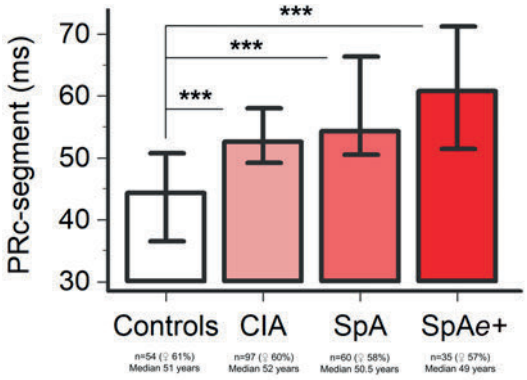
Background: It is increasingly accepted and supported by recent population studies that patients with spondylarthritis (SpA) have an increased risk of severe atrioventricular (AV)-block/pacemaker implantation,(1) possibly due to structural and immunological similarities between enthesis and aortic root ("cardiac enthesis")(2). However, available studies analyzing AV-conduction in SpA, and more generally in chronic inflammatory arthritis (CIA), found in many cases no differences to healthy controls, suggesting that traditional electrocardiographic (ECG) parameters are not suitable for early detection of high-risk patients.
Objective: Since PR-interval is deeply influenced by heart rate (HR) and atrial depolarization, the aim of this study was to perform an enhanced AV-conduction assessment in CIA patients by adding HR-correction and PR-

segment measurements to standard ECG parameters.(3,4)
Methods: In a cross-sectional study, 97 consecutive patients [60% females, median 52 years] with CIA [60 SpA, 37 rheumatoid arthritis] underwent 12-lead ECG to measure PR-interval, PR-segment and HR. The Rautaharju-Soliman formula was applied to calculate HR-corrected PR-interval (PRc-interval) and PR-segment (PRc-segment). A group of 54 healthy subjects comparable for sex and age [61% females, median 51 years] was used as control.
Results: In patients with CIA, PR-segment and even more PRc-segment were significantly longer when compared to controls (PR-segment: 50.0 [40.0-70.0] *vs.* 45.5 [36.7-58.0] ms; p=0.033; PRc-segment 52.6 [42.1-69.6] *vs.* 45.0 [34.0-55.8] ms; p<0.001). Stratification analyses revealed that such differences were observed in SpA patients only (PR-segment: 53.0 [40.0-70.0] *vs.* 45.5 [36.7-58.0] ms; p=0.012; PRc-segment: 54.3 [41.0-63.4] *vs.* 45.0 [34.0-55.8] ms, p<0.001), specifically in those with enthesitic involvement (PR-segment: 57.0 [47.0-67.7] *vs.* 45.5 [36.7-58.0] ms, p<0.001; PRc-segment: 60.8 [46.0-76.5] *vs.* 45.0 [34.0-55.8] ms, p<0.001) (**Figure**). Moreover, in this latter subset of patients, the prevalence of PR/PRc-segment prolongation (>90 ms) was significantly higher than in controls (11% *vs.* 0%, p=0.021). Conversely, no difference in PR/PRc-intervals was observed throughout the groups.
Conclusion. Enhanced ECG assessment reveals delayed AV conduction as a specific feature of patients with enthesitic SpA, supporting the hypothesis that in these subjects musculoskeletal and cardiac involvement are strictly interconnected. Our findings underscore the potential of incorporating PR/PRc-segments into routine ECG evaluation as simple and sensitive tools for the early detection of SpA patients at higher risk for severe AV-block, in whom a tighter control of disease activity may be requested and administration of drugs negatively affecting AV-conduction contraindicated.
Keywords: Cardiovascular system; Descriptive Studies; Diagnostic test
References:
1. Bengtsson K, Forsblad-d'Elia H, Lie E et al. Risk of cardiac rhythm disturbances and aortic regurgitation in different spondyloarthritis subtypes in comparison with general population: a register-based study from Sweden. Ann Rheum Dis 2018;77:541-548.
2. Sherlock JP, Joyce-Shaikh B, Turner SP et al. IL-23 induces spondyloarthropathy by acting on ROR-γt+ CD3+CD4-CD8- entheseal resident T cells. Nat Med 2012;18:1069-76.
3. Soliman EZ, Rautaharju PM. Heart rate adjustment of PR interval in middle-aged and older adults. J Electrocardiol 2012;45:66-9.
4. Soliman EZ, Cammarata M, Li Y. Explaining the inconsistent associations of PR interval with mortality: the role of P-duration contribution to the length of PR interval. Heart Rhythm 2014;11:93-8.



NATURAL LANGUAGE PROCESSING IDENTIFIES COMORBIDITIES AND PHENOTYPES ASSOCIATED WITH TREATMENT LONGEVITY IN PSORIATIC ARTHRITIS

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Background: Patients with psoriatic arthritis (PsA) present with heterogeneous clinical phenotypes and exhibit variable responses to innovative treatments, including biologic and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs). Evidence regarding treatment trajectories and predictors of therapeutic retention remains limited.
Objective: To identify factors associated with the 12-month retention of newly prescribed b/tsDMARDs in PsA patients using a natural language processing (NLP)-assisted approach.
Methods: For all patients diagnosed with PsA who attended our center between January 2019 and February 2024, the report corresponding to the first visit in which a new b/tsDMARD was prescribed was retrieved for analysys, regardless of the line of treatment. We developed a Bidirectional Encoder Representations from Transformers (BERT)-based NLP model to extract demographic and clinical data from the outpatient records, along with information on prescribed therapies. Treatment data were matched with dispensing records from the Hospital Pharmacy database to verify which medications were prescribed, discontinued, or switched during the 12-month follow-up. Model outputs were reviewed by clinicians to validate the extracted data. The resulting features were used to build a predictive model for 12-month drug retention using binary logistic regression. The model was trained and evaluated using a train-test split and k-fold cross-validation. Performance metrics were computed on the train and test sets, and logistic regression analyses were used to estimate odds ratios (ORs) for predictors of both retention and discontinuation.
Results. A total of 413 PsA cases (52% female; mean age 52 ± 12 years) initiating a newly prescribed b/tsDMARD were included. Reported PsA domain distribution included peripheral arthritis (90%), axial disease (15%), dactylitis (18%), enthesitis (18%), skin psoriasis (61%), and inflammatory bowel disease (2%). Extracted comorbidities encompassed depression-anxiety (7%), diabetes mellitus (10%), obesity (9%, defined as BMI ≥ 30 kg/m²), and smoking (14%).
Newly initiated therapies included anti-TNF agents (53%), anti-IL-17 (22%), anti-IL-23 (6%), JAK-inhibitors (2%), and apremilast (19%). At 12 months, 306 patients (73.4%) were still receiving the initial treatment with retention rates being similar for anti-TNFs (78%), anti-IL-17 (79%), anti-IL-23 (83%), and JAK inhibitors (86%), but significantly lower for apremilast (53%; p < 0.001).
Treatment retention was not associated with specific disease domains or comorbidities but was influenced by gender. Specifically, female patients were 65% of those who discontinued therapy and 48% of patients who retained it (p = 0.003). This trend remained significant among patients treated with anti-TNF agents (female proportion: 64% of discontinuers vs. 42% of retainers; p = 0.014), but not with anti-IL-17 or anti-IL-23 therapies.
The logistic regression model showed good performance in predicting treatment retention, with recall scores of 0.76 and 0.74, precision of 0.83 and 0.83, and F1-scores of 0.79 and 0.77 in the train and test sets, respectively. However, performance was lower for predicting discontinuation, potentially due to class imbalance. The overall model accuracy ranged from fair to good, with AUC-ROC values between 0.56 and 0.73.
Complementary logistic regression focusing on treatment discontinuation confirmed female sex as a significant risk factor (OR 2.5, 95% CI 2.0–4.7), whereas older age (OR 0.8, 95% CI 0.6–0.97) and diabetes mellitus (OR 0.35, 95% CI 0.1–0.7) were associated with treatment persistence (Figure). Discontinuation risk was higher with apremilast (OR 10, 95% CI 6.4–109), anti-TNF (OR 5, 95% CI 2.6–43), and anti-IL-17 agents (OR 4, 95% CI 1.8–34), but not with anti-IL-23.
When stratifying according to treatment classes, anti-TNF discontinuation was more frequent in females (OR 2.3, 95% CI 1.2–4.3), and less likely in older patients (OR 0.6, 95% CI 0.4–0.97) and in case of sacroiliitis (OR 0.15, 95% CI 0.0–0.5). For anti-IL-17 therapies, dactylitis (OR 0.1, 95% CI 0.0–0.6), obesity (OR 0.05, 95% CI 0.0–0.3), and anxiety-depression (OR 0.05, 95% CI 0.0–0.4) appeared to be protective factors against treatment discontinuation.
Conclusions. The 12-month treatment retention in PsA is significantly influenced by sex, age, metabolic and neuropsychiatric comorbidities, and selected clinical domains. Our findings were generated through a novel NLP-based analytical framework and underscore the potential of real-world data extraction from unstructured medical records to discover predictors of treatment outcomes in internal medicine and rheumatologic diseases.

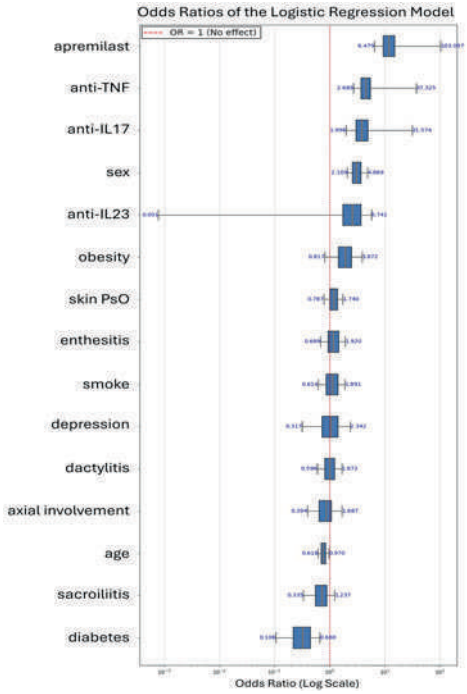

Figure. Odds ratios (Log scale) of the variables evaluated for treatment discontinuation in the logistic regression.

BIOMARKERS OF GUT EPITHELIAL DAMAGE, MICROBIAL TRANSLOCATION, AND INNATE IMMUNE ACTIVATION CHARACTERIZE PATIENTS WITH AXIAL PSORIATIC ARTHRITIS FROM PSORIASIS PATIENTS: SOLUBLE BIOMARKER ANALYSIS INSIGHTS FROM THE ATTRACT STUDY

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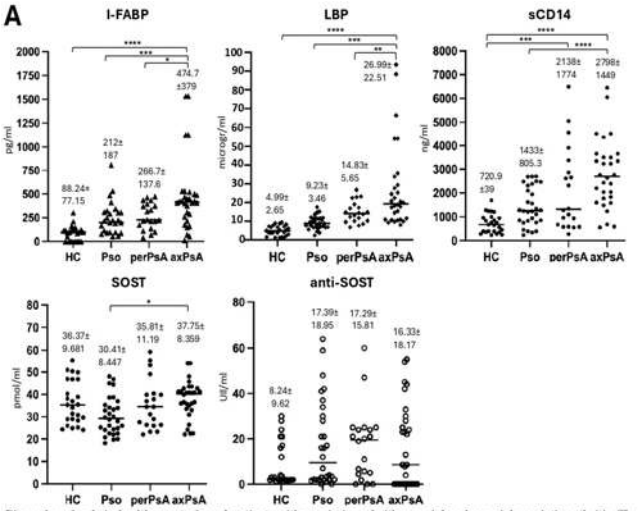
Background: Increasing evidence suggests that axial spondyloarthritis (axSpA) may be marked by intestinal damage, leading to the translocation of bacterial products into the bloodstream, potentially influencing the innate immune system.Recently, our group conducted a cross-sectional study (ATTRACT) that, through a screening strategy in 365 patients with psoriasis (PsO), found 29% with axial Psoriatic Arthritis (PsA).Considering that abnormal intestinal permeability, microbial translocation and presence of anti-SOST/IgG have been described in axSpA patients, we hypothesised that these mechanisms of innate immunity activation originating from gut epithelial impairment could modulate the expression of pathways implicated in the inflammation of axPsA patients.
Objectives: In this study, we aimed to describe the role that intestinal fatty acid binding protein (I-FABP), lipopolysaccharide-binding protein (LBP), soluble CD14 (sCD14), sclerostin (SOST), and anti-SOST/IgG plasma levels may have as putative diagnostic biomarkers of inflammation in patients with peripheral or axial psoriatic arthritis naïve to biologic DMARDs.Secondly, we aimed to analyse the correlations between these biomarkers and our patient cohort's clinical characteristics and disease activity.
Methods: The cohort studied within ATTRACT has been fully described previously. Plasma was collected from 30 PsO, 20 perPsA, 30 by axPsA naïve patients, and 25 healthy controls (HCs). I-FABP, LBP, sCD14, and SOST plasma levels were detected using commercial ELISA kits. Anti-SOST serum levels were assayed using a peptide-binding ELISA described elsewhere, respectively.
Results: Axial PsA patients show higher levels of gut epithelial damage, microbial translocation and innate immune activation than those with Pso and HCs. AxPsA patients show significantly higher plasma levels of I-FABP, LBP, and sCD14 than PsO patients and HCs and of I-FABP and LBP than perPsA patients. In comparison, perPsA patients show significantly higher plasma levels than HCs only of the sCD14. For discriminating between axPsA and Pso patients, with a cut-off of 306 pg/ml, I-FABP has a sensitivity of 70% and a specificity of 76.7% (AUC 0.7589, $p < 0.0006$), with a cut-off of 11.597 microgram/ml LBP has a sensitivity of 70% and a specificity of 77% (AUC 0.8767, $p < 0.0001$), and with a cut-off of 1991 ng/ml sCD14 has a sensitivity of 70% and a specificity of 70% (AUC 0.7933, $p < 0.001$).Contrary to previous data in axSpA patients, SOST and anti-SOST plasma levels were similar in all three groups of patients and HCs, except for significantly higher SOST levels in axPsA than in PsO patients.**Gut epithelial damage, microbial translocation and innate immune activation correlate in patients with Pso and PsA**Significant positive correlations were demonstrated between *i)* I-FABP and LBP with sCD14, SOST, and CRP; *ii)* LBP with Disease Activity Index for Psoriatic Arthritis (DAPSA), Axial Spondyloarthritis Disease Activity Score (ASDAS), and duration of back pain and arthralgias; *iii)* sCD14 with ASDAS. SOST was strongly positively correlated with all the biomarkers, clinical disease activity, duration of back pain and arthralgias, and presented a strong inverse correlation with anti-SOST.**CONCLUSIONS**-This post hoc analysis of biosamples from the ATTRACT study reveals significant elevations of gut epithelial damage, microbial translocation, and innate immune activation biomarkers in patients with axPsA compared to those with PsO and healthy controls. The elevated levels of I-FABP and LBP suggest a plausible link between intestinal damage, microbial translocation and clinical disease activity in axPsA, offering a practical approach for their screening in routine medical practice, offering a valuable alternative to complex genetic analyses.



Biomarkers levels in healthy controls and patients with psoriasis and either peripheral or axial psoriatic arthritis. The figure presents the results of the biomarkers' ELISAs from healthy controls (n=25) and patients in the ATTRACT cohort [4] with psoriasis (n=30), as well as those with peripheral (n=20) or axial (n=30) psoriatic arthritis. The median results ± the SD of each group are represented in each graph. Statistical analyses were performed using Stata software, with the ANOVA test corrected using the Bonferroni post-hoc test. P-values are shown if significance: *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001. **Abbreviations.** ELISA: Enzyme-Linked Immunosorbent Assay; ATTRACT: Axial Psoriatic Arthritis Screening Ancona Italy; HC: healthy controls; Pso: patients diagnosed with psoriasis; perPsA: patients diagnosed with psoriatic arthritis involving peripheral sites; axPsA: patients diagnosed with psoriatic arthritis involving axial sites (with or without peripheral involvement); LBP: LPS-binding protein; sCD14: soluble CD14; I-FABP: intestinal fatty acid-binding protein; SOST: sclerostin; anti-SOST: anti-sclerostin IgG antibodies.

	LBP	sCD14	I-FABP	SOST	Anti-SOST	DAPSA	ASDAS	PASI	CRP	Yrs BP	Yrs PP	NAPSI
LBP		0.408**	0.048	0.345*	0.024	0.361**	0.329**	0.229	0.484***	0.347**	0.507***	0.215
sCD14	0.408**		0.285*	0.270*	-0.286*	0.067	0.373**	-0.077	0.255*	0.194	0.190	0.115
I-FABP	0.048	0.285*		0.280*	-0.182	0.121	0.111	0.081	0.204*	0.194	0.064	0.068
SOST	0.345**	0.270*	0.280*		-0.393***	0.348***	0.433***	0.332**	0.432***	0.252*	0.345**	0.116
Anti-SOST	0.024	-0.286*	-0.182	-0.393***		-0.082	-0.076	-0.034	0.032	-0.085	-0.125	-0.260
DAPSA	0.361**	0.067	0.121	0.348***	-0.082		0.733***	-0.046	0.339**	0.184	0.418***	0.052
ASDAS	0.329**	0.373**	0.111	0.433***	-0.076	0.733***		0.054	0.334**	0.143	0.369**	0.193
PASI	0.229	-0.077	0.081	0.332**	-0.034	-0.046	0.054		0.366**	0.120	0.161	0.473**
CRP	0.484***	0.255*	0.204*	0.432***	0.032	0.339**	0.334**	0.366**		0.122	0.260*	0.125
Yrs BP	0.347**	0.194	0.194	0.252*	-0.085	0.184	0.143	0.120	0.122		0.391**	0.237
Yrs PP	0.507***	0.190	0.064	0.345**	-0.125	0.418***	0.369**	0.161	0.260*	0.391**		0.016
NAPSI	0.215	0.115	0.068	0.116	-0.260	0.052	0.193	0.473**	0.125	0.237	0.016	

Correlations between biomarkers and clinical characteristics of the ATTRACT's patient cohort. The table shows the results of the correlations between biomarkers and the clinical characteristics of ATTRACT's cohort patients with psoriasis and peripheral or axial psoriatic arthritis. Statistical analyses were carried out using "Stata" software, Pearson's chi-squared test and ANOVA test with Bonferroni posthoc test. P-values are shown in bold if <0.05, indicating significance. *p<0.05; **p<0.01; ***p<0.001. **Abbreviations**. ATTRACT: Axial psoriaTic arThritis scReening AnCona iTaly; LBP: LPS-binding protein; sCD14: soluble CD14; I-FABP: intestinal-fatty acid binding protein; SOST: sclerostin; anti-SOST: anti-sclerostin IgG antibodies; DAPSA: Disease Activity in Psoriatic Arthritis; ASDAS: Ankylosing Spondylitis Disease Activity Score with C-reactive protein; PASI: Psoriasis Area Severity Index; CRP: C-reactive protein; Yrs BP: years of back pain symptoms; Yrs PP: years of peripheral pain, with or without signs of joint inflammation; NAPSI: Nail Psoriasis Severity Index.

SELF-REPORTED OROPHARYNGEAL DYSPHAGIA AND SWALLOWING-RELATED QUALITY OF LIFE IN PEOPLE WITH SYSTEMIC SCLEROSIS: PRELIMINARY RESULTS OF A CROSS-SECTIONAL STUDY

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Background: Swallowing impairment due to esophageal involvement is frequently diagnosed in patients with systemic sclerosis (SSc). Proximal or oropharyngeal dysphagia (OD) may be secondary to oral muscle weakness, reduced range of chewing movements, poor saliva production, uncoordinated pharyngeal contractions, loss of teeth, microstomia, or anatomic anomalies causing obstruction. We previously showed that proximal swallowing abnormalities may involve up to 50% of patients1,2.Despite its prevalence, the characteristics of self-reported oropharyngeal dysphagia and its impact on quality of life (QoL) in SSc patients have not been studied.

Aim: In the present study, we aim to assess the prevalence and characteristics of self-reported oropharyngeal dysphagia and evaluate its impact on QoL using different validated questionnaires in a well-characterized cohort of SSc patients.

Methods: We recruited 60 consecutive SSc patients from the Scleroderma Unit of Marche University Hospital, Ancona, Italy (EUSTAR Center 034). Every participant completed the Italian version of three questionnaires: the Eating Assessment Tool-10 (EAT-10), the Swallowing Quality of Life Questionnaire (SWAL-QoL) and the Dysphagia Handicap Index (DHI). The EAT-10 has 10 items, each question ranges from 0 (no problem) to 4 (severe problem). EAT-10 score of 3 or greater is abnormal. The SWAL-QoL is used to assess the impact of swallowing problems on QoL, with 44 items exploring different aspects grouped into 11 lifestyle subscales. With 25 items, the DHI investigates the physical, functional, and emotional impacts, with range from 0 (no impact) to 100 (full impact), that OD may have on the patient's life and provides a self-evaluation of OD severity, with range from 1 (normal) to 7 (severe). The total scores of EAT-10, DHI and SWAL-QoL and patients' clinical characteristics were summarized using descriptive statistics. Statistically significant differences between patients self-reporting dysphagia symptoms (EAT-10 score ≥3) and non-dysphagic patients were evaluated using non-parametric tests and Chi-squared test as appropriate. Correlations between variables was estimated using the Spearman correlation coefficient. Agreement between self-reported dysphagia by EAT-10 and documentation of proximal dysphagia in medical records was assessed by Cohen's kappa.

Results: Patients' baseline characteristics and main study results are shown in the Table. Among 60 SSc patients, 30 (50%) had an EAT-10 score ≥3. Patients with OD were more likely to have esophageal involvement (78% vs 34%, p=0.001), reflux and use proton pump inhibitors (71% vs 40% and 85% vs 56%, p=0.016 and 0.015, respectively) and self-reported xerostomia (74% vs 43%, p = 0.019). They also have a higher burden of disease activity (mRSS and EUSTAR-AI, p<0.05) and poorer functioning and QoL. The median SWAL-QoL and DHI scores were all significantly lower or higher, respectively, in dysphagic patients. There was a very strong correlation between all the sub-scores of the three questionnaires. EAT-10 was moderately correlated with GIT2.0-10 (ρ 0.75), measures of physical functioning (Cochin hand function scale ρ 0.63, HAQ ρ 0.67) and global assessment (PtGA and PhGA ρ 0.54 and 0.45, respectively), but not with SSc disease activity. Importantly, EAT-10 showed a moderate correlation with SF-36 sub-scales, including limitations due to physical role and pain (ρ -0.54 and -0.53, respectively) and limitations due to emotional problems and mental health (ρ -0.43 and -0.36, respectively). Significant correlations between DHI and SWAL-QoL subscores and CHFS, HAQ, PtGA and PhGA and SF-36 were also observed. Agreement between self-reported dysphagia by EAT-10 and proximal dysphagia on medical records was excellent (Cohen's kappa 0.93, p<0.0001).

Conclusion: Proximal dysphagia involves half of SSc patients and is associated with disease burden and poor QoL. EAT-10, DHI, SWAL-QoL are valid and reliable instruments to detect self-reported OD in SSc patients. Further studies should address the correlation between self-reported and instrumental assessment and the impact of speech language therapy on swallowing impairment.

References: 1. J Scleroderma Relat Disord. 2024 Jun;9(2):143-153. 2. Clin Exp Rheumatol. 2019 Jul-Aug;37 Suppl 119(4):108-114.

METABOLIC SYNDROME AND CARDIOVASCULAR-KIDNEY-METABOLIC HEALTH: EVALUATION OF PREDICTIVE RISK FACTOR FOR MORTALITY IN SYSTEMIC SCLEROSIS

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Rationale: Metabolic syndrome (MetS) is a cluster of abnormalities including diabetes, visceral adiposity, dyslipidemia and systemic arterial hypertension. Insulin resistance and deficit of the lipoprotein lipase are responsible of the increased risks of developing diabetes and central obesity while sympathetic nervous system, hypersensitivity to the salt and increased cation transport cause systemic arterial hypertension. These factors determine an important cause of the current global cardiovascular diseases (CVD), representing the leading cause of death worldwide. In recent decades, several classifications for the MetS have been proposed. Recently, a new syndrome called the "Cardiovascular-kidney-metabolic" (CKM) syndrome was identified, to determine patients at high cardiovascular and metabolic risk. A limited number of studies have investigated MetS in patients with systemic sclerosis. The aim of the study was to evaluate if MetS and CKM assessment may predict mortality in SSc patients during a 10-year follow-up.

Methods: Ninety consecutive SSc patients fulfilled the 2013 ACR/European League Against Rheumatism criteria were enrolled to complete this retrospective study in 10 years follow-up. According to guidelines chronic kidney disease (CKD) was defined as a decreased glomerular filtration rate (GFR) of <60 mL/min/1.73 m2 for at least 3 months. Clinical assessment, anthropometric, biochemical data and urinalysis were recorded in all patients at the time of enrollment. The diagnosis of MetS was made according to the criteria of the National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATP-III), NCEP-R and the International Diabetes Federation (IDF). CKM classification is characterized by stages: stage 0 (no CKM risk factors); stage 1 (excess or dysfunctional adiposity); stage 2 (metabolic risk factors and kidney disease); stage 3 (subclinical CVD in CKM syndrome); and stage 4 (CVD in CKM syndrome with and without kidney failure)

Results: We collected data of 90 SSc patients (females 85.6 %) with a median age of 56.5 years (IQR 45; 64); 51.1 % were diffuse cutaneous SSc. The prevalence of MetS according to the different classifications was: 11.1 % for NCEP-ATPIII, 14.4 % for NCEP-R and 14.4 % for IDF. For the CKM staging the 55.6 % of patients was stage 0, the 10 % was stage 1, the 32.2 % was stage 2 and the 1.1 % both were 3 and stage 4. Mortality was observed in 21 (23.3 %) SSc patients. Kaplan-Meier curves showed that overall survival probability was shorter in patients with MetS according to NCEP-ATPIII ($p < 0.001$), NCEP-R ($p < 0.05$) and IDF ($p < 0.05$) compared to patients without MetS; while the overall survival was similar in patients with CKM 0–1 and patients with CKM 2-3-4. Cumulative incidence rate of SSc-related death was similar in patients with MetS according to NCEP-ATPIII, NCEP-R and IDF compared to patients without MetS and in patients with CKM 0–1 and patients with CKM 2-3-4. Cumulative incidence rate for all-cause mortality not-SSc related was higher in patients with MetS according to NCEP-ATPIII ($p < 0.001$), NCEP-R ($p < 0.01$) and IDF ($p < 0.01$) compared to patients without MetS; while the cumulative incidence rate all-cause mortality not-SSc related was similar in patients with CKM 0–1 and patients with CKM 2-3-4.

Conclusions: Patients with SSc and MetS exhibited a higher rate of death from causes unrelated to SSc. Thus, the assessment of MetS in SSc patients, irrespective of the diagnostic criteria used, should be integrated into their routine clinical evaluation to provide a more comprehensive risk assessment.

TAKAYASU ARTERITIS AND GIANT CELL ARTERITIS: RESULTS FROM A CROSS-SECTIONAL STUDY OF 84 ITALIAN PATIENTS

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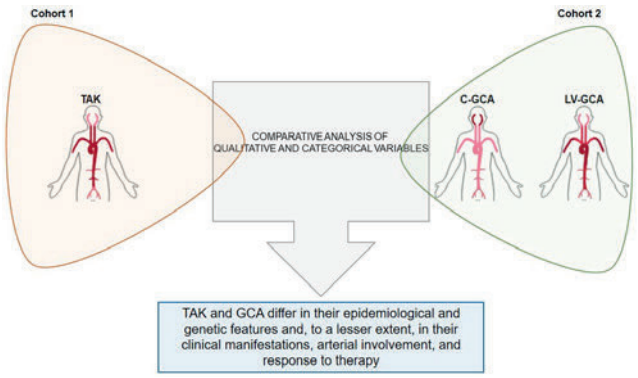
Background: Whether Takayasu arteritis (TAK) and giant cell arteritis (GCA), the most common forms of large-vessel vasculitis (LVV), are distinct clinical entities or different manifestations of the same disease is an ongoing debate. This study analyzes and compares the clinical manifestations, imaging characteristics, and diagnostic and therapeutic features of TAK and GCA in a longitudinal cohort of patients recruited from four Italian centers.
Methods: The study population comprised 59 patients with TAK and 25 with GCA [7 with cranial-GCA (C-GCA) and 18 with large vessel-GCA (LV-GCA)] who were diagnosed between January 2014 and July 2024. Most (75%) were followed up for at least 60 months. Previous studies comparing TAK and GCA are considered in the Discussion.
Results: In TAK patients, the time to diagnosis following the onset of symptoms was longer ($P = 0.025$), the prevalence of females higher ($P = 0.003$), and the presence at diagnosis of constitutional symptoms ($P = 0.008$), cardiovascular signs ($P < 0.001$), and renal involvement ($P = 0.030$) more frequent than in GCA patients. In GCA patients, the sex distribution was equal. However, in addition to the cranial and constitutional symptoms associated with the cranial and large vessel forms of the disease, respectively, the prevalence of polymyalgia rheumatica ($P < 0.001$), hypertension ($P < 0.001$), diabetes mellitus ($P = 0.020$), and osteoporosis ($P = 0.030$) was higher in GCA than in TAK patients. Vascular involvement was seen in both groups, with common carotid artery involvement more frequent in GCA patients ($P = 0.020$), and involvement of the aortic arch ($P = 0.020$) and mesenteric ($P = 0.030$) and renal ($P = 0.008$) arteries more frequent in TAK patients. Glucocorticoids were administered at a higher dose ($P = 0.002$) and combined more frequently with immunosuppressants in TAK patients. Among GCA patients, 75% received tocilizumab as second-line treatment. The two groups did not significantly differ with respect to long-term remission, but relapse was more frequent in TAK patients.
Conclusions: Despite their phenotypic similarities, TAK and GCA differ in their epidemiological and genetic features and, to a lesser extent, in their clinical manifestations, arterial involvement, and response to therapy. Our data therefore indicate that TAK and GCA are clinically distinct, requiring disease-specific approaches in their diagnosis and management.



INTEGRATIVE PROFILING OF SYSTEMIC SCLEROSIS PATIENTS THROUGH A CLUSTERING APPROACH BASED ON AUTONOMIC NERVOUS SYSTEM REGULATION, INFLAMMATORY BIOMARKERS, AND FRAILTY ASSESSMENT

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Systemic Sclerosis (SSc) is a rare autoimmune disease characterized by microvascular dysfunction, autoantibody production, extracellular matrix remodeling and collagen deposition, leading to fibrosis that affects both skin and internal organs. Given its multisystem involvement, a holistic approach is therefore essential to comprehensively assess patient health.
For this purpose, we conducted a cross-sectional study on a cohort of patients affected by SSc from the Scleroderma Unit of the Department of Internal Medicine, Policlinico Hospital, Milan. Patients with both limited cutaneous (lcSSc) and diffuse cutaneous (dcSSc) subsets, as well as patients with very early diagnosis of systemic sclerosis (VEDOSS), were enrolled. Electrocardiogram (ECG) and respiration signals were recorded at rest in clinostatic position for 10 minutes. Heart rate variability analysis was conducted to assess cardiovascular autonomic control as a proxy for the autonomic nervous system (ANS) evaluation. In particular, linear power spectrum analysis and nonlinear symbolic analysis were performed.Through the first one, we calculated total power (TP) as an index of overall heart rate variability, along with spectral power in the low-frequency (LF, 0.04–0.15 Hz) and high-frequency (HF, 0.15–0.40 Hz) bands, representing sympathetic and parasympathetic modulation, respectively. The LF/HF ratio was also derived to evaluate sympathovagal balance, with higher values indicating sympathetic predominance. In parallel, nonlinear symbolic analysis was used to assess cardiac autonomic modulation by measuring the percentage of 0V patterns (indicative of sympathetic modulation) and the percentage of 2UV and 2LV patterns (indicative of vagal modulation).
Blood samples were collected in order to assess inflammatory biomarkers through a next generation ELISA test. In particular, the systemic pro-inflammatory biomarkers Interleukin(IL)-6, Tumor necrosis factor(TNF)-α, soluble Triggering Receptor Expressed on Myeloid cells (sTREM)-1 and the anti-inflammatory biomarker IL-10 were assayed. Additionally, Electronic Health Records and the clinical history of the patients were checked to quantify the frailty according the Frailty Index developed by the Canadian Scleroderma Research Group that combines 44 items regarding the most critical aspect involved in the pathology and returns a frailty score between 0 and 1. For the calculation of this index, 4 main aspects were considered: disease-specific symptoms (e.g., presence of digital ulcers, gastrointestinal involvement), patient comorbidities, health-related quality of life (e.g., mood, sleep quality) and physical functionality. We finally performed a clustering analysis through k-means algorithm in order to profile the population through a division into groups based on cardiovascular autonomic control, inflammatory profile and state of frailty. Data were transformed into standardized values (mean = 0, SD = 1) for clustering analysis and differences between groups were explored using t-tests or one-way ANOVA (with Bonferroni post hoc comparisons).
A total of 71 SSc patients (mean age: 57 years; disease duration: 14 years; 92% female; 80% lcSSc, 16% dcSSc, 4% VEDOSS) were enrolled in the study. The mean frailty index of the analysed population was 0.30. Most of the patients were characterized as frail ($0.21 < FI < 0.45$, 59%), followed by pre-frail patients ($0.1 \leq FI \leq 0.21$, 24%), most frail ($FI \geq 0.45$, 10%) and non-frail ($FI < 0.1$, 7%). K-means clustering using standardized variables (TP, LF/HF, 0V%, 2LV%, IL-6, IL-10, and FI) revealed two distinct patient groups. Cluster 1 (n = 34) showed reduced HRV (lower TP), increased sympathetic dominance (higher LF/HF and 0V%, lower 2LV%), heightened inflammatory markers (IL-6 and IL-10), and higher frailty compared to Cluster 2 (N° of patients = 37). The two groups did not differ in age (p=0.648), disease duration (p=0.240), or sex (p=0.675), though SSc subtype distribution differed, with Cluster 1 having mainly lcSSc (74%) and dcSSc (26%) and Cluster 2 including both lcSSc (87%) and dcSSc (5%) and VEDOSS (8%) patients. Thus, Cluster 1 appears to represent a more compromised subgroup with autonomic imbalance, higher inflammation, and greater frailty.
Our findings suggest that is important to consider a multiparametric assessment when it comes to profiling SSc patients. The evaluation of ANS profile,

inflammation, and frailty could support the development of more personalized care strategies and risk stratification tools in SSc patient management.

CAN SPECKLE TRACKING GLOBAL LONGITUDINAL STRAIN PREDICT THE OUTCOME IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHY?

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Introduzione: Col termine miopatia infiammatoria si identifica un gruppo eterogeneo di disordini immunomediati sistemici dalle caratteristiche cliniche peculiari. Tra gli organi più frequentemente coinvolti vi è il muscolo scheletrico, con una presentazione clinica tipica dominata da debolezza e riduzione della forza prevalentemente a carico dei distretti prossimali. Anche il cuore, trattandosi di tessuto muscolare, può essere interessato dando luogo a manifestazioni cliniche più severe. Sebbene il coinvolgimento cardiaco possa inizialmente presentarsi in modo subclinico, è possibile un'evoluzione nel tempo dove l'eventuale concomitanza di alterazioni morfo-strutturali e/o anomalie della conduzione possono condurre verso lo sviluppo di insufficienza cardiaca e quindi costituire un'importante causa di mortalità. In un precedente studio, si è dimostrato come i pazienti affetti da miosite abbiano una significativa riduzione del Global Londitudinal Strain (GLS) rispetto ai controlli sani. Il GLS, parametro ecocardiografico che misura la deformazione contrattile miocardica, si è rivelato sensibile nel rilevare alterazioni della funzione sistolica anche in assenza di disfunzione ventricolare sinistra conclamata, suggerendo la presenza di un danno subclinico precoce.Questo lavoro si è concentrato sull'analisi della deformazione contrattile miocardica nella nostra coorte di pazienti con miopatie infiammatorie per indagare il potenziale ruolo del GLS come indicatore prognostico di eventi cardiovascolari maggiori e mortalità.
Metodi: Sono stati considerati 41 pazienti (30F/11M, età 59 ±18) seguiti presso la SOD Clinica Medica dell'AOU delle Marche, con diagnosi certa di miopatia infiammatoria con un timing di follow-up di 8 anni (4-11 anni). La popolazione in studio non aveva malattia cardiaca manifesta ed è stata eseguita una valutazione laboratoristica e clinica (CPK, MMT8, MITAX, MDI), ECG, ecocardiogramma con calcolo del GLS (basale e al follow-up) e sono stati considerati anche i fattori di rischio cardiovascolare al tempo zero (Tab. 1).
Risultati: Durante il follow-up (FU) si è osservata una progressiva riduzione della frazione d'eiezione del ventricolo sinistro (VS) (baseline LVEF: 64.53% vs FU LVEF: 60.9%, p=0.03) e del GLS del VS (baseline LGLS: -19.6% vs FU LGLS: -16.6, p=0.04), insieme ad un aumento dei volumi atriali (iLAV: +8 cm2/m2; p=0.02; iRAV: +10 cm2/m2; p=0.01) e delle pressioni di riempimento stimate (E/e': +1.4, p=0.01). Il GLS destro non era significativamente associato all'endpoint primario. Un LGLS > -16% correlava con l'endpoint primario, con una sensibilità dell'80% e una specificità del 67% (AUC 0,74). La sopravvivenza stimata dall'endpoint primario è stata dell'85% per il gruppo LGLS normale e del 35% per il gruppo con LGLS alterato.
Conclusioni: Nelle miopatie infiammatorie il coinvolgimento cardiaco può manifestarsi fino al 70% dei casi in modo subclinico, rappresentando un'importante causa di mortalità. Il GLS è un indicatore precoce di disfunzione cardiaca subclinica in grado di predire eventi cardiovascolari avversi e il rischio di morte in modo più sensibile del dato relativo alla frazione di eiezione. In conclusione, lo studio evidenzia come in questi pazienti vi sia fin dall'esordio un valore di GLS alterato, pur in presenza di una FE nella norma. Inoltre, il GLS peggiora nonostante la malattia di fondo appaia sotto controllo, dato il miglioramento della forza muscolare e il valore della CPK. Il monitoraggio attivo dei pazienti con miosite mediante GLS potrebbe permettere interventi terapeutici tempestivi riducendo il rischio di complicanze cardiache o mortalità.

Variabili	Totale (n.41)
Età	59.0 ± 18.3
F:M	30 (75%):11 (25%)
BMI (Kg/m2)	24.5 ± 4.6
Polimiosite	30 (75%)
Dermatomiosite	11 (25%)
Ipertensione	29 (70%)
Dislipidemia	24 (58%)
Diabete mellito	4 (10%)
Malattia coronarica	0 (0%)
Malattia vascolare carotidea	2 (5%)
Precedente ICTUS/TIA	2 (5%)
Fibrillazione atriale	3 (7%)

LONG-TERM OUTCOMES OF PATIENTS WITH TAKAYASU ARTERITIS IN THE ERA OF BIOLOGICAL AGENTS: A MULTICENTER STUDY

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Background: Takayasu arteritis (TAK) is a rare, chronic large-vessel vasculitis affecting the aorta and its major branches, predominantly in young adults. Given its chronic course and early onset, long-term outcome data, particularly in the era of biologic therapies, remain limited.
Objective: To evaluate long-term clinical outcomes, vascular progression, therapeutic strategies, and complication profiles in TAK patients followed for ≥60 months, with a focus on the impact of biologic agents.
Methods: A retrospective multicenter cohort study was conducted across four institutions (two in Italy, one in India, one in Turkey). Medical records of patients with a clinical diagnosis of TAK and ≥60 months of follow-up were reviewed. Data collected included baseline demographics, clinical and angiographic features, treatment regimens (glucocorticoids [GCs], conventional and biologic DMARDs), vascular interventions, and disease- or therapy-related complications. Regression models were used to identify predictors of GC discontinuation, vascular procedures, and infection risk.
Results: A total of 119 TAK patients (84% female, mean age at diagnosis: 31 ± 23 years) were included, with a median follow-up of 122 months. At baseline, the most frequently involved vessels were the subclavian (71%), carotid (66%), and descending thoracic aorta (54%). Advanced vascular damage was present in 40% of patients, and 16% had already undergone vascular procedures at baseline. GCs were initiated in 94% of patients, but sustained discontinuation was achieved in only 34%, after a median of 49 months; no predictors of GC withdrawal were identified. csDMARDs were used in 94% and bDMARDs in 71% of patients (median initiation: 17 months). The most common bDMARDs were TNF inhibitors (69%) and tocilizumab (23%), with 87% used in combination with csDMARDs.During follow-up, 21% of patients developed new arterial occlusions, 6% new aneurysms, and 19% required vascular procedures. Baseline involvement of the abdominal aorta, celiac trunk, superior mesenteric artery, and renal arteries significantly in-

creased the risk of later interventions. Infections occurred in 12% of patients (bacterial, fungal, mycobacterial), and varicella-zoster virus (VZV) reactivation in 6%. Older age at onset was associated with higher infection risk ($p = 0.003$). Other complications included hypertension (13%), ischemic heart disease (6%), diabetes (3%), fractures (3%), stroke (2%), and pulmonary embolism (2%). Two patients (2%) died of unknown causes.
Conclusions: Despite widespread use of biologic therapies, sustained GC withdrawal was achieved in only one-third of patients, often after prolonged treatment. Vascular complications-particularly involving the abdominal vessels-remain a major concern and frequently require interventional procedures. Long-term morbidity in TAK is driven by cardiovascular and infectious complications, the latter being more frequent in older individuals.

POSTER

PRIMITIVE HYPERPARATHYROIDISM: CASE REPORT

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Introduction: The authors present a case report of primary hyperparathyroidism in a 78 aa woman came to our attention by state stupor and severe hypercalcemia.
Case report: The authors present a case report of primary hyperparathyroidism in a 78 aa woman came to our attention by state stupor and severe hypercalcemia. In history we record BBS, high blood pressure, multi-infarct encephalopathy with cognitive impairment
During the stay the following tests are performed:
It undertakes moisturizing therapy, phosphonates, cortisone, diuretici.Si monitor during hospitalization of serum calcium values, phosphorus, PTH until normalization predi mission. It undertakes to treatment with cinacalcet discharge cp 30 cp 1 mg / day.
Discussion: Current international guidelines focus on normalizing serum calcium by surgery and reducing the impact of PHPT on target tissues with preservation of renal and skeletal health. The impact of a nonsurgical approach to lowering serum calcium is thus an important consideration in the medical management of PHPT among those individuals with clinically important hypercalcemia who are not candidates for parathyroid surgery. Thus, cinacalcet would be a useful treatment option for subjects who have hypercalcemia and have failed surgery or are unable to proceed with surgery. In addition, in subjects with multiple endocrine neoplasia (MEN), cinacalcet has been shown to be useful in delaying surgery, if necessary, while maintaining normocalcemia. The dose regimens of cinacalcet required to lower serum calcium in MEN1-associated PHPT appear to be similar to those required in sporadic PHPT. Medical management in PHPT also includes correction of vitamin D insufficiency with cholecalciferol in order to achieve a 25-hydroxy vitamin D level of at least 50 nmol/l. Supplementation requires monitoring of both serum and urine calcium to ensure that hypercalcemia and hypercalciuria do not worsen. Bisphosphonates (including alendronate) may provide skeletal protection and are a medical option in the management of PHPT. Treatment with alendronate in a 24-month trial for subjects with asymptomatic PHPT resulted in improvements in bone mineral density at the lumbar spine in comparison with placebo. Reductions in bone remodeling were observed. However, serum calcium and PTH remained elevated and were unchanged over the 24-month study period. Combination therapy with both alendronate and cinacalcet has been found to both lower serum calcium and provide skeletal protection. Vitamin D inadequacy should be corrected in patients with PHPT. Vitamin D inadequacy has been associated with increased weight of parathyroid adenomas and higher levels of serum calcium and PTH. Neither vitamin D nor bisphosphonates are approved to treat hypercalcemia in patients with PHPT. Recent studies of HRQOL in patients with PHPT concluded that neurological features appear to be relate to preoperative levels of serum calcium. Improvements in HRQOL were observed following parathyroidectomy. Furthermore, in a randomized study, improvements in two domains on SF-36 and favorable trends on other measures were noted in surgical patients compared with those who did not undergo the operation. Perrier et al. further evaluated cognition in asymptomatic PHPT (mean calcium 10.5 mg/dl) and also utilized functional magnetic resonance imaging (fMRI) to assess brain function in a randomized controlled trial comparing parathyroidectomy with observational studies. There were no differences in cognition between the two groups or in fMRI voxel counts. Therefore, the improvements seen in HRQOL from observational studies following parathyroidectomy were not confirmed in this randomized controlled trial.
Conclusions: The authors present a case report of primary hyperparathyroidism in a 78 aa woman came to our attention by state stupor and severe hypercalcemia.

INFERIOR VENA CAVA AGENESIS. CASE REPORT.

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Background: Congenital defects of the inferior vena cava as well as its absence or atresia are rare vascular defects and result from an altered development during embryogenesis.
Case summary: We present the case of a 28-year-old man with agenesis of the inferior vena cava, deep vein thrombosis of the right lower limb and left renal hypoplasia. He comes to our attention in the Emergency Department reporting a worsening turgidity of the right lower limb after a contusive-distracting trauma to the right thigh (while he was in elevation during a volleyball game he received a contusion to the thigh). The patient is subjected to the following tests in the Emergency Department: ELECTROCARDIOGRAM: Sinus rhythm, 90 b/m; BLOOD COUNT: Within limits; D-DIMER: 3.45 microgr./mL (normal value < 0.25 microgr./mL); CHEST X-RAY: No active pleuroparenchymal lesions. Cardiovascular shadow within limits; POPLITEO-FEMORO-ILIAC-CAVAL VENOUS AXIS COLOR DOPPLER: Massive deep vein thrombosis of the right iliac, femoral and right popliteal. Venous thrombosis of the internal saphenous vein of the thigh. Partial inferior caval venous thrombosis. In light of the findings obtained, it is decided to admit the patient to the Internal Medicine I° Emergency Department in order to complete the diagnostic process. In fact, the patient is subjected to: THROMBOPHILIC MARKER STUDY: The study of thrombophilic markers reveals positivity of MTHFR C677T heterozygous genotype with normal homocysteine (12 micromoles/l VN= <15 micromoles/l), protein S deficiency (60% VN=70%-140%), coagulative protein C deficiency (42% VN=70%-140%) with normal rPCA (ratio greater than 3.2); THORACIC-ABDOMINAL CT WITH MDC: Spiral CT with intravenous MDC. Absence of tomodensitometric alterations in the liver, spleen, pancreas. Hypoplasia of the left kidney; hypertrophic appearance of the right kidney. Regulate the nephrographic effect and the elimination of the contrast medium bilaterally. The inferior vena cava is visualized in its distal pre-atrial tract and in the retrohepatic location up to the confluence of the suprahepatic veins; in the remaining abdominal tract, multiple vascular structures of tortuous and ectatic appearance are observed, attributable to collateral circulations. In particular, an ectatic and tortuous venous vascular structure is highlighted, which from the right iliac space moves upwards, partially surrounding the right kidney and merging with the other collateral circulations. Ectasia of the deep iliac veins, of the lumbar venous plexuses, of the azygos and hemiazygos veins. The external iliac veins are visualized bilaterally only for a portion beyond which they merge into collateral vessels. Thrombosis of the right external iliac vein in the visualized portion and of the ipsilateral superficial femoral vein. ANGIO-MR ABDOMEN: Examination performed with axial T1-weighted FLASH sequences before and after MDC and with axial and coronal TRUE FISP sequences; angio-MR with coronal 3D FLASH sequences after MDC and MIP reconstructions. The arterial phase of the angiographic phase shows no alterations in the caliber and course of the abdominal aorta and iliac arteries; the emergence of the celiac trunk and superior mesenteric artery are normal. The right renal artery has a caliber within the upper limits of normal with a normal course; the left renal artery has a uniformly reduced caliber without ostial stenosis and has an extremely reduced course. The picture reflects the condition of the two kidneys with evidence of a small harmonic kidney on the left with normal nephrographic effect and elimination of the contrast medium and a right kidney with increased volume that has normally excreted the contrast medium. The sequences acquired in the venous phase do not show certain visualization of the inferior vena cava except in the distal pre-atrial tract, from the confluence of the suprahepatic veins. In the retrohepatic upstream tract the vessel appears markedly hypoplastic as well as in the abdominal course where in the cava site there are tortuous and ectatic vascular structures probably due to collateral circulations as well as the perivertebral venous circulations appear significantly ectatic. Furthermore, to the left of the aorta there is a vascular structure visible in the venous phase that could be compatible with hemiazygos. CAVOGRAPHY: The examination performed via the left transfemoral route shows: agenesis of the inferior vena cava with the presence of a paravertebral embryonic type vicarious circulation to which the main district venous vessels belong and which flows into the azygos vein and patency of the intrahepatic inferior vena cava. The patient is subjected during hospitalization to treatment first with LMWH and then with Apixaban.
Discussion: This clinical case represents an extremely rare event in the scientific literature for various reasons: presentation modality, thrombophilic predisposition, vascular defect.
Conclusions: The case we described presents a very rare vascular anomaly consisting of agenesis of the inferior vena cava associated with deep vein thrombosis of the right lower limb and left renal hypoplasia.

HUGHES SYNDROME: CASE REPORT

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Background: and purpose of the study: We describe the case of a 28-year-old woman with shortness of breath, chest pain, swelling of the left lower extremity. We propose the following objectives: present the case report of Hughes syndrome and its association with venous thromboembolism.

Materials and methods: The patient was subjected to thoraco-abdominal and pelvic CT scan with contrast medium (thrombosis of lower lobar branch of pulmonary artery and of left segmental branches of right pulmonary artery, thrombosis occluding iliac-femoral axis on the left); echocardiography; venous Doppler ultrasound of lower extremity s (thrombosis of iliac-femoral-popliteal axis on the left); research of tumour and thrombophilic markers.
Results: IgG anticardiolipin antibodies 2694.00 U/mL (0-10 VN); IgM anticardiolipin antibodies 33.00 U/mL (VN 0-10); baseline aPTT (repeated) always >85 sec.; MTHFR C677T positive with mutated homozygous genotype; Homocysteine 18 micromol. (VN <15); Protein S 53% (VN 70-140); rPCA 1.25 (ratio >2.45); LAC (lupus anticoagulant) present; Russell viper venom 3.10 (ratio <1.21); Silica clotting time 2.62 (ratio <1.31); IgG anti-beta glycoprotein antibodies 100.00 SGU (VN <11); IgM anti-beta glycoprotein antibodies 17.00 SMU (VN <11); antinuclear antibodies (ELISA screening): positive; antinuclear antibodies (IIF title): positive 1:160 homogeneous pattern (VN <1:80).
Conclusions: This case report illustrates a result pathogenetically related to Hughes syndrome, characterised by LAC positivity, anticardiolipin antibodies and anti-beta glycoprotein.

PESCORE STUDY: CORRELATIVE ANALYSIS IN 30 PATIENTS WITH VENOUS THROMBOEMBOLISM. THREE-YEAR EXPERIENCE (2022-2024)

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Introduction: The "PESCORE" study, an acronym derived from "Pulmonary Embolism Severity index and eCg scORE", enrolled 30 patients, aged between 48 and 82 years, with venous thromboembolism (central pulmonary embolism) hospitalized in the three-year period January 2022-December 2024. The clinical picture of onset was characterized in all patients by severe respiratory failure (arterial blood gas analysis value of pO2<60 mmHg) possibly associated with chest pain, confusional state, hemodynamic instability (PAS<90 mmHg). In all patients, the PESI and the ECG Score were calculated. The PESI values at entry were compared with the ECG Score values at entry in the 30 enrolled patients. A correlative analysis was performed for continuous variables with a parametric Pearson test to verify whether there is a significant relationship between the PESI values at entry (independent variable A) and the ECG Score values at entry (dependent variable E).
Purpose of the work: The "PESCORE" study has the following objectives: 1) to verify any existing relationships between the PESI values at entry and the ECG Score values at entry in the 30 patients enrolled in the "PESCORE" study during the three-year period January 2022 – December 2024; 2) verify the statistical significance found by applying the parametric test of Pearson as a test of correlative analysis for continuous variables to establish whether the relationships of the variables considered are due to chance.
Material and method: The 30 patients enrolled with central pulmonary embolism were examined according to the fields of the database created called "PESCORE". The parametric correlation test of Pearson correlates the independent variable A (PESI at entry) with the dependent variable E (ECG Score at entry) in the 30 enrolled patients. In the column "Variable A (PESI)" the values of PESI are expressed for each patient at entry.
Analysis of the results: The Pearson test applied to the 30 patients shows a highly significant correlation ($p<0.001$) of the two variables examined (PESI values at entry and ECG Score values at entry) and, therefore, not attributable to chance. In fact, the value of "r" obtained is -0.02 and the VC (critical value) of "r" for p=0.001 is <0.207 with GL=29.
Discussion: The data obtained suggest that the increase in PESI values at entry in the 30 patients enrolled in the "PESCORE" study correlates with the increase in ECG Score values at entry observed in all patients. This suggests that the severity of the clinical picture, measured by PESI is correlated with the ECG Score score obtained as can be seen from the values of PESI and ECG Score at entry.
Conclusions: The "PESCORE" study has demonstrated that in the group of 30 patients with venous thromboembolism (central pulmonary embolism) there is a correlation between the two variables considered: PESI and ECG SCORE. This correlation shows an absolute negative concordance according to the Pearson correlation coefficient "r" and is the expression not of a casual association but of a close correlation between the increase in PESI values and the increase in ECG SCORE value in the 30 patients with central pulmonary embolism.

MIATEV STUDY: COMPARATIVE ANALYSIS, BY SEX AND AGE, IN A POPULATION OF 228 PATIENTS WITH VENOUS THROMBOEMBOLISM. FOUR-YEAR EXPERIENCE (2021-2024)

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Background: and purpose of the study: The MIATEV study enrolled 48 males with VTE, 124 females with VTE, 16 males with PE, 40 females with PE.
Objectives: to verify differences in presentation between the 4 groups and the statistical significance of the differences between the two pairs of groups being compared (TEVU–TEVD and EPU–EPD).
Materials and methods: A created database analyzed the patients according to 4 fields: sex, age, VTE, PE. The Student t-test was applied for the comparative analysis. The test compares the equality between the two means of the two groups (M1-M2, M3-M4) and calculates t using the formula applied to the two groups being compared: (M1-M2)/√DS12/N1+DS22/N2 for the TEVU-TEVD groups, (M3-M4)/ √DS32/N3+DS4/N4 for the EPU–EPD groups.
Results: The VR of t in the M1-M2 comparison is lower than the expected value for which there is no significant difference in the 2 groups (TEVU and TEVD) in relation to age. The VR of t in the M3-M4 comparison is higher than the expected value for p = 0.001 and the difference for age appears highly significant in the 2 groups (EPU and EPD). The VR of t in the M1-M2 comparison is -0.5 with VC of t = 1.65 ($p > 0.05$) while the VR of t in the M3-M4 comparison is 3.78 with VC of t = 3.5 (GL 170 and 54).
Discussion: The MUTEV study has demonstrated that pulmonary embolism in men is more frequent over 70 years of age while VTE affects both sexes over 60 years of age.
Conclusions: These data are in line with Stein's experiences and the reasons for the differences found must be sought in the different expressiveness of risk factors in patients with VTE and pulmonary embolism.

PLANCET STUDY: CORRELATIVE ANALYSIS IN 30 PATIENTS WITH VENOUS THROMBOEMBOLISM. TWO-YEAR EXPERIENCE (2023-2024)

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Introduction: . The "PLANCET" study, an acronym for "Pesi cLearANCE lactates", enrolled 30 patients, aged between 48 and 82 years, with venous thromboembolism (central pulmonary embolism) in the two-year period 2023-2024 and subjected to loco-regional fibrinolysis. In all patients, lactate clearance was calculated on arterial blood gas analysis (lactate dosage at T0 pre-lysis and at T1 post-lysis at 6 hours) according to the formula: lactates (T0)-lactates (T1)/lactates (T0)x100 (VN lactates 0.5-1.6 mEq/l) and the Pulmonary Embolism Severity Index (PESI) whose values were compared with those of lactate clearance. A correlative analysis for continuous variables was performed with Pearson's parametric test to verify whether there is a significant relationship between the PESI values at entry (independent variable A) and the lactate clearance values (dependent variable E).
Purpose of the study: The "PLANCET" study has the following objectives: to verify any existing relationships between the PESI values at entry and the lactate clearance values in the 30 patients enrolled in the "PLANCET" study during the two-year period January 2023 – December 2024; to verify the statistical significance found by applying the Pearson parametric test as a correlative analysis test for continuous variables to establish whether the relationships of the variables considered are due to chance.
Material and method: . In the 30 enrolled patients, the PESI values (independent variable A) were compared at entry with the lactate clearance values (dependent variable E) by applying the Pearson parametric correlation test. The Pearson correlation coefficient "r" formula is used to calculate the test: $\Sigma(A- \bar{A})\ (E- \bar{E})\ /\ \sqrt{\Sigma(A- \bar{A})2\ \Sigma\ (E- \bar{E})2}$.
Results: The Pearson test applied to the 30 patients shows a highly significant correlation ($p<0.001$) of the two variables examined (PESI values at entry and lactate clearance values) and, therefore, not attributable to chance. In fact, the value of "r" obtained is 0.62 and the VC (critical value) of "r" for p=0.001 is 0.207 with GL=29.
Discussion: The data obtained suggest that the increase in PESI values at entry in the 30 patients enrolled in the "PLANCET" study correlates with the increase in lactate clearance values observed in all patients. This suggests that the severity of the clinical picture, measured by PESI, is correlated with the lactate clearance values, as can be seen from the PESI and lactate clearance values, by

virtue of the therapeutic efficacy obtained with loco-regional thrombolysis. In fact, thanks to this procedure, it is possible to obtain a reduction at 6 hours of the lactate value in arterial blood gas analysis with an increase in the clearance values reported in all patients, particularly in those patients with a high PESI score.
Conclusions: The "PLANCET" study has demonstrated that in the group of 30 patients with venous thromboembolism (central pulmonary embolism) there is a correlation between the two variables considered: lactate clearance and PESI. This correlation shows an absolute positive concordance according to the Pearson correlation coefficient "r" and is the expression not of a casual association but of a close correlation between the increase in lactate clearance values and the increase in the PESI value in the 30 patients with central pulmonary embolism.

AMEBIASIS: CASE REPORT

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Introduction: The Authors presented the case report of a 41-year-old patient, of Bangladeshi nationality, who has been living in Italy for years, who came to our attention for evening fever for about 10 days resistant to antibiotic therapy. The last trip to Bangladesh dates back to 18 months before, during which at his family home he took water directly from the local water supply as required in Bangladesh.
Case report: During hospitalization, the patient underwent the following tests: 1) Skull CT scan with contrast medium: shows no areas with enhancement of pathological significance; 2) Thorax CT scan with contrast medium: shows atelectasis phenomena in the middle lobe with mediastinal lymphadenopathy (max 12 mm diameter); 3) CT scan of the abdomen with contrast medium: in the right hepatic lobe, a large polylobed formation (11x9.3x7 cm) with fluid content and thin walls is appreciated, showing impregnation after contrast medium, as for an abscess focus; 4) MRI of the facial massif with contrast medium showing the presence of solid tissue measuring 23x23x13 mm that occupies part of the posterior portion of the right middle and upper nasal choana up to the ipsilateral posterior ethmoidal cells, adhering to the nasal septum and the middle concha; after contrast medium, marked and homogeneous enhancement of the tissue occurs; 5) Ultrasound-guided abdominal drainage: under ultrasound and fluoroscopy guidance, a 16 Fr drain is positioned inside the hepatic abscess, 250 cc of purulent-corpuscular material, chocolate-colored, is aspirated; 4 days later, a check of the drainage of the liver abscess is performed and by administering water-soluble contrast medium, the collection disappears, so the percutaneous drainage is removed; 6) EGDS: no lesions and the biopsies show signs of chronic inflammation; 7) ILEOCOLONSCOPY: The ileum, traversed for 20 cm, shows small erosions and the biopsies do not show active phenomena; there are erosions with a fibrin base in the cecum and the biopsies show chronic lymphoplasmacytic infiltrate; in the colon-rectum, no findings; the histological examination on fragments of mucosa of the large intestine shows acute and chronic inflammation of the lamina propria with granulation tissue findings in the context of which microorganisms compatible with Ameba Histolytica are found; 8) FIBROBRONCHOSCOPY: in the middle lobe, viscous and stringy secretions are present and bronchial lavage is performed, negative for neoplastic cells; 9) Serial ECG: show sinus rhythm 10) Blood tests: SGOT, SGPT, ALP, WBC and PCR values show regression trend at discharge; lymphocyte typing is within limits; HIV test negative; ANA, ENA, native antiDNA within limits; sterile urine culture; search for neoplastic markers negative; HAV, HBV, HCV negative; electrophoretic protein test shows hypoalbuminemia (35.9%, NV 55.8-66.1%), hyperalpha 1 (10.7%, NV 2.9-4.9%), hyperalpha 2 (17.5%, NV 7.1-11.8), hyperbeta 2 (7.8%, NV 3.2-6.5%), hypergamma (21.7%, NV 11.1-18.8); direct BK negative; negative parasitological examination of stool; Entamoeba Histolytica IgG present evaluated with ELISA method. Therapy is started with intravenous metronidazole at a dose of 750 mg every 8 hours for 10 days and subsequently with oral paromomycin at a dose of 200 mg every 8 hours for 7 days.
Discussion: The pathogenic action exerted by E. histolytica is a consequence of three basic properties of trophozoites: adhesion to tissues, cytolytic and proteolytic powers of the parasite, ability to evade the body's immune defenses. The trophozoites overcome the layer of mucus that covers the intestinal wall, adhere to the epithelium and mucin via a lectin (adhesin). Contact with the extracellular matrix induces in trophozoites, through structures called "amebapores", the release of proteolytic enzymes capable of degrading collagen, laminin, matrix macromolecules and local secretory IgA. The parasites penetrate between the separated epithelial cells, erode the lamina propria and spread (amoeboid movements) in a lateral direction causing extensive necrotic events (flask ulcers). The amoebae can "metastasize" to other organs and cause extra-intestinal amoebiasis (hepatic, pulmonary, cerebral). Liver abscess is present in >50% of cases without prodromes or positive anamnesis for intestinal form (as in the case of our patient) with septic type fever, right hypochondrial pain, hepatomegaly, neutrophilic leukocytosis, h ESR, h ALP, dense, chocolate-colored "pus". For the diagnosis of intestinal form, the following is performed: parasitological examination of "fresh" stool (<30'); presence of trophozoites and/or cysts, trichrome staining of cysts, search for fecal antigens with ELISA; for other forms: serological tests: + >90% hepatic forms, ELISA for antigens on abscess material. For therapy, tissue amebicides such as metronidazole, other nitroimidazoles (tinidazole), dihydroemetine hydrochloride in severe forms.
Conclusions: The Authors presented the case report of a 41-year-old Bangladeshi patient with a liver abscess caused by entamoeba histolytica.

INCIDENTAL VENOUS THROMBOEMBOLISM IN 30 CANCER PATIENTS: ROLE OF THE KHORANA SCORE. KONCER STUDY. FIVE-YEAR EXPERIENCE (2020-2024)

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Introduction: The "KONCER" study, an acrostic from "KhOraNa score and canCER", enrolled 30 patients, aged between 58 and 84 years, with incidental complete venous thromboembolism and cancer in the five-year period January 2020-December 2024. All patients underwent: thoracic-abdominal-pelvic CT with contrast medium); echocardiography; venous color Doppler ultrasound of the lower limbs and possible elastic compression; search for thrombophilic and neoplastic markers. In all patients, the Khorana score48 was measured. Therefore, a database was created called "KONCER". The database contained the following fields: 1) patient number, 2) Khorana score48 for each patient. All patients were analyzed, during recruitment, according to the aforementioned 2 fields, collected from time to time in masks created in "structure view" and "datasheet view" mode as allowed by the database program. A comparative analysis was performed for continuous variables with a parametric Cochgran Q test to verify whether there is a significant relationship between the values of the Khorana score (dependent variable E) and the extent of the incidental venous thromboembolic manifestation (independent variable A).
Purpose of the work: The "KONCER" study has the following objectives: 1) to verify any existing relationships between the values of the Khorana score and the venous thromboembolic manifestation in the 30 patients enrolled in the "KONCER" study during the five-year period January 2020 – December 2024; 2) verify the statistical significance found by applying the Cochran Q parametric test as a comparative analysis test for continuous variables to establish whether the relationships of the variables considered are due to chance. A comparative analysis was performed for continuous variables with the Cochran Q parametric test to verify whether there is a significant relationship between the values of the Khorana score (dependent variable E) and the extent of the venous thromboembolic manifestation (independent variable A).
Material and method: The 30 patients enrolled with venous thromboembolism were examined according to the fields of the database created called "KONCER". To calculate $\chi 2$, the following formula is applied: $\chi 2 = (k-1)[(k\ x)-y2]/(k\ y)-z=20.95$. "k" indicates the 3 variables considered, "x" indicates the total of the squares of the 3 variables considered. "y" indicates the total of the clinical conditions. "y2" indicates the square of the total of the clinical conditions. "z" indicates the total of the squares of the clinical conditions. The relative value (VR) of the $\chi 2$ obtained is 60 with Degrees of Freedom (GL)=2.
Analysis of results: The Cochran Q test applied to the 30 patients involved in the "KHONCER" study, shows how the clinical situation "TEV" (complete venous thromboembolism) highlighted in all patients is not attributable to chance but assumes a high statistical significance since the relative value (VR) of the $\chi 2$ obtained is 60 with Degrees of Freedom (GL) = 2 and the critical value (VC) of the $\chi 2$ for $p = 0.001$ is 13.816. The differences in choice are, therefore, highly significant with $p < 0.001$.
Discussion: The data obtained in the 30 patients enrolled in the "KONCER" study demonstrate a statistically significant correlation in incidental venous thromboembolism between the Khorana score and the extent of the venous thromboembolic manifestation. The Cochran Q test expresses a highly significant difference whose clinical significance lies in the high reliability of predicting the venous thromboembolic risk in cancer patients.
Conclusions: The "KONCER" study has demonstrated that in the group of 30 patients with complete venous thromboembolism there is a highly significant correlation between the Khorana score and the extent of the venous thromboembolic manifestation according to the Cochran "Q" test. The "KONCER" study demonstrates the high predictivity of the venous thromboembolic risk in cancer patients.

NEUROCYSTICERCOSIS: CASE REPORT

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Case report: We report the case of a 34-year-old woman who came to our attention for recurrent syncopal episodes in the last 6 months lasting a few minutes with spontaneous resolution. The frequency of the last episodes with the reduction of the free interictal interval are the reasons that led her to the emergency department. The objective examination does not reveal any noteworthy findings. The CT is 36.6°C, the BP 110/70 mmHg, the HR 74/m RS. The patient is perfectly conscious and well oriented, does not present focal deficits or signs of meningism. The following tests are performed during hospitalization: Laboratory tests: the blood count shows microcytemia, probably constitution, electrolytes are normal, liver, pancreatic, renal function are normal. Muscle and myocardial enzymes are repeatedly negative. Arterial blood gas analysis is within limits. Coagulation function, electrophoretic protein analysis, urine test with urine culture are within limits. The search for neoplastic markers is within limits. The parasitological test is repeatedly negative. The search for markers for hepatitis, TORCH complex, HIV, treponema is negative. Spinal puncture is performed, showing clear liquor and the bacterioscopic and culture test is negative. ECG: within limits Chest X-ray 2P: no other pleuroparenchymal changes are observed Abdominal ultrasound: no alterations of the intra-abdominal organs are observed Muscle ultrasound and subcutaneous layers: negative search for cystic nodules. Electroencephalogram: shows bihemispheric graphoirritative anomalies. Cranial CT scan without contrast medium: reveals the presence of some bihemispheric cystic formations and highlights edema of the right prefrontal gyrus. Encephalon MRI: sequences are performed on the three orthogonal planes of space with SE, FSE, DWI, GR and FLAIR techniques weighted in T2 and T1, the latter before and after administration of intravenous paramagnetic contrast medium. Numerous small nodular-shaped areas with a ubiquitous distribution are observed, predominantly supratentorial and bihemispheric, with dimensions varying from punctate to approximately 10 mm, the largest of which appears localized in the right frontal subcortical region (superior frontal gyrus) and appears surrounded by vasogenic edema. The lesions show different intensitometric behavior alternating from hypointense to hyperintense in the long TR sequence (with a small halo of hypointensity from paramagnetic substance and in GR, where some appear hypointense as from initial calcium deposit. After contrast medium, enhancement in the form of rings is observed in most of them (the larger ones) while others show homogeneous enhancement (the smaller ones). At least one of these lesions appears to have a meningeal implant. In the left frontal area, a venous angioma with a "caput medusae" appearance is observed. The subarachnoid spaces of the vault, base and Sylvian valleys are normally represented. The finding of multiple nodular lesions appears suggestive of neurocysticercosis Intracranial ANGIORM: 3D TOF sequence with VR reconstructions was performed. Good representation of the polygon of Willis and the main branches. No evidence of aneurysmal formations. Therefore, antiparasitic therapy for neurocysticercosis is undertaken with Albendazole 15 mg/kg/day (e.g. 800 mg) PO divided bid with meals for 1 month in cycles. Antiepileptic is administered with Levetiracetam (Keppra) 500 mg tablets 1 cpx2/day for the first week, progressively increasing the dosage. Therapy is performed with Prednisone 60 mg/day for 1 month, to reduce the edema caused by the larger lesions, associated with H2 antagonists PO. During the hospital stay, the patient did not present further epileptic equivalents (syncope) and is discharged with an outpatient schedule for angioRMN of the brain and control electroencephalogram.
Discussion: It is clear that the syncopal episodes reported by the woman must be considered equivalent to epileptic ones as evidenced by the electroencephalogram and the CT and MRI images of the brain suggestive of neurocysticercosis. Once the antiepileptic and antiparasitic therapy was started, the patient did not present further critical episodes. Antiepileptic therapy is recommended over time due to the high risk of recurrent convulsive crises with possible suspension only in case of radiological resolution of the lesions. The case of neurocysticercosis presented by us in a 34-year-old woman from Madagascar, who had been in Italy for 8 months and who came to our attention for recurrent syncopal episodes, integrates the data found in the literature.
Conclusions: We presented the case report of a young woman aged 34, from Madagascar, who had been in Italy for 8 months and who came to our attention for recurrent syncopal episodes that, from the diagnostic investigations conducted, were equivalent to epileptic. Our experience integrates the data from the literature.

INDIRECT ECHOCARDIOGRAPHIC SIGNS OF PULMONARY EMBOLISM: THE SERIND STUDY. COMPARATIVE ANALYSIS IN 20 PATIENTS WITH VENOUS THROMBOEMBOLISM. THREE-YEAR EXPERIENCE (2022-2024)

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Introduction: SERIND study, acrostic of "Signs EchocardIogRaphic INDirect Central of pulmonary Embolism" enrolled 20 patients, between 48 and 82 years old, with venous thromboembolism (central pulmonary embolism) hospitalized in the three-year period 2022-2024. The results obtained from the case history showed a severe respiratory failure in all patients (arterial blood gas analysis value pO2<60 mmHg), associated with chest pain, confused state of mind, hemodynamic instability (PAS<90 mmHg). In the 20 patients, we examined echocardiographic values at the entrance, both direct and indirect, of the overload of the right ventricle according to Kurzyna criteria. As a consequence we carried out a comparative analysis for nominal variables with the Cochrna's Q test to check if there is a significant relationship between A conditions (RV overload criteria), B (60-60 SIGN), C (Mc Connell Sign).
Purpose of the experiment: SERIND study has the following goals: to test any association with A conditions (RV overload criteria), B (60-60 SIGN), C (Mc Connell Sign) in 20 patients enrolled in SERIND study. Moreover, to check its statistical importance by applying the Cochran's Q test in order to determine if the differences are due to chance.
Procedures used: To calculate $\chi 2$ we apply the following formula: $\chi 2 = (k-1)[(k x)-y2]/(k y)-z=28,9$. "K" refers to 3 variables, "X" refers to the total sum of squares of the 3 variables. "Y" stands for the total of the chosen scores. "Y^{2}" is the square of the total chosen scores. "Z" means the sum of the squares of the chosen scores. The $\chi 2$ relative value (VR) is 28,9 with Degree of Freedom (GL) =2. The $\chi 2$ critical value (VC) per p=0,001 is 13,816.
Observation/data/results: By applying the Cochran's Q test, the results demonstrate how A, B, C conditions are not at all due to chance. They have indeed a significant importance because the $\chi 2$ obtained relative value (VR) is 20,95 with Degrees of Freedom (GL)=2, and the $\chi 2$ critical value (VC) per p=0,001 is 13,816. The differences in choice are consequently strongly significant with p<0,001.
Discussion: The results obtained show how the significant association in SERIND study, reveals the coexistence, according to Kurzyna criteria, of A conditions (RV overload criteria) + B conditions (60-60 Sign) + C conditions (Mc Connell Sign). This means that the case report begins with right ventricular distress. From the literature we survey the following experiences that come out. Pech connects PEI with the survival of patients with pulmonary embolism. Miller focused on a scoring system based on the number of obstructive vascular segment during pulmonary angiography. Fava explains the effectiveness of mechanical fragmentation linked to pulmonary intra arterial thrombolysis with urochinasi. Nakazawa looked into the risk of distal embolization with pulmonary hypertension after loco-regional lysis combination with thromboembolism fragmentation. Kurzyna and Toosi considered indirect central echocardiographic criteria in order to assess the ventricular overload in those patients affected with severe pulmonary embolism. Casazza studied Mc Conell's signs, concerning those patients with acute right ventricular failure, a particular marker for pulmonary embolism.
Conclusions: SERIND study showed how in 20 patients affected with venous thromboembolism (central pulmonary embolism), the most significant association is linked to the coexistence of A conditions (RV overloaded criteria) + B conditions (60-60 SIGN) + C conditions (Mc Connell Sign). This correlation is very significant according to the Cochran's Q test, in 20 patients with central pulmonary embolism. Among all the similar case reports in literature, SERIND study reveals data that complete those provided from Kurzyna, Toosi, Casazza.

OLEANDER POISONING: CASE REPORT

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Introduction: Exposure to plants containing cardiac glycosides is rare in the United States. Of 1,390,000 non-drug toxic exposures reported by the American Association of Poison Control Centers (AAPCC). Exposure to cardiac glycosides from plants accounts for only 1% of all plant exposures and 0.1% of all exposures. The deliberate ingestion of a yellow oleander seed (Thevetia peruviana), known as "lucky nuts," has recently become a common practice in northern Sri Lanka to reduce stress outside the home by slowing the heart rate,

according to social ecologist Vandana Shiva. Shiva also reports how Indian farmers who cannot pay their debts resort to ingesting Thevetia seeds for mass suicides. In fact, thousands of cases are reported annually in India with a mortality range for untreated patients between 5% and 10%. Mortality according to the AAPCC is rare. Morbidity associated with exposure to plants containing cardiac glycosides tends to be less severe than that associated with pharmacological cardiac glycosides. Pharmacological exposure generally occurs in patients > 60 years of age and is very often due to acute or chronic intentional ingestion. Exposure to plants containing cardiac glycosides according to AAPCC data shows that 57% of children < 6 years old are affected, 19% of children between 6 and 19 years old, and 23% of adults > 19 years old. The most common plants containing cardiac glycosides are Digitalis purpurea, Digitalis lanata, Strophantus gratus, Convallaria maialis, Nerium oleander, Thevetia peruviana, Urginea maritima.
Case report: Patient AJ, 42, comes to our attention at 7:00 p.m. We learn from the anamnestic story that she chewed and ingested about 10 pink oleander leaves around 3:30 p.m. with the onset of vomiting and subjective dizziness after about two hours, for which the poison control center is consulted and we proceed with ECG monitoring, electrolyte control, fluid therapy, gastrolysis with activated charcoal. The blood pressure is 100/55 mmHg, the heart rate is 40 b/m, the respiratory rate is 18 breaths/minute, the SpO2 is 96% in room air, the blood tests show a digoxinemia of 8.47 mg/ml (VN=0.5-2 mg/ml) and the electrocardiogram reveals sinus bradycardia with HR 40/m. Therapy is started with atropine 0.5 mg iv followed by the infusion of orciprenaline 10 fl in 500 cc SF at an initial rate of 5 ml/h to be increased, if necessary, to 10-15 ml/h: in fact, the heart rate increases up to 70 b/m after about 24 hours for which the infusion with orciprenaline is suspended while digoxinemia is reduced to 1.97 mg/ml after 12 hours, to 1.18 mg/ml after 24 hours, to 0.58 mg/ml after 36 hours.
Discussion: Like all cardiac glycosides, those contained in pink oleander (oleandrin, oleandroside, digitoxigenin) inhibit the Na+/K+ ATPase-dependent pump with depletion of intracellular K+, increase of intracellular Na+, reduction of Na+/Ca++ exchange, increase of intracellular Ca++ with increased activation of contractility. This results in a reduction of the normal resting membrane potential and a secondary impairment of the pacemaker function of myocytes that can lead to bardyarrhythmias and asystole and, considering the structural analogy of the cardiac heterosides contained in oleander with that of digoxin, the cross-reactivity described in the "immunoassays" by Osterloh and Dasgupta should not be surprising. The biological activity of the heterosides is mediated by the allosteric effect produced by the rearrangement of the receptor complex upon interaction according to the Thomas model.
Conclusions: In light of the pharmacodynamic and pharmacokinetic aspects inherent to the cardiac glycoside molecules contained in oleander leaves, the cross-reactivity of the "immunoassay" between digoxin and oleandrin with digitalis overdose is evident.

MONDOR SYNDROME: CASE REPORT

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Introduction: We present the case report of a 21-year-old woman with superficial venous thrombosis (SVT) of Mondor.
Material and methods: The patient came to our attention for a few days after a mild contusive trauma of a hard, painful and tender cord. She denies fever. In her anamnesis, migraine is reported. She does not take estrogen-progestins. She has an umbilical piercing and a tattoo. The search for thrombophilic markers is negative. Abdominal ultrasound shows no alterations or lymphadenomegaly. ESR, CRP, leukocytes are increased. ANA and ENA are within limits. A swab is performed at the piercing site (hyperemic skin) which shows positivity for staphylococcus aureus. The echocolordoppler shows TVS of Mondor. The brain MRI shows no alterations and the study of the venous sinuses does not show thrombosis. The patient is treated with LMWH and oral antibiotic therapy.
Discussion: Mondor's TVS involves the anterolateral chest wall (lateral thoracic and thoracoepigastric veins) and the dorsal vein of the penis. It is benign and characterized by the appearance of a single or branched, painful cord. It is related to trauma or infection.
Conclusions: The authors presented a case report of Mondor's TVS associated with Staphylococcus aureus contamination and blunt trauma of the abdominal wall.

THE ΔP-PESI STUDY: CORRELATIVE ANALYSIS IN 20 PATIENTS WITH VENOUS THROMBOEMBOLISM. BIENNIAL EXPERIENCE (2023-2024)

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Introduction: The "ΔP-PESI" study, an acronym derived from "DELTA(PAO2-PaO2)-Pulmonary Embolism Severity Index", enrolled 20 patients, aged between 48 and 82 years, with venous thromboembolism (central pulmonary embolism) in the two-year period January 2023-December 2024. The clinical picture of onset was characterized in all patients by severe respiratory failure (arterial blood gas analysis value of pO2<60 mmHg) possibly associated with chest pain, confusion, hemodynamic instability (PAS<90 mmHg). In all patients, the PESI at admission and the ΔP at admission were calculated. The ΔP is an index of gas exchange impairment with an increase in the alveolar (A)-arterial (a) gradient of O2 = PAO2 – PaO2= [(PBar-PH2O)FiO2-PaCO2/R]-PaO2= [(760-47)FiO2-1.25PaCO2]-PaO2. The normal value corresponds to age/4 +/-4, therefore = 10-15. If > 20, an alteration of gas exchange is detected, if > 50, a serious alteration of gas exchange is detected. Compared to P/F, a simpler parameter to calculate, it is a more reliable index of gas exchange as it takes PaCO2 into account.
Purpose of the study: The ΔP-PESI study enrolled 20 patients, aged between 48 and 82 years, with venous thromboembolism admitted in the two-year period 2023-2024. The ΔP-PESI study has the following objectives: 1) to verify any existing relationships between the ΔP values at admission and the PESI values at admission in the 20 patients enrolled in the ΔP-PESI study during the two-year period January 2023 - December 2024; 2) to verify the statistical significance found by applying the Pearson parametric test for the correlative analysis.
Materials and methods: The Pearson test correlates the variable A (ΔP at entry) with the variable E (PESI at entry) in the 20 patients enrolled in the ΔP-PESI study. To calculate the test, the formula of the Pearson correlation coefficient "r" is applied: $\Sigma(A-\bar{A})(E-\bar{E})/\sqrt{\Sigma(A-\bar{A})2\,\Sigma(E-\bar{E})2}$. Therefore, the value of "r" obtained with Degrees of Freedom (GL)=19 is 0.97.
Results: Since the Critical Value (VC) of "r" is equal to 0.693 with GL=19 for p=0.001, the Relative Value (VR) of "r" expresses an absolute positive agreement of the covariation between the values of the two variables considered (A and E) which is highly significant with p<0.001. The Pearson test applied to the 20 patients shows a highly significant correlation (p<0.001) of the two variables examined (ΔP values at entry and PESI values at entry) and, therefore, not attributable to chance. In fact, the value of "r" obtained is 0.97 and the VC (critical value) of "r" for p=0.001 is 0.693 with GL=19.
Discussion: The data obtained suggest that the increase in ΔP values at entry in the 20 patients enrolled in the ΔP-PESI study correlates with the increase in PESI values at entry observed in all patients. This suggests that the severity of the clinical picture, measured by ΔP at entry, is correlated with the PESI score obtained with the tomographic finding, as can be seen from the ΔP and PESI values at entry. From the examination of the literature, the following experiences emerge, which we propose below.
Conclusions: The ΔP-PESI study has demonstrated how there is a correlation between the two variables considered: ΔP and PESI. This correlation shows an absolute positive agreement according to the Pearson "r" coefficient and is an expression of a close correlation between the increase in the ΔP values and the increase in the PESI value.

HORTON'S ARTERITIS: CASE REPORT

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Introduction: The authors have presented the case of a 58 year old patient, of Italian nationality, who was admitted for observation for serotonin fever, masseter claudication, fatigue, headache and hyperalgesia in the right temporal area which was resistant to treatment with NSAIDs and antibiotics. No pathologies worthy of note emerged on taking the clinical history.
Case report: During hospitalisation, the patient was subjected to the following examinations:
Treatment was undertaken with deltacortene tablets 25 mg until remission of the clinical picture.
Discussion: Giant cell arteritis, which is also called Horton's arteritis or temporal arteritis, plays a part in vasculitis of the large vessels; of all the inflammatory diseases that affect the arteries, it is without doubt the most common.

It is a disease that emerges after reaching the age of 50; the average age of patients with this disease is approximately 73 years. The female: male ratio favours women by circa 2 to 1. This disease is closely related to another frequently encountered inflammatory disease: rheumatic polymyalgia. Approximately 16-21% of patients with rheumatic polymyalgia develop giant cell arteritis and 40-60% of patients with giant cell arteritis also have rheumatic polymyalgia. Precisely because of this important correlation between both diseases, many experts believe it is, in fact, just a different clinical manifestation of the same pathological entity. Giant cell arteritis affects mainly the arterial branches arising from the aortic arch and, in particular, the extra cranial vessels. This preference alone is the basis for another name often given to this disease: temporal arteritis; this artery, which supplies blood to the tissues of the cheek-bone area, the front of the face and the parietal area of the scalp, is often affected; the involvement of this artery is the cause of one of the most feared complication of this disease, which is the loss of vision, characteristically in one eye. Involvement of the temporal artery is the reason for the most common symptoms that patients complain about: severe headache of new onset; pain on merely touching the scalp, pain on combing the hair, pain in the cheeks and/or tongue and/or throat whilst chewing and/or swallowing. As already mentioned, the ocular symptoms can be amaurosis, diplopia and visual hallucinations. In addition to these symptoms, patients can also present systemic, non-specific symptoms: fever, malaise, anaemia, weight loss. Symptoms linked to involvement of the cranial vessels are those that allow us to make the diagnosis. Although the temporal artery is the most frequently affected, other arteries can also be involved, and depending on the arteries affected, will have different symptoms. Treatment should be continued for an average of 1-2 years. More specifically: - the initial prednisone dose is 1 mg/kg/day; this dose should be maintained for a month and then gradually fall. During the dose reduction, the treatment should not be used on alternate days. At three months, the dose should be between 10 and 15 mg per day. This dose should then be reduced much more slowly. Patients with Horton's arteritis are at a higher risk of developing cardiovascular and cerebral accidents. The addition to aspirin therapy (75-100 mg daily) might be helpful in the prevention of these events. Introduction of this drug, with gastric protection, could be recommended when evaluating treatments for individual patients. Finally, given the chronic nature of steroid therapy, a bone protection with calcium, vitamin D and possibly anti-resorptive medications is always introduced.

Conclusions: The Authors have presented a case report from a patient with Horton's arteritis.

ECHINOCOCCOSIS: CASE REPORT

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Introduction: Echinococcus granulosus. Humans are the accidental intermediate host in the development cycle of hydatid disease. It is an endemic disease in the sheep and cattle raising countries Middle East, North Africa, New Zealand, Australia, and South America.

Case presentation: A 63 years male patient farmer by occupation presented to our internal and emergency ward with a mass in the left upper quadrant of the abdomen. There was left hypochondriac dull aching pain which did not shift or radiate. Patient complained of malaise with nausea, vomiting and weight loss since one year. Also there was intermittent fever every fifteen days since last six months. Physical examination showed an asymmetric abdomen and a growing lump with smooth surface in left hypochondriac, epigastric and umbilical region. There was no lymphadenopathy. Routine laboratory investigation CBC, coagulation profile, biochemistry, renal function test, liver function test and electrolytes revealed no abnormalities. Plain radiograph of the abdomen revealed a well-defined, rounded soft-tissue opacity with calcified margins in the left hypochondrium. Chest radiograph was normal. Abdominal ultrasonography showed round, well defined, cystic lesion of size 165 × 140 mm over pancreas which moving left kidney and spleen. Abdominal CT scan shows large homogenous cystic lesion in spleen measuring 20 × 22 cm loculated cyst with many septa, originating from the spleen. The cyst in the spleen appeared to fill the left quadrant of the abdominal cavity, displacing the intestines to the right, most likely suggestive of hydatid cyst. There were no cysts in other abdominal viscera. A CT scan of his chest did not show any cysts. Surgical exploration revealed a hydatid cyst occupying whole splenic parenchyma only thin rim of splenic tissue was present in inferior surface. The mass measuring approximately 250 × 200 mm was attached to left diaphragm. The cyst was resected en-bloc with the spleen. Histopathological examination showed the classic laminated cyst wall encircling many scolices with a double layer of hooklets; which is consistent with Echinococcus granulosus infection thus confirmed the diagnosis of splenic hydatid cyst. On cut section there was hydatid sand and fluid around 3.9 litres.

Discussion: Hydatid disease is a major health problem worldwide, mainly in sheep- and cattle-raising areas of the world. Hydatid disease of spleen is a rare clinical condition as even in the endemic region the frequency is reported to be 0.5–4% of abdominal hydatid diseases. The most common sites of hydatid disease are the liver (60–70%), which acts as a first filter and the lungs (10–40%), which acts as second filter. Primary infestation of spleen through the arterial route. Splenic hydatid disease may also arise with retrograde spread of parasites via the portal and splenic veins bypassing the lung and liver. The hydatid cyst consists of three layers. The presentation of splenic hydatid disease can vary greatly. Splenic hydatid cysts are usually asymptomatic, solitary slow-growing and incidentally diagnosed. Severe anaphylactic reactions due to rupture of the cyst are also reported leading to fever, pruritus, dyspnoea, stridor and oedema of the face. Pre-operative diagnosis may be difficult due to the similarity of the presenting symptoms and the radiological findings to those of other more commonly encountered lesions of the spleen. The Casoni skin test is sensitive but not specific. Radiological diagnosis by plain X-Ray, Ultrasonography (USG), CT and MRI can also be used to diagnose hydatidosis. Serological tests are highly sensitive and specific for Echinococcosis. The standard treatment is splenectomy as complete resection removes all parasitic and pericystic tissues. Antihelminthic drug therapy using Benzimidazole chemotherapy drugs with Albendazole 10–15 mg/kg/day for one month or Mebendazole 40–50 m/kg/day for 3–6 months, in addition to Praziquantel 40 mg/kg/wk for 2 weeks pre and postoperative to reduce the chance of anaphylactic shock and decrease the tension in the cyst wall are used. We performed total splenectomy.

Conclusion: The splenic hydatid cyst may become a challenging surgical problem. Computerised tomography scan is the most sensitive investigation for diagnosis. The anatomical relations of splenic hydatid cyst should be demonstrated before surgery on account of varied presentations. Although the management must be individualized for each patient, a surgical resection is the best curative procedure.

PRE/POST-LYSIS PAPS CORRELATION. PROMP STUDY. COMPARATIVE ANALYSIS WITH STUDENT TEST IN 30 PATIENTS WITH VENOUS THROMBOEMBOLISM. THREE-YEAR EXPERIENCE (2022-2024)

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Introduction: The PROMP study on PRe-pOstlysis systolic arterial pulMonary Pressure enrolled 30 patients, aged between 48 and 82 years with venous thromboembolism (central pulmonary embolism) and hospitalized in the period January 2012 to December 2024. The clinical onset was characterized in all patients with severe respiratory failure (value arterial blood gas levels of pO2 <60 mm Hg), on occasion accompanied by chest pain, confusion, hemodynamic instability (SBP < 90 mm Hg). All patients underwent: a thoracic-abdominal and pelvic CT with contrast medium, pulmonary angiography with loco-regional fibrinolysis in combination with heparin sodium in peripheral vein, mechanical thrombectomy; echocardiography pre-lysis and post-lysis at 30 days with measurement of systolic pulmonary artery pressure. In all patients, systolic pulmonary artery pressure (PAPs) was measured pre-lysis and post-lysis at 30 days according to the formula in mm Hg measured at doppler: 4XTRV2 + RAP, where TRV is the speed of tricuspid regurgitation and RAP the right atrial pressure. We remind you that pulmonary hypertension is mild if the PAPs is between 25 and 35 mm Hg, moderate between 36 and 45 mm Hg, severe at > 46 mm Hg. A comparative analysis was performed for continuous variables with parametric Student "t" test to see if there is a significant relationship between PAPs values pre-lysis and post-lysis measured in mmHg.

Scope of the work: The "PROMP" study has the following objectives: to verify any relationship between the values of pre-lysis and post-lysis PAPs at 30 days in 30 patients enrolled in the "PROMP" study during the period January 2022 to December 2024, and to assess the statistical significance found by applying the Student "t" test as a parametric test of comparative analysis for continuous variables, to determine whether the relationships of the variables considered could be due to chance.

Materials and method: OLOGY In the 30 patients enrolled with central pulmonary embolism, the values of pre-lysis and post-lysis PAPs at 30 days were examined and compared by applying the "t" test of Student. The test then calculated the relative value (RV) of the index t to be associated with the difference found using the following formula: t = (M1-M2) / √DS12 /N1 + DS22 /N2.

Analysis of results: The "t" test of Student applied to 30 patients shows a highly significant correlation (p <0.001) of the two variables examined (PAPs values pre-lysis and post-lysis at 30 days), and therefore not attributable to chance. In fact, the "t" value obtained was 5.14 and the VC (critical value) of "t" of p=0,001 is 3.65 with GL=29.
Discussion: The data obtained suggest that the co-variation of the PAPs values pre-lysis and post-lysis in the 30 patients enrolled in the "PROMP" study expresses a highly significant difference in the clinical significance lies in the efficacy of loco-regional thrombolysis associated with mechanical thrombectomy which was followed by a reduction of systolic pulmonary artery pressure values post-lysis in 30 days in 30 patients enrolled in the study "PROMP".
Conclusions: ; The "PROMP" study showed that in the group of 30 patients with venous thromboembolism (central pulmonary embolism) there is a highly significant correlation between the two variables considered: pre-lysis and post-lysis PAPs. This correlation shows an absolute positive correlation according to the Student "t test for comparative analysis and expresses not a random association but a close correlation between the PAPs values pre-lysis and post-lysis in the 30 patients with central pulmonary embolism.

CORRELATION BETWEEN CK RATIO AND PRIMARY CANCER SCREENING: CABOTO STUDY

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Introduction: In the three year period 2022-2024, the authors enrolled 30 patients, aged between 45 and 83, 20 female and 10 male, with CK-MB values equal or superior to those of total CK. In the 30 patients an acute coronary disease was excluded. All patients underwent total body CT scan with contrast material and in all patients an undetected and asymptomatic neoplasm was identified as an incidental finding. The CABOTO study, an acrostic deriving from "creatine kinase (ck) mb - to - total ck ratio", indicates in the CK - MB an indicator for the screening of neoplasia. Therefore, a database was created with Microsoft Access © called CABOTO. The database contained the following fields: 1) patient number, 2) CK ratio values, 3) presence and type of neoplasia. All the patients were analyzed, during the recruitment, according to the above mentioned 3 fields, collected from time to time in masks created in "structure visualization" and "visualization data sheet" mode as allowed by the database program. A comparative analysis was performed for nominal variables with Cochran "Q" test to verify if the CK ratio is statistically significant.
Aim of study: The CABOTO study proposes the following objectives:1) to verify the CK ratio values in the 30 patients with unrecognized neoplasia enrolled in the period 2022-2024;2) verify the statistical significance found by applying as a benchmark test for nominal variables the "Q" test by Cochran to determine if the degree of lysis takes statistical significance.
Materials and methods: The 30 patients enrolled were examined according to the fields of the database created with Microsoft Access © called "CABOTO". The 3 comparative nominal variables, "K conditions", were named with the letter A (CK ratio <1)), B (CK ratio = 1), C (CK RATIO> 1). The 30 patients (100%) presented the C condition (CK ratio> 1). The 30 patients involved in the CABOTO study were listed in the left column. The presence of variables examined in conditions A, B, C, in the 30 patients it is reported in the 3 central columns. The sum of the number of variables present in each enrolled patient is indicated by the letter y and the relative high value in the square is indicated by the letter y2 in the 2 columns on the right. With xA the sum of the number of variables analyzed in column A is indicated, with xB the sum of the number of variables examined in column B, with xC the sum of the number of variables examined in column C. With xA2, xB2, xC2 are shown the related squares. With y, y2, z the sum of the number of conditions present in each patient, the square of their sum, the sum of their squares are respectively indicated. With the abbreviation tQ the name of the Cochran test is indicated applied to the 3 conditions according to the formula xA2 + xB2 + xC2. The formula for the calculation of X2 is shown at the bottom right. At the bottom center are the obtained values of X2 with the values of DF (Degrees of Freedom = k-1) and the high statistical significance (p <0.001) obtained on the basis of the DF and the critical value (VC) of the X2 that for p = 0.001 it is 13.86.
Analysis of results: The Cochran Q test applied to the 30 patients, shows, to the comparative analysis, highly significant differences (p <0.001) and, therefore, not attributable to the case. In fact, the value of X2 obtained is 60 and the VC (critical value) of X2 for p = 0.001 is 13.86 with GL = 2.
Discussion: Accumulating evidence indicated that the estimated activity of CK-MB could be falsely increased in patients with neoplasms rather than myocardial disease. The spuriously high expression CK-MB could be explained by the interference of CK-BB or maro-CK, as the immunoinhibition method was used for the CK-MB activity determination. This aberrancy of overestimated CK-MB expression in patients without obvious thoracic symptoms may confuse physicians, leading to inappropriate diagnosis and unnecessary examination and management. Here, we conversely take advantage of the characteristics of overestimated CK-MB expression and high CK-MB-to-total-CK ratio in patients with potential neoplasms to evaluate the efficacy of CK-MB-to-total-CK ratio as a laboratory indicator for primary cancer screening. According to the literature review, the elevation of CK-BB activity had been observed in various malignancies, including lung, breast, liver, colon, and prostate cancers. It was believed that the enhanced CK-BB activity could originated from the release of enzyme due to tumor necrosis. In tumorigenesis, increased localization of CK-BB to nuclear matrix was observed in colon cancer. Besides, unmethylation of the CK-BB promotor and therefore higher CK-BB mRNA expression in hematological cancer cell lines was identified.

THE PENSE STUDY: CORRELATIVE ANALYSIS IN 10 PATIENTS WITH VENOUS THROMBOEMBOLISM. BIENNIAL EXPERIENCE (2023-2024)

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Introduction: The PENSE study, an acronym for "Pulmonary Embolism and Neuron-SpEcific enolase", enrolled 10 patients, aged between 45 and 78 years, with venous thromboembolism (central pulmonary embolism) and increased serum levels of NSE (V.N. 0-16.3 mg/ml), admitted in the two-year period January 2023 - December 2024. All patients underwent: CT skull-neck-thoraco-abdomino-pelvic with contrast medium; pulmonary angiography with loco-regional fibrinolysis; bronchiolo-alveolar lavage with search for neoplastic cells; fibrobronchoscopy; pre-discharge echocardiography with measurement of pulmonary artery pressure (PAP); venous echocolordoppler of the lower limbs; search for thrombophilic and neoplastic markers which showed an isolated increase in all patients of the NSE marker at the time of admission. In all patients involved in the PENSE study, the search for unknown neoplasms had a negative outcome; those patients with venous thromboembolism associated, after diagnostic integration with total body CT with contrast medium, with neoplastic pathology were excluded from the study. Therefore, a database called PENSE was created with the following fields: 1) patient number, 2) arterial pO2 at admission, 3) arterial pCO2 at admission, 4) clinical picture of central PE, 5) loco-regional fibrinolysis procedure, 6) state of consciousness, 7) SBP at admission, 8) NSE dosage on day 1, 9) NSE dosage on day 8, 10) arterial pO2 on day 8, 10) SBP on day 8. All patients (Table 1) showed an arterial pO2 at admission < 60 mmHg, underwent intra-arterial loco-regional fibrinolysis, presented confusional state, increased NSE values at admission (day 1), reduced NSE values and increased arterial pO2 on day 8.
Purpose of the work: The PENSE study has the following objectives: to verify any existing relationships between the values of arterial pO2 at admission (1st day) and the values of NSE at admission (1st day) in the 10 patients enrolled in the PENSE study; to verify the statistical significance found by applying the Pearson parametric test as a correlative analysis test for continuous variables to establish whether the relationships of the variables considered are due to chance.
Material and method: The 10 enrolled patients were examined according to the fields of the database called PENSE which compares the values of arterial pO2 on day 1 (independent variable A) with the values of NSE on day 1 (dependent variable E) in the 10 enrolled patients. The Pearson test correlates the independent variable A (arterial pO2 on day 1) with the dependent variable E (NSE on day 1) in the 10 patients enrolled in the PENSE study and for the calculation the formula of the Pearson correlation coefficient "r" is applied: $\Sigma(A- \bar{A}) (E- \bar{E}) / \sqrt{\Sigma(A- \bar{A})2 \Sigma (E- \bar{E})2}$. The Pearson test shows a highly significant correlation (p<0.001) of the two variables examined (arterial pO2 values on day 1 and NSE values on day 1) and, therefore, not attributable to chance. In fact, the value of "r" obtained is 0.99 and the VC (critical value) of "r" for p=0.001 is 0.89 with GL=9.
Analysis of results: The Pearson test shows a highly significant correlation (p<0.001) of the two variables examined (arterial pO2 values on day 1 and NSE values on day 1). In fact, the value of "r" obtained is 0.99 and the VC (critical value) of "r" for p=0.001 is 0.89 with GL=9.
Discussion: The increase in NSE values on day 1 in the 10 enrolled patients correlates with the reduction in arterial pO2 values on day 1 because severe arterial hypoxia can cause transient neuronal suffering with an increase in NSE values.
Conclusions: The PENSE study demonstrated that in the group of 10 patients with central pulmonary embolism and increased serum NSE levels there is a

correlation, with absolute positive concordance, between the two variables considered, NSE and arterial pO2, in agreement with the experiences of Nguyen, Yang, Kärkelä, Reisinger, Rech, Ekmektzoglou, Wunderlich, Chekhonin, Kecskes, Celtik, Liu, Szturmowicz.

AN AUTOIMMUNE CAUSE OF ATRIO-VENTRICULAR BLOCK

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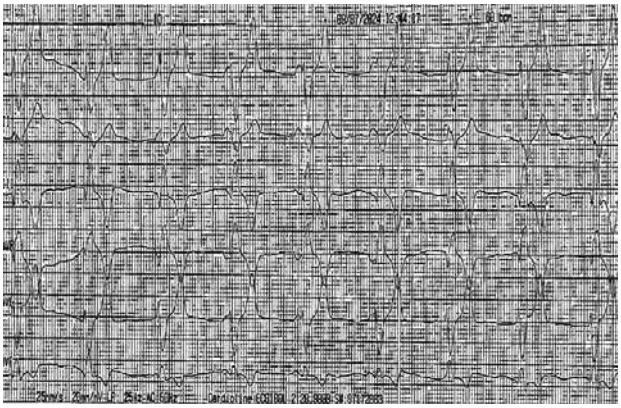
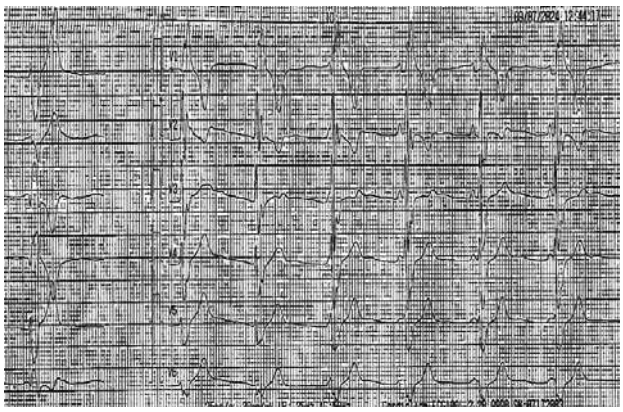


A 62-year-old male diagnosed with myasthenia gravis (MG) positive for antibodies against acetylcholine receptors (AchR-Ab), was admitted to the internal medicine department due to a worsening of symptoms. Over the past 15 days the patient experienced a rapid progression of severe dysphagia and weakness, with two episodes of presyncope, unresponsive to home-administered steroids, despite his chronic treatment regimen consisted of pyridostigmine. Apart from arterial hypertension, no other comorbidities were present. At admission, the patient exhibited severe neurological scores (MGFA IVb, MG-ADL 10, QMG 20), with regular vital signs (blood pressure 120/80 mmHg, heart rate 75 bpm, SpO2 98%, GCS 15). However, the electrocardiogram (EKG) revealed an advanced atrioventricular (AV) block. The patient promptly underwent permanent pace-maker (PMK) implantation, received supportive care with parenteral nutrition and was started on eculizumab in addition to pyridostigmine.
MG is a chronic autoimmune disease primarily affecting skeletal muscle by producing antibodies that bind to receptors at the neuromuscular junction, in wich the most common antibodies are AchR-Ab. In 60-70% of patients, there is an abnormality of the thymus, with thymoma occurring in 20%.Treatment of MG typically requires long-term use of acetylcholinesterase inhibitors and immunosuppressive agents. Bradyarrhythmias are a possible consequence in patients treated with parasympathomimetic agents. However, 16% of MG patients have cardiac involvement, with arrhythmias being the most common manifestation (8%).
Specifically, several cases of pyridostigmine-induced bradycardia and heart block have been documented in the literature. In a previous case report, a patient with pyridostigmine-induced high-grade AV block and syncope was treated with hyoscyamine, a muscarinic antagonist, resulting in complete resolution. In a similar case, another patient was treated with hyoscyamine without success, requiring a permanent PMK implant. In another case of complete heart block, the patient avoided long-term PMK placement by discontinuing pyridostigmine treatment, resulting in the reversion to sinus rhythm. Moreover, other medications involved in MG treatment could may contribute. Immunosuppressive agents may affect cardiac autonomic function (CAD), increasing the risk of arrhythmia. In particular, azathioprine has been associated with an increased incidence of atrial arrhythmias. Corticosteroids also influence CAD. Specifically, prednisone significantly reduces sympathetic nerve activity. Moreover, steroids may predispose to hypokalemia or other electrolyte disturbances, which can induce arrhythmias.
In addition, MG itself can show cardiovascular involvement. EKG abnormalities are common in patients with MG, particularly in severe forms of the disease. A frequent cause of cardiac manifestations in MG is myocarditis, that may contribute to cardiac conduction abnormalities. Moreover, malignant arrhythmias are often not linked to underlying coronary artery disease. Similarly, heart failure often lacks a clear etiology, suggesting a myocardial dyskinesia MG related. Any other cardiac complications may be secondary to skeletal muscle exhaustion. Additionally, myocarditis often coexists with concomitant skeletal muscle myositis. Another potential cause of cardiac involvement is the presence of antibodies that crossreact with skeletal and heart muscle. Some patients, indeed, have anti-striational antibodies. Finally, immune activation and the related chronic inflammation appear to be the main factors responsible for CAD in MG. The overactivation of sympathetic nervous system, results in increased sympathetic outflow to the heart and vasculature, as well as decreased parasympathetic outflow to the heart. Another possible mechanism involves the presence of autoantibodies targeting nicotinic acetylcholine receptors in autonomic ganglia, or cross-reactivity with skeletal muscle nAChR, with some idiotypes also binding to ganglionic AChR. Studies have shown a sympathovagal imbalance favoring sympathetic tone, a predisposing factor for arrhythmias, and parasympathetic insufficiency. Finally, it is possible that the same autoimmune process that causes MG, affects cardiac conduction, and this may be aggravated by the use of pyridostigmine.
Our patient was subsequently subjected to coronary angiography and no underlying coronary disease was found. Moreover, historically he showed transient, mildly elevated creatine kinase (CK) levels, that can be observed in patients with anti-titin antibodies, revealing a concurrent underlying myositis.
In conclusion, determining which is the etiology responsible for cardiac manifestations in MG is challenging, and in most cases it remains unknown. Nevertheless, in patients with MG who present heart block and bradyarrhythmias while currently being treated with pyridostigmine, medication-induced arrhythmia should always be considered.



MULTIDISCIPLINARY SKILLS IN ACUTE CARDIOGENIC PULMONARY EDEMA: INTEGRATION OF KNOWLEDGE FOR EFFECTIVE DIAGNOSTIC-THERAPEUTIC MANAGEMENT

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Background: A critical factor in the management of acute cardiogenic pulmonary edema is the multiplicity of professionals involved in the diagnostic-therapeutic path, and therefore the need to integrate different knowledge and skills and to converge on better care objectives.
Clinical case: A seventy-year-old patient with post-infarction dilated cardiomyopathy, diabetes mellitus, and previous lung cancer treated with surgery and subsequently with polychemotherapy, arrives in the emergency room with acute pulmonary edema with hypertensive crisis and oliguria. Laboratory findings show mild normocytic-normochromic anemia, very high troponin and BNP, mild renal failure with hyperkalemia, moderately elevated D-dimer. Blood gas analysis shows severe hypoxemia and minimal hypocapnia, without acidosis or alkalosis. The ECG shows atrial fibrillation tachyarrhythmia with high ventricular response and complete left bundle branch block. Chest X-ray shows extensive interstitial-alveolar edema with a dubious bronchopneumonic focus. A chest CT scan is therefore performed, which confirms the extensive pulmonary edema associated with a neoformation likely of neoplastic nature. An echocardiogram was performed and revealed a picture of dilated cardiomyopathy with an ejection fraction of 45%, mid-apical hypokinesia, moderate-severe mitral and tricuspid valve insufficiency. Treatment was immediately started with high-dose furosemide, nitroglycerin, morphine, amiodarone and digoxin intravenously; low molecular weight heparin subcutaneously. After being stabilized, the patient was admitted to intensive care where he was further subjected to non-invasive mechanical ventilation with CPAP, levosimendan infusion and ultrafiltration session. With the restoration of sinus rhythm on

the electrocardiogram and the resumption of diuresis, a gradual clinical-objective improvement was observed; blood gas analysis was also within normal limits, although the patient was maintained on medium-flow oxygen therapy. In consideration of the radiological resolution of the acute pulmonary edema picture, a targeted therapy for heart failure is set up, also providing the patient with diagnostic-therapeutic indications for mitral-tricuspid valvulopathy and the probable recurrence of the lung neoplastic disease.
Conclusions: Acute cardiogenic pulmonary edema causes a severe alteration of gas exchange with an in-hospital mortality of 5-20%. It is characterized by high filling pressures of the left heart, resulting in an increase in pressures at the level of the pulmonary capillaries and an accumulation of intra-alveolar fluid. This occurs in the presence of heart disease (acute coronary syndromes, tachyarrhythmias, myocarditis, acute valvular disease, Takotsubo cardiomyopathy), but also in cases of fluid overload, hypertensive crisis and acute renal failure. The clinical presentation of acute heart failure can be classified based on the adequacy of peripheral perfusion ("warm patient", "cold patient") and the presence of congestion ("dry patient", "wet patient"). The wet patient corresponds to the picture of acute cardiogenic pulmonary edema, the cold patient to that of cardiogenic shock. This categorization predicts prognosis and directs clinical management. Acute cardiogenic pulmonary edema represents a multidisciplinary challenge to be faced in a team, with solid cardiological management. Only through the identification of shared management paths, which involve numerous specialists in the hospitalization and post-hospital phase, is it possible to create a system suited to the needs of patients, which includes rapid clinical evaluation and diagnosis as well as timely initiation of therapy, with choices who know how to combine rigor and clinical appropriateness.

HIGH-SENSITIVITY TROPONIN AND ACUTE CORONARY SYNDROMES: USEFULNESS AND INDICATIONS FOR USE FOR AN APPROPRIATE DIAGNOSTIC-THERAPEUTIC PROCESS

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Background: Acute coronary syndrome is confirmed by the increase and/or reduction of cardiac troponin (cTn) values, in a clinical context of myocardial ischemia. In patients with symptoms of myocardial ischemia, high cTn concentrations are related to the extent of coronary artery disease and to a lower coronary perfusion. Therefore, they identify patients at high risk of cardiac events.
Clinical case: A sixty-year-old patient, smoker, hypertensive, dyslipidemic, obese, hypothyroid and with previous alcoholic habits, is taken to the emergency room for dyspnea at minimal effort, poorly productive cough and asthenia. Familiarity for ischemic heart disease and type 2 diabetes mellitus. He denies angor, fever and other significant signs and/or symptoms. The standard vital parameters are all within normal limits. The general and system-specific objective examination is also within normal limits. Troponin at admission is within the normal range, but will be significantly increased at a subsequent control blood test two hours after time zero, also performed due to the insidious appearance of poorly defined, subcontinuous chest pain with apparently pleuritic characteristics. Routine blood chemistry shows in particular alterations in liver function such as liver stasis, neutrophilic leukocytosis, increased inflammation indices and mild macrocytic anemia. The ECG documents sinus tachycardia with sporadic ventricular extrasystoles (but sometimes bigeminy) and incomplete right bundle branch block, with nonspecific anomalies of the ventricular repolarization phase. Chest X-ray shows cardiomegaly and unilateral elevation of the diaphragm, with a layer of right mid-basal pleural effusion. The echocardiogram documents hypertensive heart disease with dilated evolution, pericardial leaflet separation, moderate aortic valve stenosis-insufficiency, mild ectasia of the aortic bulb and ascending aorta, indirect signs of pulmonary arterial hypertension. A chest CT scan without contrast medium confirms the aforementioned radiological and echocardiographic findings. The patient is admitted to a cardiology unit, where he will undergo coronary angiography and subsequent percutaneous myocardial revascularization, due to the presence of right-dominant stenosing coronary atheromatous disease.
Conclusions: Having become the biochemical standard for the diagnosis of acute coronary syndrome, elevated troponin is associated with an unfavorable prognosis. More recent tests than the standard ones are preferable, highly sensitive for cardiac troponin (hs-cTn) and precise; hs-cTn should be measured at onset and 2-3 hours later. The increase in cTn alone should not dictate the diagnostic-therapeutic pathway. It is advisable to integrate cTn into an evaluation algorithm based on pre-tests of probability of coronary artery disease. In subjects with positive cTn and high a priori probability (symptoms, risk factors, medical history, electrocardiogram, echocardiogram) it is reasonable to start antithrombotic treatment and proceed with coronary angiography, which should be performed quickly if the risk of short-term ischemic events is high, while it can be postponed or cancelled if the probability of these events is low and the clinical outcome is favorable. On the contrary, patients with high cTn and low pre-test probability of coronary artery disease generally do not benefit from an aggressive treatment strategy. Instead, the approach to patients without cTn elevation, but with high pre-test probability of coronary artery disease, should be aimed at recognizing other global risk indicators. The latest generation, highly sensitive cTn measurement allows the presence of myocardial damage to be recognized in patients with known or unknown cardiovascular disease. The doctor's eye is thus equipped with a magnifying glass capable of identifying the damage before it leads to significant functional consequences.

CONTROL OF CORE TEMPERATURE IN MAJOR ORTHOPEDIC SURGERY AND NEUROTRAUMATOLOGY IN OLD PATIENTS WITH DELIRIUM AND EVALUATION MINI MENTAL TEST

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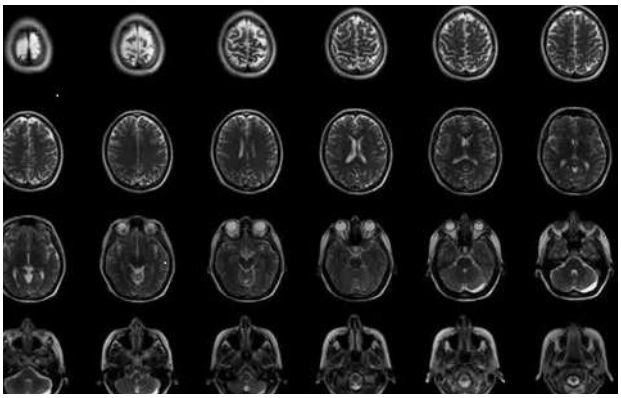
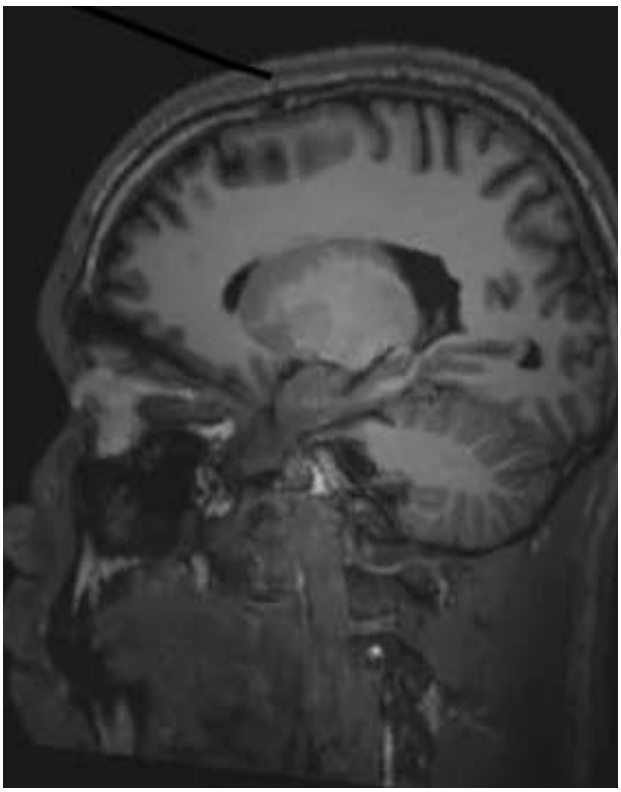
Randomised study of geriatric patients aged between 75±85 divided into two groups with and without intraoperative heating undergoing major orthopaedic surgery. 46% of patients manifest delirium in the postoperative stage. From the study, postoperative pain is correlated to the onset of delirium in the postoperative stage. In major orthopaedic surgery in geriatric patients (N=25) aged between 75±85 with intraoperative heating, the incidence of overall delirium is 15%; delirium with a single event in the controls during the stay 40%; severe delirium 5%; delirium in the postoperative stage 15%; delirium on discharge 5%.
In major orthopaedic surgery in geriatric patients (N=25) aged between 75±85 without intraoperative heating, the incidence of overall delirium is 15%; delirium with a single event in the controls during the stay 40%; severe delirium 5%; delirium in the postoperative stage 15%; delirium on discharge 5%.
Pharmacological treatment of delirium: with intraoperative heating quetiapine 25 ½ or 1 pill twice/day,Haloperidol 8 drops; without intraoperative heating quetiapine 25 1 pill twice/day and Haloperidol 1 dose i.m.; without intraoperative heating with mini nutritional assessment low olanzapine 1 pill once/day, quetiapine 25 2 pills once/day, Haloperidol 1 dose i.m
Preoperative IADL score in geriatric patients (N=50 pt.; aged between 75±85) undergoing major orthopaedic surgery is 5±4.
Postoperative IADL score in geriatric patients group A (N=25 pt.) undergoing major orthopaedic surgery with intraoperative heating is 3±2.
Postoperative IADL score in geriatric patients group B (N=25 pt.) undergoing major
Orthopaedic surgery without intraoperative heating is 2±1.
In the 50 patients before the operation, the mini nutritional assessment is 23±24, on discharge in group A with intaroperative heating the mini nutrional assessment is 21±20, in group B without intaraoperative heating, the mini nutritional assessment is 19±18.
Postoperative pressure sores in geriatric patients group A undergoing major orthopaedic surgery with intraoperative heating, the incidence is: 15% sacrum pressure lesions first stage; 5% sacrum pressure lesions second stage. Postoperative pressure sores in geriatric patients group B undergoing major orthopaedic surgery without intraoperative heating, the incidence is: 8% sacrum pressure lesions fourth stage; 10% sacrum pressure lesions third stage. Mini mental test postoperative score in geriatric patients group A is 22±18 and in group B is 18±15. The delirium is most freqent in geriatric patients. Mild Perioperative Hypotermia- N Engl J Med-2000-336-1730.





PURPLE URINE BAG SYNDROME (PUBS): WHEN COLOURS DON'T LIE

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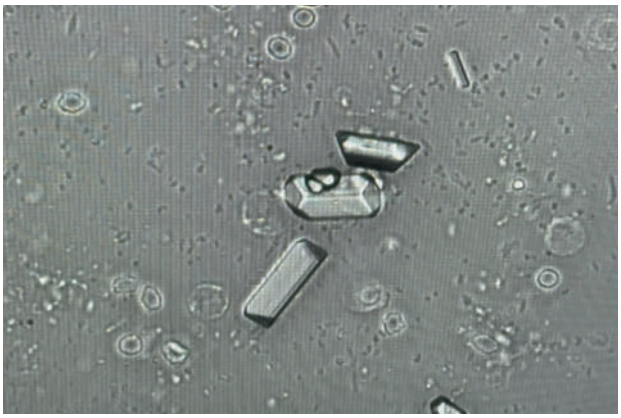
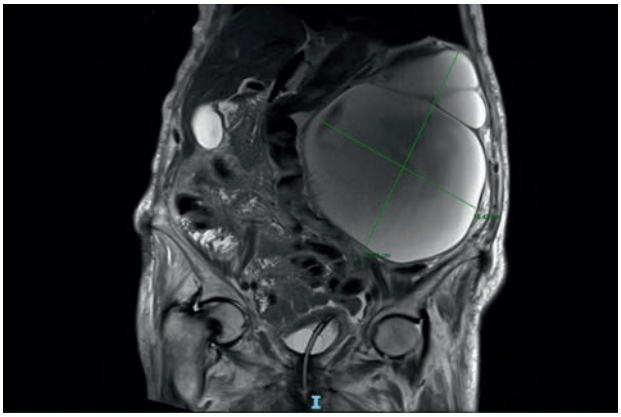
Introduction: Purple urine bag syndrome (PUBS) is a condition characterized by purple discoloration of urine; it is rarely seen in clinical practice and may signify pathology. It is often associated with urinary tract infections occurring in catheterized patients, generally elderly females with severe comorbidities and chronic constipation. Urinalysis is usually characterized by an alkaline pH; while urine culture shows the presence of Gram-negative bacteria with sulfatase and phosphatase activity which have a role in the formation of indirubin and indigo. By the way, these pigments cause discoloration.
Case description: We present the case of an 88-year-old woman admitted from the ED to our Internal Medicine ward for nausea and vomiting. Her past medical history included chronic kidney disease (CKD), anaemia, hypertensive cardiopathy, and severe chronic left kidney hydronephrosis of unknown origin. On examination, she was afebrile, had epigastric pain, had hypotension and sinus tachycardia. Furthermore, she had an indwelling urinary catheter since admission to the ED.
Biochemical investigations revealed severe dehydration with azotemia91mg/dL and elevated serum creatinine1,84mg/dL with eGFR26ml/min/1,73m2(CKD-EPI2021). Her white blood cell count (WBC) was6x10^3/µL, and her C-reactive protein (C-RP) was0.11mg/dL, with both values remaining stable throughout the admission period (Table1). Also, urine culture was positive for P. mirabilis; however, we decided to treat the patient only for acute dehydration with intravenous fluids and she soon began to feel better.
Moreover, we decided to perform a magnetic resonance imaging of the abdomen to better characterize the left kidney, which appeared cystic on bedside ultrasound. The scan showed features of a voluminous lobulated formation with a fluid signal, which extended from the left renal lodge to the entire left hemiabdomen reaching up to the iliac fossa; the overall dimensions were 164 x 170 mm on the axial plane and 207 mm of cranio-caudal extension (Figure 1). This finding was suggestive of severe inveterate hydronephrosis (grade IV) with clearly dilated pyelico-calyceal cavities and marked atrophy of the renal parenchyma. The formation had mass effect displacing intestinal loops, stomach, pancreas and spleen.
Therefore, we consulted a urologist to surgically address the formation but eventually, the patient refused any surgical treatment.
On the seventh day of catheterization, we saw a purplish discoloration of the urine bag. Urinalysis was characterized by a pH 8.0, absent nitrites, leukocyturia, hematuria while urine microscopy showed the presence of tricalcium phosphate crystals (Table 1)(Figure 2-3).
Discussion: PUBS is an uncommon condition characterized by the purple discoloration of urine. It is mostly seen in patients with an indwelling urinary catheter, although purple diaper syndrome has also been described.
There are not definitive data on PUBS epidemiology. A recent meta-analysis reviewing cases from the last three decades reported a mean age of 75.6 years with a slight female prevalence and an overall mortality rate of 6,9%.
The predisposing factors seem to be: advanced age, use of an indwelling urinary catheter, chronic constipation, high-protein intake, intestinal hypomobility and small intestine bacterial overgrowth.
The pathophysiology of PUBS originates from the dietary absorption and digestion of tryptophan. A certain amount of this amino acid gets intact to the small intestine, where it is metabolized to indole by resident bacteria. Indole reaches the liver through portal circulation, and it is conjugated to indoxyl sulphate. This compound is bound to albumin and excreted into the urinary system; here, if phosphatase/sulfatase-producing bacteria are present, it is further metabolized to indoxyl and may convert to indigo and indirubin through oxidation. The purple colour seems to be the result of the combination of the red pigment, indirubin, and the blue one, indigo.
Pseudomonas aeruginosa, Proteus mirabilis, Morganella morganii, Escherichia coli, Providencia stuartii and Klebsiella pneumoniae have been identified to be the most common bacteria with sulphatase and phosphatase activity.
Learning points: PUBS is a rare disease and there is not a standard approach to it. It is often considered a sign of urinary tract infection (UTI) and treated with antibiotic therapy; however, some authors consider PUBS to be just a manifestation of bacterial colonization of the catheter and the urinary tract rather than infection.
We considered our patient as having asymptomatic bacteriuria (ASB) as she didn't meet CDC criteria for catheter associated urinary tract infection (CAUTI) and so, we opted to not introduce an antibiotic therapy to avoid her any harm from unnecessary therapy and further selection of drug resistant bacteria.
Keywords: urinary infection, purple urine, elderly, indirubin.





Urinalysis		Laboratory tests	Day 1	Day 7
pH	8	Hb	7.7 g/dL	7,7 g/dL
Leukocyturia	40 – 60 p/HPF	WBC	6,1 x 10^3/µL	5 x 10^3/µL
Nitrites	Absent	Creatinine	2,24 mg/dL	1,78 mg/dL
Red blood cells	60 – 100 p/HPF	eGFR (CKD-EPI 2021)	21 ml/min/1,73 m^2	27 ml/min/1,73 m^2
Urine protein	30 mg/dL	Urea	127 mg/dL	74 mg/dL
Urine glucose	0.0 mg/dL	Na^+	143 mmol/L	141 mmol/L
HCO_3^-	19,4 mmol/L	K^+	3,3 mmol/L	3,7 mmol/L
Crystals	Tricalcium phosphate	Ca^{2+}	8,48 mg/dL	7,78 mg/dL
		C-RP	0,21 mg/dL	0,19 mg/dL
		PTH	119.6 pg/mL	

24. HYPOGLYCEMIA: AN INSIDIOUS SYMPTOM IN THE BARIATRIC PATIENT

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Introdution: Obesity is a chronic, relapsing disease that represents a global epidemic. To date, bariatric surgery is the most effective and cost-effective treatment for long-term morbid obesity. Roux-en-Y gastric bypass (RYGB) is one of the most performed bariatric surgeries, with excellent long-term results. However, approximately one-third of patients may experience weight regain over time, as well as dumping syndrome. Both conditions are difficult to manage and require a multidisciplinary and personalized approach. Dietary modifications, behavioral interventions, and medications are the first therapeutic step. Revision surgery is the traditional approach when non-invasive treatments fail. However, reoperations can be technically difficult and are associated with increased morbidity and mortality.
Case report: A.G. a 39-year-old man came to our clinical observation in day hospital to undergo clinical tests for postprandial hypoglycemia in the suspicion of dumping syndrome. With an initial weight of about 120 kg, being affected by metabolic syndrome with hyperinsulinism and insulin resistance, he underwent mini-gastric bypass surgery with marked weight loss. No supplementary replacement therapy was prescribed. No eating disorders were reported. After a period of well-being of about 18 months, following a large meal during a party, he showed episodes of melena until severe normochromic and normocytic anemia and syncope were found, therefore, the patient was hospitalized. The admission blood tests confirmed anemia for which he underwent urgent esophagoduodenoscopy with the finding of ischemic ulcer and active bleeding involving the surgical anastomosis subjected to injection and thermal hemostasis and colonoscopy, within the norm. He was a candidate for re-do surgery with conversion of mini gastric bypass to gastric bypass (RYGB) with further weight loss. After 5 months from surgery, he reported the appearance of multiple episodes of severe hypoglycemia despite frequent meals of small quantities during the day (about 6-8) and persistent diarrhea. Hypoglycemia occurred approximately 2 hours after the meal, up to blood glucose values below 30 mg/dl, with suggestive symptoms. An oral glucose load test was performed which showed altered values already at 60 minutes with an insulin peak and altered glycated hemoglobin values. Type 2 diabetes was diagnosed.
Conclusion: Dumping syndrome is a condition that can occur in patients who have undergone bariatric surgery, particularly gastric bypass. In patients with dumping syndrome, the bolus passes too quickly from the stomach to the small intestine, due to a reduced capacity of the gastric sac or incorrect eating habits, which leads to the onset of chronic malabsorption syndrome and persistent diarrhea. There are two different forms of symptoms: one called "early", which occurs less than an hour after a meal, and one called "late", which appears only 1-3 hours after a meal. To diagnose dumping syndrome, an objective examination and evaluation of the clinical history are sufficient. Blood tests can determine whether the patient, especially after meals containing sugar, suffers from reactive hypoglycemia, which can sometimes be confused with reactive hypoglycemia due to hyperinsulinism. It is essential to make a differential diagnosis and establish a dietary regimen that limits the possibility of hypoglycemia to a minimum.

25. A CASE OF MULTIDISCIPLINARY MANAGEMENT OF THE PATIENT WITH PULMONARY-RENAL SYNDROME

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Introdution: Pneumorenal syndrome is the association of diffuse alveolar hemorrhage and rapidly progressive acute glomerulonephritis, often the consequence of numerous pathologies, including some autoimmune disorders, such as vasculitis. The initial diagnosis can be complex and a significant number of patients rapidly deteriorate. It is essential to make a differential diagnosis to characterize the clinical picture and choose the best therapy.
Case report: A 55-year-old man was admitted to the Emergency Department of a primary care hospital for the onset of edema of the lower limbs, hemoptysis, worsening dyspnea, and asthenia for about a week. No new medications had been taken in recent months, nor had any recent infections been reported. The anamnesis reported recent radiotherapy treatment for prostatic adenocarcinoma, arterial hypertension, and obesity. The objective findings were acute respiratory failure type I and bilateral alveolar hemorrhage on imaging, while laboratory tests showed a picture of acute renal failure, alteration of inflammation indices, normocytic normochromic anemia with microhematuria and proteinuria compatible with nephritic syndrome. Hospitalized in Internal Medicine, he underwent antibiotic therapy, low-flow oxygen therapy and blood support, however, in relation to the still unclear and mild clinical picture, corticosteroid therapy was not administered. As the days passed, the clinical course was characterized by a very rapid decline with acute anemia not responsive to blood support secondary to massive hemoptysis, severe type I respiratory failure subjected to NIV, emergency hemodialysis treatment for acute renal failure not responsive to medical therapy. A diagnosis of pneumorenal syndrome was made, and a complete antibody panel was sent elsewhere, making the patient a candidate for urgent plasmapheresis, however with little clinical improvement. In relation to the severe clinical picture, methylprednisolone 1 g was administered for 3 consecutive days and an ultrasound-guided renal biopsy was indicated, with benefit especially from a respiratory point of view. Antibody positivity for p-ANCA antibodies led to the diagnosis of microscopic polyangiitis, therefore therapy with cyclophosphamide was started and due to the potential fibrotic evolution of the hemorrhage, it was decided to continue immunomodulatory treatment with steroid and cyclophosphamide (2 mg/kg orally or IV once/day for 6-12 months) with resolution of the respiratory picture. The patient was started on chronic biweekly hemodialysis as he had not recovered renal function resulting in end-stage chronic renal failure.
Conclusion: The suspicion of vasculitis must always arise in the face of systemic manifestations not otherwise justified with other diagnostic hypotheses. It is almost always a diagnosis of exclusion of other diseases that can simulate vasculitis. Microscopic polyangiitis is a systemic necrotizing vasculitis of small-caliber vessels without immune complex deposition, associated pANCA, which

mainly affects the kidney and lung. It can manifest as a pulmonary-renal syndrome. High doses of corticosteroids and cyclophosphamide or rituximab are used for treatment. An important problem remains the lack of a universal PDTA able to clearly define the treatment pathway, ensuring multidisciplinary management, especially in peripheral hospitals where it is not always possible to send specific tests, with consequent delay in diagnosis and initiation of therapy. It is reasonable, at times, to start an empirical therapy during a strong diagnostic suspicion to allow the diagnosis to be excluded or confirmed.

SARS COV-2 INFECTION AND COLD AGGLUTININ DISEASE: A RARE CASE OF POST-COVID19 AUTOIMMUNE HEMOLYTIC ANEMIA

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Introdution: Autoimmune hemolytic anemia is an anemia due to a high and early destruction of red blood cells due to autoantibodies that react with red blood cells at temperatures above 37° C (warm antibody hemolytic anemia) or below 37° C (cold agglutinin disease). Warm antibody hemolytic anemia, frequently IgG, is the most common form, it is often idiopathic or secondary to other hematological diseases, while cold antibody hemolytic anemia, always IgM, is generally linked to bacterial or viral infections (H. influenzae, Mycoplasma, Epstein Barr virus, coronavirus etc.) or lymphoproliferative disorders. Some subjects may be asymptomatic, especially when the destruction of red blood cells is modest and develops gradually, or have symptoms similar to those of other anemias including jaundice, fever, chest pain, syncope. The direct Coombs test establishes the diagnosis and may suggest the cause, as does the determination of the autoantibody involved. Treatment depends on the cause and includes corticosteroid therapy, splenectomy, intravenous immunoglobulins, immunosuppressants, and avoidance of triggers.
Case report: A 49-year-old man with congenital deafness came to the Emergency Department for jaundice and syncope. No family history of autoimmune diseases or recent use of new medications was reported. He denies any previous or current infections, including SARS CoV-2. His medical history dates back to approximately 14 days after hospitalization when he developed a flu-like syndrome characterized by fever and productive cough; the general practitioner prescribed antipyretic therapy as needed and antibiotic therapy with Cefixime without benefit. After approximately 7 days, he showed jaundice and syncope at home for which he was hospitalized. Haematological tests on admission showed severe normocytic normochromic anemia and indirect hyperbilirubinemia, increased LDH values and reduced haptoglobin for which, in the suspicion of hemolytic disease, direct and indirect Coombs tests were performed, both of which were positive. A nasopharyngeal swab was performed to screen for influenza viruses and, given the positivity to SARS CoV-2, a chest CT scan was performed in an emergency regimen, which documented bilateral interstitial "ground glass" pneumonia. The blood gas analysis performed in an emergency regimen did not show acute respiratory failure, therefore oxygen therapy was not prescribed and antiviral therapy with Remdesivir was started as per guidelines. To better characterize the anemia, an abdominal CT scan was performed in an emergency regimen and no acute lesions affecting the abdominal parenchyma were found, thus excluding splenomegaly and lymphadenopathy. Blood culture tests were sent to exclude infections such as HIV, Chlamydia, Mycoplasma, these were positive for Mycoplasma and H. influenzae and therefore, under haematological indication, blood support was performed with bags of slow-infusion concentrated red blood cells and therapy was set up with Methylprednisolone 1 mg/kg/day with partial benefit and stabilization of haemoglobin values no higher than 9 g/dl. An anti-erythrocyte antibody of the IgM type was typed suggestive of cold agglutinin disease therefore a bone marrow biopsy and bone marrow needle aspiration were performed not suggestive of lymphoproliferative disorders. Given the poor response to cortisone and the failure to achieve normalization of Hb values, it was decided to progressively decrease corticosteroid therapy without adverse effects. As per haematological advice, therapy with Rituximab 375 mg/week was started.
Conclusion: Hyperactivation of the immune response to the SARS-CoV-2 Coronavirus may often lead to the development of autoimmune diseases. Molecular mimicry, the presence of circulating autoantibodies and concomitant autoimmune diseases in some patients are a clear sign of the potential trigger effect of the SARS-CoV-2 virus on the human immune system for the development of autoimmune disorders. A wide range of systemic or organ-specific manifestations have been reported in association with COVID-19, in particular antiphospholipid antibody syndrome, Kawasaki syndrome, Guillain-Barré syndrome, Miller Fisher syndrome, idiopathic thrombocytopenic purpura and autoimmune hemolytic anemia. The existing evidence, different according to the specific pathology, is scarce mainly because it is based on case reports or case series without long-term follow-up. Since it is still unknown whether these autoimmune manifestations are a transient post-infection phenomenon or a nosological entity in itself, further studies are needed to better understand the relationship between COVID-19 and autoimmunity.

THE RARITY IN THE ORDINARY

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Background: HIV infection and lymphoproliferative neoplasms are closely linked, often presenting concurrently. We describe an unusual case of NK/T-cell lymphoma presenting as an anal lesion in a newly diagnosed AIDS patient.
Clinical case: A 59-year-old male presented to the emergency department with persistent anal pain and mucopurulent discharge, ongoing for two months. Symptoms included fatigue, nocturnal fevers with chills, and pelvic pain. Initial evaluation by a proctologist revealed a protruding anal lesion suspicious for carcinoma. Laboratory tests showed only moderate leukopenia. Abdominal CT and pelvic MRI identified a mass in the anal region with multiple enlarged retroperitoneal lymph nodes. During hospitalization, serologic testing confirmed HIV infection with a CD4+ count of 5 cells/mm^3. Additional virologic testing for CMV, EBV, HSV-1/2, and VZV was negative. Lumbar puncture ruled out central nervous system involvement.
Histopathologic analysis of the anal lesion demonstrated a lymphoid infiltrate with numerous blastic cells, consistent with NK/T-cell lymphoma. Bone marrow biopsy was negative for lymphocytic infiltration. The patient was started on antiretroviral therapy and referred for hematologic follow-up.
Discussion: This case highlights the rare presentation of NK/T-cell lymphoma in an HIV/AIDS patient [1], [2]. Non-Hodgkin lymphoma (NHL) is the second most common malignancy in HIV/AIDS, with aggressive B-cell lymphomas typically being the predominant subtype, often EBV-associated, which was excluded in our case. However, NK/T-cell lymphoma is an uncommon entity, with only 10 reported cases in HIV/AIDS patients [1]. It is more frequently diagnosed in Asia and South America, with a predilection for extranodal involvement, including the nasopharynx, tonsils, and lung, but rarely the lymph nodes [3].
NK/T-cell lymphoma is highly aggressive, with a historically poor prognosis (median overall survival of 12 months). However, the introduction of antiretroviral therapy has significantly improved outcomes. Studies indicate a marked increase in median survival from 12 months before 2006 to 42 months in the ART era, particularly when combined with standard chemotherapy [1].
This case underscores two critical considerations: first, malignancies are a common complication of HIV, necessitating a high index of suspicion in clinical evaluations; second, advancements in ART play a pivotal role in improving outcomes for HIV-associated malignancies.
Conclusion: We present a rare case of NK/T-cell lymphoma with an unusual anal mucosal localization in an AIDS patient. This case highlights the evolving role of internal medicine in managing complex conditions traditionally seen in other specialties. As HIV becomes a chronic condition, internal medicine physicians will increasingly encounter its complications, emphasizing the need for a multidisciplinary approach to care.
[1] R.U. Hernández-Ramírez, M.S. Shiels, R. Dubrow, e E.A. Engels, «Cancer risk in HIV-infected people in the USA from1996to2012: a population-based, registry-linkage study», T*he Lancet HIV*, vol.4, fasc.11, pp. e495–e504, nov.2017, doi:10.1016/S2352-3018(17)30125-X.
[2] K. Perez, J. Castillo, B.J. Dezube, e L. Pantanowitz, «Human immunodeficiency virus-associated anaplastic large cell lymphoma», *Leukemia & Lymphoma*, vol.51, fasc.3, pp.430–438, mar.2010, doi:10.3109/10428190903572201.
[3] M.J. Koh et al., «Comparative outcomes for mature T-cell and NK/T-cell lymphomas in people with and without HIV and to AIDS-defining lymphomas», *Blood Advances*, vol.6, fasc.5, pp.1420–1431, mar.2022, doi:10.1182/bloodadvances.2021006208.

ACUTE VIRAL HEPATITIS: A RARE CAUSE THAT SHOULD BE CONSIDERED

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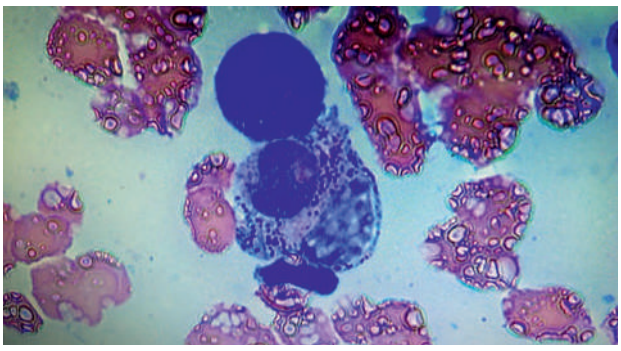
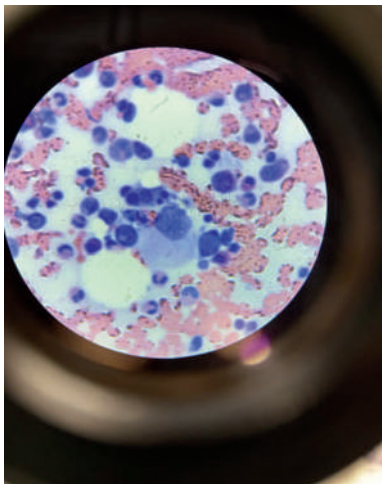
A 68 years-old man was admitted to our department because of acute hepatitis. A few days before, he started to complain about low-grade fever, weakness, abdominal pain, nausea, vomiting, and inability to tolerate oral intake. He had no history of hepatic disease or other illnesses. He used to drink about three beers weekly but he denied smoking habits. He took only one pill of paracetamol (1 g) in the last days; he denied use of antibiotic or other drugs, intravenous substances or unprotected sexual activity.
On admission, the patient was febrile, normotensive and tachycardic. Physical

exam was notable for tenderness in the right upper abdomen without defense. The skin was warm, dry and free of rashes or jaundice. He had normal bowel sounds and no organomegaly. No lymphadenopathy was noted. Initial laboratory findings revealed a white blood cell count (WBC) of 1,7 x 10^3/mm3 (reference value [RV]: 4,800-10,800 10^3/mm^3) with slight neutrophilic predominance (80.6%), lymphocytopenia (0,3 x 10^3/mm^3), a normal red blood cell count (RBC) of 4.51 x 10^6/mm^3 (RV: 4.9-5.5 x 10^6/ mm^3), haemoglobin 12.1 gm/dL (RV: 13.1-17.1 g/dL), and platelets 122 x 10^3/ mm^3 (RV: 150-450 x 10^3/ mm^3). Electrolytes were normal, with normal kidney function (creatinine concentration of 1.06 mg/dL (RV: 0.73-1.18 mg/dL). The alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were elevated at 1671 U/L (RV: 4-34 U/L) and 1091 U/L (RV: 10-49 U/L), respectively. The alkaline phosphatase (ALP), colinesterasis and bilirubin were at 98 IU/L (RV: 46-116 IU/L), 9493 U/L (RV 7000-19000 U/L) and 1 mg/dL (RV: 0.2-1.1 mg/dL), respectively; the international normalized ratio (INR) was 2.21 (RV: 0.8-1.2) without any drug possibly interfering with this value, CRP 9.5 mg/dL (RV: 0-0.5 mg/dL).
Subsequently, he was admitted to our ward. The viral hepatitis panel was negative for hepatitis A, hepatitis B surface antigen and core antibodies, and within the reference range for Hepatitis C antibodies. A panel of autoantibodies and minor hepatic viruses (CMV, EBV, VZV, and TORCH-profile including Herpes Simplex Virus HSV1-DNA and HSV2-DNA), was also performed; zoonosis, iron and copper state were studied. The abdomen ultrasound didn't show relevant findings except for some hepatic cysts. A total body computed tomography was also performed, revealing a suspected pneumonia and thrombosis of the left jugular vein. Empiric therapy with Ceftriaxone was started, together with rehydration therapy and Vitamin K supplementation.
The clinical and mental status of the patient deteriorated within the first 24 hours after admission, with altered mental status and worsening of liver function (AST> 6000, ALT >3300, out of the reference range, bilirubin 2.7 mg/dL and INR 3.18), thus he was referred for liver transplantation and NAC (N-acetyl cysteine) infusion protocol was started. Nevertheless, the laboratory values revealed acute pancytopenia (WBC 0.7 x 10^3/ mm^3, acute anemia with RBC 2.62 x 10^6/ mm^3 and a severe drop in hemoglobin levels to 7.3 g/dL; PLT decreased to 24 x 10^3/ mm^3; ferritin level arises (622 ng/mL, RV 22-322 mg/mL), and also LDH >4500 U/L (RV 120-246 U/L) and beta-2 microglobulin (13,91 mg/dl, RV 1-2,4 mg/L). A peripheral blood smear showed schistocytes compatible with haemofagocytic syndrome. The patient developed acute kidney injury (4.27 mg/dL), worsening lactic acidosis, clinical signs consistent with multiorgan failure, and eventually died on day 4 after admission. RT-PCR for HSV became available after the patient died (HSV1-DNA > 25.000.000 copies/mL).
Herpes simplex virus hepatitis is a rare complication of HSV infection that has the propensity to cause fulminant liver failure and death. The rate of HSV infection is very high (over 60% of the general population for HSV-1) thus fulminant hepatitis is a rare manifestation (1% of acute liver failure cases). It has been recognized especially in drug-induced immunosuppressed individuals but it has been reported also in immunocompetent patients, such as in our case. Diagnosing HSV hepatitis can be difficult due to the absence or non specificity of clinical features. Encephalitis (altered mental status, fever, focal or global cerebral dysfunction) and disseminated intravascular coagulation (DIC) are reported in literature, but no haemofagocytic syndrome, so far.
The prognosis of HSV hepatitis is dismal, with a mortality rate of 80-90%. Therefore, early detection and treatment of HSV hepatitis are crucial in preventing rapid clinical deterioration and death. Empiric treatment has not yet been established; however, there is evidence that acyclovir can improve the clinical status of patients with HSV hepatitis and should be tried to reduce the mortality rate.





HYPERHOMOCYSTEINEMIA AND VENOUS THROMBOSIS

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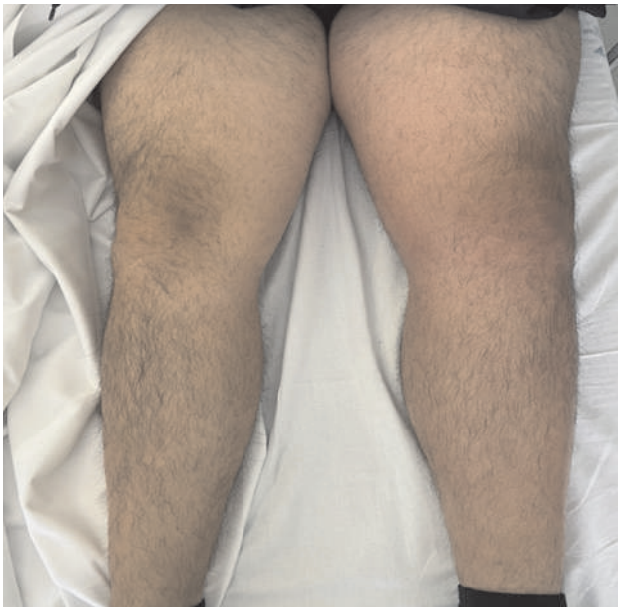
Hyperhomocysteinemia is an established risk factor for premature atherosclerosis and cardiovascular disease; more recently, it was also associated with venous thrombosis (VT). Until the early nineties the relationship with venous thrombosis was controversial; only in 1991 the first formal studies on the association between hyperhomocysteinemia and VT were reported. Meta-analyses have reported a 2- to 3-fold increased risk of VT in individuals with hyperhomocysteinemia; however, confounding factors were generally not considered. In contrast, randomized trials of homocysteine-lowering therapy and VT risk have been negative.
The mechanisms by which hyperhomocysteinemia might contribute to atherogenesis and thrombogenesis are incompletely understood. VT is now believed to be a multifactorial disease. Since hyperhomocysteinemia is a common abnormality, it is likely to interact with other inherited and acquired prothrombotic factors (e.g. MHTFR mutations) to increase the over-all risk of VT; however it may represent a potentially reversible cause of thrombophilia by itself. Hyperhomocysteinemia is due to genetic and acquired factors (unhealthy lifestyle with poor diet in folate and vitamin B, elderly, renal impairment, thyroid diseases, malignancies), and an exciting aspect is the chance of easily correcting the abnormality with appropriate vitamin supplementation. The primary agent for treatment is folic acid, with or without the addition of vitamins B12 and B6. A meta-analysis of the short-term trials of therapy with folic acid showed a reduction of 25% of homocysteinemia and a further reduction of 7% when vitamin B12 was associated. This situation may be associated with a 10% to 20% decreased risk of VT. Although there is now clear evidence that it is possible to normalize high homocysteine levels, there is, at present, no evidence to treat those both in primary or secondary prophylaxis. Further trials are required to estimate if this is worthwhile from the clinical point of view.
We report the cases of three male patients who were admitted to our department in the last year (April 2024-March 2025) for proximal VT and who had not other evident risk factors for VT (no recent trauma or surgery, no neoplastic or autoimmune disease, no foreknown thrombophilic abnormalities), which resulted affected by hyperomocysteinemia. Homocysteine levels were 58,63, 24,72, 43,21 Umol/L respectively (RV > 3,7-13,9 Umol/L), folate levels were 2,66, 4,06, 2,16 ug/mL (RV>5,38 ug/mL). Age at admission was 51, 24 and 30 years respectively. All three had sedentary habits; only one of them was a smoker. No one suffered from any disease but all of them were found to be overweight/obese (BMI was 30,8, 32 and 28,6 respectively). Only one of them had a MTHFR eterozygosis mutation. One had familiar history of thrombophilia but no evident mutation was founded.
All of them started folic acid and vitamin B12 supplementation and anticoagulant therapy (two with direct oral anticoagulant, the one who exceeded 100 kg weight with warfarin), under clinic and ultrasound follow-up: homocysteinemia levels were found in the normal range at medium 4 weeks after the start of vitamin supplementation, otherwise VT required about 3-6 months of anticoagulation to go back. One of the patient with one-year follow-up is keeping low dosage anticoagulant therapy (apixaban 2,5 mg bid). Other two are also candidates to low-dosage long-term therapy, as recommended for idiopathic VTE without significant hemorrhagic risks.
In medical practice the measurement of homocysteine may be indicated in unexplained idiopathic VT, or recurrent episodes or VT occurred at an early age

or at an uncommon site. Our brief study suggest a possibile correlation of unhealthy lyfestyle, overweight and hyperhomocysteinemia, and support hyperhomocysteinemia as a risk factor for VT. Further research are still needed to understand pathophysiology of this relationship and the clinical effects of reducing homocysteine levels by vitamin supplementation.



HAEMOFAGOCYTIC SYNDROME

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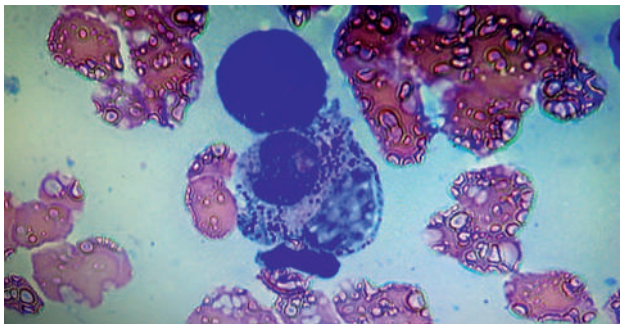
Haemophagocytic syndromes (haemophagocytic lymphohistiocytosis, HLH and macrophage activation syndrome, MAS) are clinical life-threatening syndromes characterized by hyper-inflammatory response, cytokine release syndrome and organ damage, that are mainly reported in pediatric patients, thus reports of adult presentation are increasing. Insufficient knowledge of the molecular pathophysiology of these syndromes may have contribute to poor prognosis until now. Early diagnosis is needed to avoid high mortality of this rare condition, but it is often misdiagnosed because of heterogeneity of clinical presentation and a broad spectrum of differential diagnosis.
Red flags are represented by fever, elevated ferritin and other markers of systemic inflammation, high levels of triglycerides, inappropriately low blood cell counts (BCC), disseminated intravascular coagulopathy, hepatitis, and central nervous system inflammation. There is high risk for progression to multiple organ dysfunction, shock and often death.
HLH/MAS typically develops in the setting of infectious, malignant (especially lymphoma) or rheumatological diseases, or less commonly as a manifestation of underlying genetic inborn errors of immunity that predispose to hyper-inflammation. Treatment of patients with suspected HLH/MAS requires a dynamic risk-benefit assessment and should be directed towards 3 main presenting features: stabilization of the patient and organ support, actively search for trigger like infection or malignancy with appropriate management, suppression of overactive inflammatory response with immunosuppressive treatment as high-dose glucocorticoids (GCs), anti-CD20 monoclonal antibody rituximab and/or intravenous immunoglobulin (IVIg), etoposide or haemopoietic stem cell transplantation.
In the last year (April 2024-March 2025) we diagnosed four case of HLH in our ward; only one of them survived from this condition.
Haemophagocytic syndromes are rare conditions, often mis-diagnosed, which course can be lethal. Among predisposing conditions, infection is the most common acute trigger of HLH/MAS, but also malignancy (especially lymphoma) is a major contributor. Nevertheless, practice patterns in recognising and managing these conditions are challenging and vary widely. Delay in diagnosis and multi-organ involvement is associated with worsened outcomes and hence quick diagnosis and prompt therapy is the key to better outcome.



A QUALITATIVE STUDY TO IMPROVE THE IMPLEMENTATION OF NURSING DELIVERIES: BEDSIDE DELIVERIES

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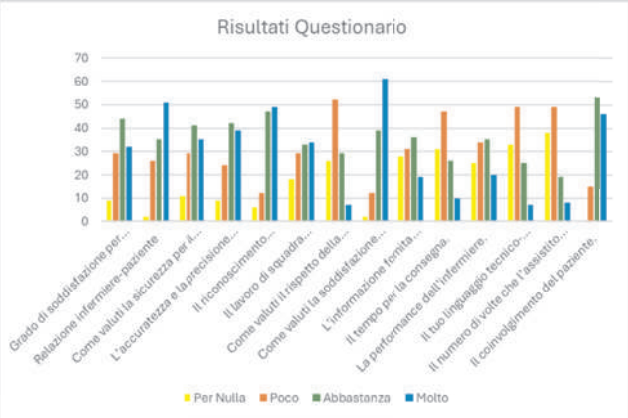
Background: The transfer of information between health care professionals is crucial for patient safety, as flaws in communication are the cause of about two-thirds of sentinel events.Effective communication betweenpatients and health professionals, moreover, is essential for patient-centered care based on quality interactions and trust and helps reduce the risk of errors,improving overall safetyof care. To reduce the risk of information loss, aneffective strategy is handover at the patient'sbedside (Bedside handovers), directly involving the patient in the process. This premise was the motivation that guided the project. The purpose of this study was to investigate whether nursinghandover that takes place betweennurses, with active participation of the patient, i.e., through the use of bedside handovers, can bring important benefits to both health care workers and patients.
The study was carriedout from June 2023 to October 2023 by administering a validatedquestionnaire, which was useful for investigating nurses' opinions about bedside deliveries. The questionnaire was written online via social channels, anonymously, subject to informed consent.This questionnaire consistsof fourteen closed- ended items, to which practitioners respond by expressing their degree of agreement or disagreement on a Likert scale (1 to 4). The studysample consisted of 189 nurses;from these, however,75 nurses were excluded because they were uninformed about this delivery methodology and/or because it had never been applied in their work context;in addition, nursesfrom the areas of emergency, mental health, and resuscitation were excluded because the literature shows difficulty in applying bedsidedeliveries in these settings (patients who are not very alert, incapacitated, emergency situations with little time available).
Ofthe 189 nursescompleted the questionnaire, only 114 nurseswere included in the study.The results show that nurses believe there are numerous benefits to bedside handover for both the patient and the nurse, including: 86.8% of nurses reported higher patient involvement in the care process and 75.4% reported improved nurse-patient relationship. Handover at the patient's bedside also enhances the safety of the caregiver, as felt by 70.7 % of professionals, improving the completeness and accuracy of information. However, some difficulties and objections from nurses also emerged. Among the most frequent are: violation of privacy (68.4 %); nurse performance (51.8 %); time taken for delivery (68.4 %); and use of technical-professional language (71.9 %), which is difficult for the patient to interpret.
"Bedside" handovers prove to be a good method of nursing delivery, presenting many advantages, but also some difficulties. An "intermediate" form of handover,in which thereare moments of handover both away from and near the patient's bedside, considering the time of day, the type of patient and the information to be conveyed, should be the idealform, to be preferred. Future goals will be to detect the quality of care perceived by the patient through patient involvement. With regard to this study, further the steps of evaluation and verification of actions are then planned.



PREVALENCE OF CATHETER-RELATED BLOODSTREAM INFECTION WITH MIDLINE CATHETERS AND PERIPHERALLY INSERTED CENTRAL CATHETERS: EXPERIENCE OF A SINGLE CENTRE

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Due to increasing popularity, ease of insertion, low rate of complications, reduced cost, Midline and PICCs are currently used in internal medicine wards as reliable and durable vascular access. Their use has become essential to allow the delivery of medical treatment for inpatients, also in difficult intravenous access patients (DIVA) despite ultrasound-guided attempts, when a central venous access is not required or controindicated.
Infection and thrombosis are the main adverse effects of these catheters. Catheter-related bloodstream infection (CRBSI) is defined as bacteremia or mycoemia after catheter insertion, related with the presence of the device. CRBSI is a serious complication, closely related to the length of hospital stay, cost, and prognosis of patients.
We want to determine the prevalence CRBSI after peripheral, midline and central catheters placement occurred in our ward during one year (January-December 2024). In this interval, patient admitted were 1572 (52% female, 48% male). About 31% (487) of the patients admitted during last year required midline (MC) insertion; 5% (77) required a CVC and 4% (62) required PICC implantation. Median age of device recipients was 74.8 years.
To determine the incidence of CRBSI, we conducted a retrospective study based on discharge diagnoses of "sepsis". Patient dismissed with main diagnosis of "sepsis" were 256 (16% of total admissions), within which 34% patients died during the hospital stay. Regarding the source of sepsis, 34% were related to pneumonia, 31% to urinary tract infections, 12% were related intra-abdominal infections (including gallbladder and biliary tract), 10% derived from soft tissue infections, and 9% (24 patients) were associated with CRBSI. 4% were of unknown origin even after diagnostic work-up.
CRBSI were considered in case of bloodstream infection in a patient with an IV device, confirmed by positive blood cultures with no other source of infection (e.g., in patients with sepsis, laboratory microbiology tests showed positive bacteria or fungi from venous blood cultures collected from the device or pathogens of the same species with the same drug sensitivity resulted from catheter segments and peripheral blood cultures). There were excluded sample contaminations.
Within CRBSI, 16 were female, 8 were male, 6/24 were infections of central cathethers (7% of total CVC placed), 4/24 were PICC or port-a-cath related (6% of total PICC positioned), 14/24 were MC related (2% of total implantation). All infections required replacement of the colonized device; only in one case it was performed a lock-therapy without removal of MC. Co-morbidities founded associated were chiefly chronic kidney disease (11/24), neurological diseases including dementia, epilepsy, mental retardation, multiple sclerosis (9/24), malignancies (7/24), diabetes mellitus (6/24), need for enteral or parenteral nutrition (6/24 and 3/24, respectively). Deaths were 6/24. Agents responsible for CRBSI were: S. aureus (6), S. haemolyticus (3), S. epidermis, S. hominis, E. faecalis (3), E. faecium, Enterobacter spp. (cloacae, ludwigii, 3), Proteus mirabilis (2), P. aeruginosa (2), Serratia spp (marcescens, liquefacens), Klebsiella pneumoniae (2), Acinetobacter pittii, Corynebacterium striatum, C. albicans (3), C. parapsilosis. Coinfections were founded in 5/24. Time from catheter insertion to first episode of fever and positive blood cultures was on average 4 days.
Our study has several limitations: first of all, we enrolled only patients with main diagnosis of sepsis, but CRBSI were reported in a subtle number of patients discharged with other main diagnoses. Otherwise, in some patients the device was implanted before the hospital admission as outpatients or during a previous hospitalization. Mortality was lower than other studies (about 25%), maybe because of rapid improvement after device removal; most critical patients might have been transferred to ICU wards (more likely patients requiring CVC). Actually it still remains to determine the percentage of serious infections of devices implanted during the year.
In literature, all intravenous access can develop CRBSI to varying degrees, but the risk of CRBSI of MC is 0–0.9%, that of PICC ranged from 0.3% to 7.3%, that of CVC exceed 10% with higher mortality. Our study showed that Midline catheters may represent a safer vascular access option compared to PICCs and CVC in selected patients, with a lower incidence of bloodstream infections. The mortality rate observed in the MC-group was higher than in previous studies and it can be attributable to non adequate protocols of placement and subsequent nursing care. The mortality rate in CVC-group was lower, maybe for a major attention for device care or because of the transfer of the more critical patients to ICU wards. Patient selection and strict adherence to insertion and maintenance protocols remain critical to minimize infection risk for both catheter types. With this study we want to remark that the use of peripheral devices is strongly needed in internal medicine wards and must be preferred to central venous line, but it requires trained personnel and standardized procedures.

HPOS STUDY: BRIDGING INTERNAL MEDICINE AND OCCUPATIONAL HEALTH IN HELICOBACTER PYLORI SCREENING AND CANCER PREVENTION

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Background: *Helicobacter pylori (Hp)* is recognized as a Group 1 carcinogen for gastric cancer. This infection is widespread worldwide, with an estimated prevalence of 30% in Italy. Since Hp eradication can help prevent cancer, implementing test-and-treat strategies is essential. The HPOS study aimed to assess the feasibility of integrating Hp screening within occupational health programs for hospital workers (HW).
Methods: This study was conducted between2023and2025at S. Orsola University Hospital in Bologna, Italy, targeting HW aged40to65. Screening was based on a stool antigen test (SAT) for Hp. Participants completed a questionnaire covering sociodemographic, occupational, lifestyle, and clinical data, with a focus on Hp awareness and infection history. Those who tested positive were referred to their general practitioner (GP) for eradication therapy. A follow-up phone interview at three months assessed general health, gastrointestinal symptoms, treatments received, additional tests performed, and participants' feedback on the study. Descriptive analyses were conducted to evaluate screening participation, and preliminary multivariate regression analysis estimated odds ratios (OR) and95% confidence intervals (CI) to explore enrollment determinants.
Results: A total of 399 HW (67.3%) actively participated, including 291 women (72.9%) and 108 men (27.1%), while 194 individuals (26.1%) declined. An additional 151 HW volunteered (79.5% women, 20.5% men), bringing total enrollment to 550. After excluding 93 dropouts, the final study population comprised 461 HW (83.2% of total enrolled). The most common reasons for refusal included a recent Hp test (n=25), lack of time (n=12), and working in a remote location (n=3). Nurses (40.2%) and health assistants (21.1%) made up the majority of participants, with nurses representing nearly half of volunteers (48.3%). The highest dropout rate was observed among physicians and researchers (31.2%). Women were more likely to participate than men (OR=0.68, 95% CI=0.47-0.99) after adjusting for age and job title. No other strong associations emerged, although a borderline positive relationship was noted for "other health professionals and technicians" (OR=1.62, 95% CI=0.96-2.73).
Conclusions: This study demonstrated that Hp screening could be successfully integrated into occupational health programs for Italian HW, achieving a participation rate of approximately 70%, which increased to 83.2% when including volunteers. To enhance the effectiveness of hospital-based Hp screening, targeted engagement strategies may be needed. Moreover, a multidisciplinary team composed of clinicians and occupational health physicians can identify the health needs of healthcare workers and provide more appropriate responses.

36. THE LADY IN YELLOW: A CASE OF JAUNDICE

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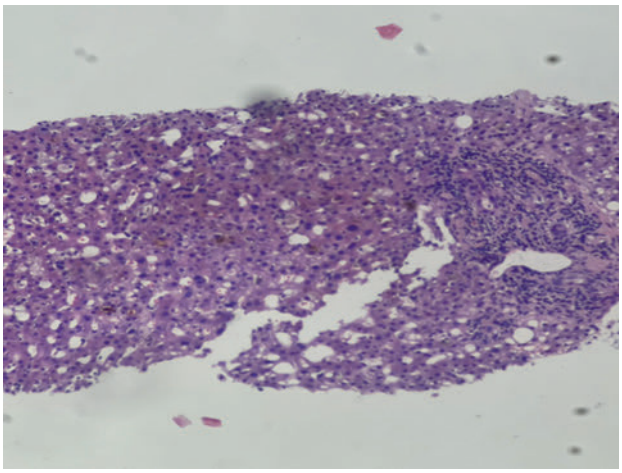
Drug-Induced Liver Injury (DILI) is the most frequent cause of acute liver failure and liver transplantation in Western countries, and it accounts for 50% of cases of acute jaundice in patients with newly onset jaundice. The clinical manifestations can vary: from a mild and asymptomatic increase in liver enzyme levels to fulminant hepatic failure that may necessitate liver transplantation. The pathophysiological mechanisms leading to liver damage are of two types: type A, or intrinsic, and type B, or idiosyncratic. Clinically, liver damage can present in a predominantly hepatocellular form, predominantly cholestatic, or mixed. Potential risk factors for DILI include advanced age, female gender, type 2 diabetes mellitus, chronic viral hepatitis, and genetic predisposition. DILI is a diagnosis of exclusion. After rigorously excluding possible causes of liver damage, such as viral hepatitis, autoimmune hepatitis, alcoholic liver disease, metabolic or biliary diseases, a thorough history is essential to identify a specific substance that could have caused the damage. It is important to know the time elapsed between the intake and suspension of the substance and the onset of liver damage, the clinical course after suspension, risk factors, concomitant therapies, and any recurrence after re-administration of the substance. The definitive diagnosis relies on histological examination, which allows identification of the type and extent of liver damage, although it does not identify the specific drug responsible. The treatment and prognosis depend on the type of liver damage that has occurred. In mild cases, discontinuing the responsible substance typically leads to a remission of symptoms and signs of the disease. In more severe and irreversible cases, such as fulminant hepatitis or cholestatic damage leading to ductopenic syndrome (with disappearance of bile ducts), liver transplantation is required. However, supportive therapy with corticosteroids, ursodeoxycholic acid, and cholestyramine may be useful. In September 2024, a 66-year-old Egyptian female patient was admitted to the emergency department, referred from a rehabilitation facility after laboratory tests revealed hyperbilirubinemia. The patient's medical history included breast cancer treated with chemotherapy, radiotherapy, and surgery in 2022, brain metastasectomy in August 2024, hypertension, type 2 diabetes, and a past history of HBV infection. Upon arrival in the emergency department, the patient was clinically stable, alert, oriented, cooperative, and breathing normally, with no abdominal tenderness. The laboratory results showed acute liver damage, cholestatic injury, and pancreatic damage (Total bilirubin 9.79 mg/dl, Direct bilirubin 7.79 mg/dl, AST 283 U/L, ALT 527 U/L, GGT 594 U/L, Alkaline phosphatase 754 U/L, pancreatic amylase 748 U/L, pancreatic lipase >1250 U/L) with normal results in other tests. An emergency abdominal CT was performed, which did not show any abnormalities in the liver or pancreas. The patient was subsequently evaluated by specialists who, based on the laboratory results and medical history, did not consider the situation urgent but recommended a whole-body CT or PET scan and the testing of hepatitis markers. The patient was transferred to our department. Upon admission, the patient was clinically stable, with jaundiced skin, dark-colored urine, and denied any abdominal pain in all quadrants. In light of the clinical picture, our focus was on investigating potential causes of jaundice, specifically intra-hepatic causes with cholestatic damage. The patient underwent a whole-body CT and MR cholangiography, considering the laboratory findings that did not suggest damage to the hepatic parenchyma or any morphological alterations in the gallbladder. After excluding all possible causes, including infectious ones, we performed a liver biopsy. The result revealed an acute-on-chronic inflammatory picture with vanishing bile duct syndrome, cholestasis, and an attempt at re-generation of the hepatic parenchyma. The report concluded with acute hepatitis with a cholestatic imprint and damage likely due to a toxic drug origin. But which drug? After reviewing the patient's detailed medical history, it was found that she had received a course of antibiotic prophylaxis for the surgical wound post-surgery. Due to the clinical history and comorbidities, the patient was not a candidate for liver transplantation. Therefore, in consultation with the hepatologist and the patient's family, palliative care measures were initiated. It was noted that DILI, particularly from amoxicillin-clavulanate, is estimated to occur in about 1-2/100,000 prescriptions. A total of 758 hepatic reactions have been reported from amoxicillin out of 24,606 prescriptions, including 156 hepatitis cases and 73 cholestatic hepatitis cases. Reactions from the amoxicillin/clavulanate combination number 112 out of 808 total cases, including 12 hepatitis cases and 26 cholestatic hepatitis cases.



EFFICACY OF EMPAGLIFOZIN ON CLINICAL PRESSURE AND AMBULATORY BLOOD PRESSURE MONITORING (ABPM 24 H) IN A POPULATION OF PATIENTS WITH HYPERTENSION AND TYPE 2 DIABETES MELLITUS

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Background: In clinical practice, arterial hypertension is often associated with type 2 diabetes mellitus (T2DM) contributing to increase the patients cardiovascular risk. In registration studies, the SGLT2i molecule Empaglifozin has been shown to reduce not only blood glucose but also clinical blood pressure, in particular systolic blood pressure. Ambulatory blood pressure monitoring 24 h (ABPM) can be useful to evaluate the effect of Empaglifozin on the reduction of blood pressure values over 24 hours.
Material and methods: In this study, 22 patients (mean age: 64.6 years; M: 16, F: 6) with T2DM of mean duration of 9 years and hypertension in treatment (mean clinical SBP: 148.2 ± 18.4 mmHg; mean clinical DBP: 88.6 ± 10.2 mmHg) were evaluated with ambulatory blood pressure monitoring 24 h (ABPM Spacelabs 90207) before and after 8 months of therapy with Empaglifozin 10 mg/day, prescribed for a non-optimal glycemic control (fasting blood glucose: 146.7 ± 37.9 mg/dl; HbA1c 56.3 ± 10.6 mmol/mol).

Results: After 8 months of therapy, Empagliflozin was associated with reduction of clinical systolic blood pressure (SBP: 135.8 ± 17.7 mmHg (p<0.001), clinical diastolic blood pressure (DBP: 81.5 ± 12.5 mmHg (p= 0.0069) and statistically significant reduction (p< 0.001) of SBP (129.6 ± 2.7 mmHg; 124.6 ± 2.7 mmHg), DBP (75.7 ± 1.6 mmHg; 73.6 ± 1.6 mmHg) and PP values (54.0 ± 2.4 mmHg; 50.6 ± 2.4 mmHg) with ambulatory blood pressure monitoring 24 h (ABPM), in particular during the morning sourge. The biohumoral tests showed a significant reduction in fasting blood glucose: 127.4 ± 20.4 mg/dl (p= 0.0030) and HbA1c: 52.1 ± 8.4 mmol/mol (p= 0.0031). No significant differences were found between LDL cholesterol values (83.0 ± 35.0 mg/dl; 82.3 ± 40.6 mg/dl).
Conclusions: Our study confirms the efficacy of Empaglifozin on the reduction of blood glucose and blood pressure, both clinical and ambulatory blood pressure monitoring 24 h (ABPM). The reduction in blood pressure observed in the early hours of the morning, contrasting the phenomenon of the "morning surge", could contribute in large part to explain the protective effect of Empaglifozin on cardio and cerebrovascular events, as observed in clinical trials.

OPTIMIZATION OF LIPID-LOWERING THERAPY IN A POPULATION OF DIABETIC PATIENTS WITH VERY HIGH CARDIOVASCULAR RISK

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Background: As the recent ESC Diabetes 2023 Guidelines underline, diabetic patients have a higher risk of developing cardiovascular disease. It is also dem-

onstrated that the association of diabetes mellitus and cardio-renal comorbidities increases not only the risk of cardiovascular events but also all-cause mortality. Therefore, control of the main CV risk factors such as high blood pressure and LDLc values in diabetic patients with ASCVD and organ damage is even more necessary and recommended by the Guidelines. The presence of alterations in the lipid profile and apolipoproteins in diabetic patients, such as high triglyceride levels, moderately elevated LDL and reduced HDL, makes it even more difficult to reach and maintain the target and requires adequate and increasingly early combination lipid-lowering therapy. In recent years, the introduction of PCSK9i and bempedoic acid has represented a potential therapeutic able to reducing teh LDLc levels by 60 to 85% on top of statin and ezetimibe therapy. Therefore, the aim of this observational study was to evaluate the prevalence of non-target LDL values in a population of diabetic patients with high CV risk, stratified according to the EAS/ESC 2019 Guidelines, as well as to evaluate the lipid-lowering therapy prescribed in clinical practice and in particular the role that new drugs could have i achieving the therapeutic target.

Materials and methods: The study population is represented by 329 diabetic patients with an average age of 67.2±10.4 years (67.2% male and 32.8% female), visited at the diabetology clinics of the Gardone Val Trompia Hospital in the first three months of 2024 with very high CV risk according to the ESC Dyslipidemia Guidelines 2019. Among the most frequent comorbidities of the population, arterial hypertension was present in 83% of patients followed by dyslipidemia in 66%, heart failure in 14.6%, cardiac arrhythmias in 12.2% and chronic kidney disease in 29.8%. Among macrovascular complications, the prevalence of coronary heart disease was 15.8% and arteriopathy was 33%; in relation to microvascular complications, 40.4% of patients had microalbuminuria, 25.5% retinopathy and 2.7% peripheral neuropathy. All patients underwent clinical examination, anamnestic and pharmacological collection, measurement of BP and blood tests such as glycemia, HbA1c, creatinine, microalbuminuria and lipid profile.

Results: Of 329 patients, mean glycemia was 141.5 ±39.5 mg/dl, HbA 1c 6.9 ±0.3%. LDLc 139.7 ±37.6 mg/dl, HDL 48.8 ±14.3 mg/dl and triglycerides 127.5±72.9mg/dl. The percentage of patients with LDL < 55 mg/dl was 37.7% with a mean excess gap from the goal of 29.4 mg/dl. Prevalence of statin prescriptions was 82.1%, ezetimibe 33.7%, bempedoic acid and PCSK9i 0.3%, omega 3 7.9% and fenofibrate 3.3%. 16.7% of patients were not taking any therapy. Among patients on combination therapy with statin and ezetimibe the 62.6% were on target; and the mean excess of LDLc of patients not on target was 38.3%. Patients on statin alone met the goal in 31.3% of cases, with a mean excess of 27.4%.

Among patients taking ezetimibe alone or no therapy, respectively 25% and 7.6% achieved the target, with a mean LDLc excess of 43.5% and 36.4%, respectively. In the study population, it was hypothesized that the introduction of ezetimibe woud have reduced LDLc 20% in 112 patients on monotherapy, leading to target achievement in 32.4%. Simulating the introduction of bempedoic acid in patients with a mean LDLc excess between 5 and 20% despite statin and ezetimibe therapy, the therapeutic target would be achieved in 12.2% of the total population. In patients on combination therapy with a mean LDLc excess greater than 20%, the introduction of PCSK9i would allow to therapeutic optimization in 13.1% of the total population considering the age prescription limits.

Conclusions: In this observational study, 62.3% of patients did not reach the LDLc goal < 55 mg/dl recommended by the EAS/ESC 2019 Guidelines. From the data processing, it emerges that the combination of statin and ezetimibe remains the first-line strategy, allowing the achievement of the therapeutic objective in the majority of cases (63%).

Access to new lipid-lowering therapies is a fundamental resource for achieving the therapeutic objectives recommended by the guidelines in those patients in whom traditional lipid-lowering therapy is insufficient.

In particular, the introduction of bempedoic acid could be a valid therapeutic strategy for the effect that the inhibition of ATP citrate lyase has on lipid profile, reducing not only plasma LDLc cholesterol values, but also non-HDL cholesterol and Apo B in addition to a modest effect on the reduction of HbA1c values.

OMI OR NOMI: THAT IS THE QUESTION

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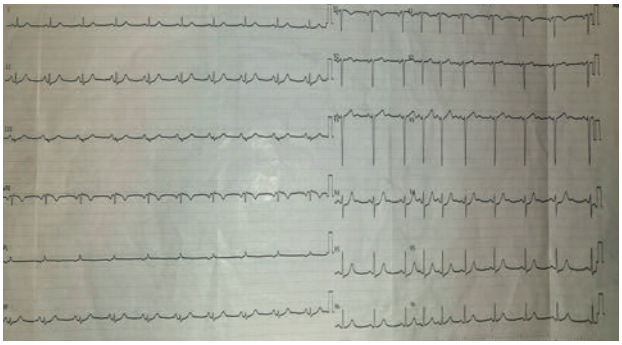
Case presentation: A 64-year-old woman presented to the emergency room (ER) with oppressive chest pain started at rest the previous evening, partially relieved by NSAIDs, but reappearing in the morning. Her medical history included active smoking and dyslipidemia, with no significant cardiovascular history.

Upon arrival at the ER, her vital signs and clinical examination were within normal limits. An ECG (figure 1) was performed, revealing sinus rhythm at 60 bpm, normal intra-atrial and interventricular conduction, and ST-segment depression in leads V4 and V5 (<1 mm). Blood tests were ordered, showing values within normal ranges except for troponin T at 217 ng/L. A second measurement after 3 hours revealed an increase to 529 ng/L. A cardiology consultation was requested, and based on the clinical picture, laboratory tests, and echocardiography findings (preserved ejection fraction, no regional wall motion abnormalities, no pericardial effusion), the diagnosis suggested pericarditis, leading to initiation of NSAIDs therapy and continued observation. However, a third troponin measurement showed a rapid rise (2600 ng/L). A repeat ECG was unchanged, while echocardiography revealed mild hypokinesia of the inferior wall. Urgent coronary angiography was therefore indicated, revealing an acute thrombotic occlusion of the mid-left circumflex artery, which was subsequently treated with percutaneous revascularization and implantation of a drug-eluting stent. The patient was admitted to the coronary care unit. An echocardiogram performed during hospitalization showed hypokinesia of the mid-basal inferior and posterolateral walls. The clinical course was uneventful.



Discussion: The treatment of acute myocardial infarction includes prompt reperfusion, prioritizing revascularization in ST-segment elevation myocardial infarction (STEMI) [1]. The scientific community classifies STEMI and non–ST-segment elevation myocardial infarction (NSTEMI) as surrogates for occlusion and non-occlusion myocardial infarction, respectively. Unfortunately, approximately one-third of high-risk patients with occlusion myocardial infarction do not meet STEMI criteria, preventing some NSTEMI patients with acute coronary occlusion from receiving emergent reperfusion [2]. In the presented case, for example, revascularization occurred approximately 30 hours after the patient presentation at the emergency department. This has led to the proposal of classifying patients into two categories: OMI (occlusion myocardial infarction), which benefits from emergent reperfusion therapy, and NOMI (non-occlusion myocardial infarction), in which emergent angiography is not required [3]. Several ECG patterns have been described that warrant urgent revascularization despite not meeting the STEMI criteria [4]. Among these is OMI of the "posterior" wall, which may appear solely as ST-segment depression on a standard 12-lead ECG, without any accompanying ST-segment elevation. This pattern can be attributed to acute occlusion of various posterior branches of either the right coronary or left circumflex artery. Posterior and lateral wall OMIs are among the most frequently missed cases, with more than 50% of circumflex artery occlusions failing to receive urgent reperfusion. [5].

Conclusions: Acute myocardial infarction is a medical emergency. If not promptly recognized and treated, it is associated with a worse prognosis. The diagnostic process begins with clinical suspicion and is based on a multiparametric evaluation of laboratory, ECG, and echocardiographic data. Acute coronary occlusion does not always present with ST-segment elevation; therefore, ECG interpretation must be critical and integrated with other available diagnostic findings.

References:

[1] R.A. Byrne *et al.*, "2023ESC Guidelines for the management of acute coronary syndromes: Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC)," *Eur. Heart J.*, vol.44, no.38, pp.3720–3826, Oct.2023, doi:10.1093/EURHEARTJ/EHAD191.

[2] H.P. Meyers *et al.*, "Comparison of the ST-Elevation Myocardial Infarction (STEMI) vs. NSTEMI and Occlusion MI (OMI) vs. NOMI Paradigms of Acute MI," *J. Emerg. Med.*, vol.60, no.3, pp.273–284, Mar.2021, doi:10.1016/J.JEMERMED.2020.10.026.

[3] H.P. Meyers, S.W. Smith, A. Bracey, e S.D. Weingart, *The OMI Manifesto: Rethinking the STEMI/NSTEMI Paradigm*,2018.

[4] F. Ricci et al., "ECG Patterns of Occlusion Myocardial Infarction: A Narrative Review," *Ann. Emerg. Med.*, vol.85, no.4, pp.330–340, Apr.2025, doi:10.1016/J.ANNEMERGMED.2024.11.019.

[5] H. Pendell Meyers *et al.*, "Ischemic st-segment depression maximal in v1–v4(Versus v5–v6) of any amplitude is specific for occlusion myocardial infarction (versus nonocclusive ischemia)," *J. Am. Heart Assoc.*, vol.10, no.23, p.22866,

Dec.2021, doi:10.1161/JAHA.121.022866/SUPPL_FILE/ JAH36862-SUP-0001-SUPINFO.PDF.

ASSOCIATION BETWEEN INSULIN SENSITIVITY AND ISLET AUTOANTIBODY PROFILE IN RELATIVES OF INDIVIDUALS WITH TYPE 1 DIABETES

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Background: and Aim: Insulin sensitivity (IS) is associated with a reduced risk of developing type 1 diabetes (T1D) when adjusted for insulin secretion. This study investigates whether the Matsuda Index, a well-established measure of IS, is associated with the presence and titers of islet autoantibodies (AAbs) in relatives of individuals with T1D.
Materials and methods: We analyzed five islet AAbs—GAD, IA2, MIAA, ICA, and ZnT8—in AAb-positive relatives of T1D patients (n=7,137) enrolled in the TrialNet Pathway to Prevention study [age: 16.8 (±12.5) years, 51.3% female; T1D Stages: 36.4% Not Staged, 34.8% Stage 1, 21.4% Stage 2, 7.4% awaiting Stage 3 confirmation]. Associations between islet AAb type/titer and Matsuda Index were assessed using linear and logistic regression models, adjusting for Index60 (a marker of insulin secretion) and age.
Results: After adjusting for Index60, the Matsuda Index was inversely associated with the presence of IA2 and ZnT8 ($p<0.0001$), as well as GAD and ICA ($p<0.001$). Similarly, it was inversely associated with AAb titers ($p<0.0001$ for GAD, IA2, and ICA; $p=0.004$ for ZnT8), except for MIAA, which showed a positive association for both presence ($p<0.0001$) and titer ($p<0.0001$). After an additional adjustment for age, the positive association with MIAA was no longer significant, whereas the inverse associations for the other AAbs remained robust (presence: $p<0.0001$ for IA2, ZnT8, and ICA; $p=0.001$ for GAD; titer: $p<0.0001$ for IA2, ZnT8, and ICA; $p=0.0003$ for GAD).
Conclusions: After accounting for insulin secretion and age, higher IS is inversely associated with the presence and titer of most islet AAbs. However, MIAA exhibits a distinct pattern, suggesting a potential age-related influence.

A "COLD" CASE OF MYXEDEMA COMA

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Case presentation: We present a case of a 77-year-old male who was brought into the emergency room as a suspected stroke for the onset of dysarthria and alterated state of consciousness.On medical examination, the patient was less responsive with a GCS of 10/15, hypothermic (TC 30°C), hypotensive (PA 80/60 mmHg), bradycardic (45 bpm), diffuse non-pitting edema. Oxygen saturation on pulse oximetry was unrecordable. On electrocardiogram junctional rhythm was observed. Chest examination revealed bibasal fine crepitation and the bed-side ultrasound showed bibasal B pattern, no pleural effusion, no free abdominal fluid, right kidney with cortical thinning (known finding), no left hydronephrosis. External warming, volume resuscitation with warm fluid and subsequent circulatory support with norepinephrine were performed, in the suspicion of severe sepsis in anergic patient. So the patient was admitted to our internal medicine department (UOC Medicina Interna di Continuità, Azienda Ospedialiero-Universitaria of Parma).His past medical history was significant for Alzheimer disease (diagnosed in 2008), chronic renal failure (baseline creatinine of 2 mg/dl), ischemic cardiomyopathy with hypokinetic-dilated heart due to previous STEMI (2018) and history of paroxysmal supraventricular tachycardia, for which amiodarone therapy was initiated.He also normally took bisoprolol 2.5 mg once at night, aspirin 100 mg, atorvastatin 40 mg once at night, furosemide 25 mg once in the morning, canrenone 50 mg once in the morning and memantine 10 mg once in the morning. He did not have any evidence of a known thyreopathy. Given the electrocardiogram (ECG) findings, amiodarone, beta-blockers and memantine were discontinued, with restoration of a sinus bradycardia with a heart rate of 38-40 bpm. The arterial blood gas analyses on 21% FiO2 (fraction of inspired oxygen) showed mild hypoxemia, so hewas put on 2 liters of oxygen via nasal cannula. His admission blood tests showed mild rise of inflammatory markers, increased transaminases, abnormalities of the blood count including mild anemia and moderate thrombocytopenia, sign of acute-on-chronic kidney failure (Table 1). At the beginning we approached the patient as having severe sepsis, so we continued fluid resuscitation, aminergic support and antibiotics (piperacillina/tazobactam), with effective hemodynamic stabilization. Due to such a high Thyroid Stimulating Hormone (TSH) value and the persistence of hypothermia, somnolence and bradycardia, he was discussed with the Endocrinologist regarding the probability of myxedema coma as a contributing factor of the clinical condition. The Myxedema coma Score at our evaluation was 70. (Table 2).
Discussion: Myxedema coma is a rare life-threatening complication of severe hypothyroidism. It can occur in patients with undiagnosed or undertreated hypothyroidism and it may remain undiagnosed due to the sudden onset, the lack of reliable history in patients presenting with altered sensorium and overlap of symptoms with common medical conditions like sepsis, metabolic encephalopathy, cerebrovascular events. Our patient was affected by Alzheimer's disease without a known history of hypothyroidism, which made the diagnosis even more insidious due to the pre-existing cognitive decline. He was initially treated as septic shock with the administration of fluid resuscitation, antibiotics and vasopressors, showing an initial clinical response and improvement in his level of consciousness. The suspicion of underlying severe hypothyroidism arose only in the following days due to the persistence of bradycardia, maintenance of body temperaturearound 35°C and significant psychomotor slowing, along with the anamnesis of amiodarone use in the home therapy. For this reason, in our case, we consulted the Endocrinologist only after obtaining a definitive laboratory confirmation of overt severe hypothyroidism (TSH 124 uU/ml, FT4 0.28 ng/dl). For the management of MC, American Thyroid Association (ATA) endorses the use of intravenous LT4 and glucocorticoids irrespective of the severity of disease, although randomized clinical trials are still lacking and not realistic since the rarity and severity of the disease, so the recommendations regarding the type and route of replacement therapy are based on expert opinions and isolated case reports. Due to the limited availability of intravenous LT4 in many countries most of the patients are managed with oral LT4. In our case the decision to start with low-dose of oral LT4 rather than high-dose of intravenous LT4, regardless its unavailability in our country, was justified by the patient's clinical improvement after sepsis treatment, thus indicating sepsis as the trigger of the clinical presentation.

THE CHALLENGE TO HAVE IT BOTH WAYS IN THE PRECARIOUS BALANCE BETWEEN AF-RELATED EMBOLISM AND GI-BLEEDING IN ELDERLY PATIENTS

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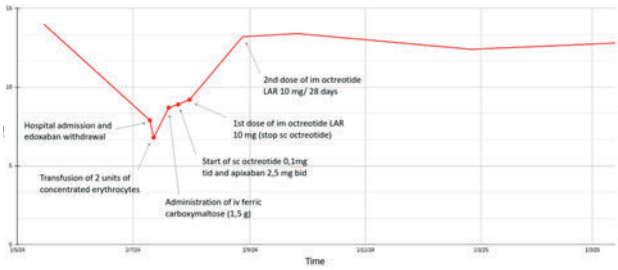
We report the case of an elderly multimorbid patient, who presented hemorrhagic complications of direct oral anticoagulation (DOAC) treatment for atrial fibrillation (AF) and AF-related embolic events during DOAC discontinuation.
The patient is a 91-year-old caucasian woman admitted to our internal medicine unit in July 2024 for dyspnea, fatigue and melena. She had a medical history of AF on edoxaban treatment (CHA2DS2-VASc 5), hypertensive cardiomyopathy, chronic kidney disease (KDIGO stage G3b), hyperthyroidism (toxic nodular goiter), chronic venous insufficiency, obesity. Her skin was pale but vital signs were normal. Blood tests showed severe normocytic anemia, with an acute drop in haemoglobin (Hb) levels (from 14 to 6,8 g/dl in a few days).
Thus, we stopped edoxaban and we administered 2 units of concentrated erythrocytes and IV pantoprazole infusion obtaining Hb values stabilization and symptoms resolution. The patient also received IV ferric carboxymaltose. The patient underwent esofago-gastro-duodenoscopy (EGDS) and subsequently colonoscopy, which were both normal. We then offered the patient videocapsule enteroscopy in the suspicion of small bowel angiodysplasia, but the patient refused to undergo the exam, even because she was not suitable to undergo any eventual surgical intervention due to an elevated anesthesiological risk.
Meanwhile, keeping DOAC stopped, the patient developed acute pain in the inferior left limb, which on physical examination appeared pale, cold and without arterial pulse. We performed urgent Doppler-US that confirmed artery occlusion, so she underwent a successful embolectomy by Fogarty catheter, resolving the acute limb ischaemia. Thus, considering the high risk of a new embolic event, the stabilization of Hb values and the absence of active melena, we re-instituted DOAC treatment, switching edoxaban for apixaban for the shorter half-life with better safety profile.
Assuming the presence of intestinal angiodysplasias, we also started octreotide at the dose of 0,1 mg/8h by subcutaneous route, with good tolerance and no adverse events. Hb levels remained stable during the subsequent days, so we prescribed off-label octreotide LAR (Long Acting Release) at the dose of 10 mg/28 days by intramuscular injection and the patient was discharged.

She did not experience new bleeding episodes / hospitalization / transfusion, while continuing both apixaban and octreotide LAR and her Hb levels progressively rose achieving 13 g/dL and remained stable over time. Furthermore, despite old age and multiple comorbidities, the patient did not experience any adverse events of octreotide therapy.
The clinical case underlines that, in elderly multimorbid patients, internal medicine specialists have to face the precarious balance between thromboembolism and haemorrhage taking difficult decisions in the management of anticoagulation. Several reports from the literature and a randomized controlled trial support the use of octreotide LAR to prevent or reduce bleeding from small bowel angiodysplasias which account for up to 60% of cases of obscure gastrointestinal bleeding.1, 2, 3, 4, 5 Octreotide acts by augmenting platelet aggregation, decreasing splanchnic blood flow, and antagonizing angiogenesis.2
Nevertheless the aim of this case is to remark the good safety and tolerability of octreotide LAR, also among elderly and multimorbid patients as reported in the literature5, and to highlight the efficacy in preventing or reducing the need for rehospitalization or blood transfusion for rebleeding from small bowel angiodysplasias or from occult intestinal bleeding in multimorbid patients who need DOAC treatment for AF. Our personal opinion is that in case of small bowel bleeding, even in elderly patients, the use of octreotide LAR should be encouraged to avoid DOAC discontinuation because of the detrimental effects on morbidity, mortality and quality of life related to AF embolic events.

References:

1. Goltstein LCMJ et al. Standard of care versus octreotide in angiodysplasia-related bleeding (the OCEAN study): A multicenter randomized controlled trial. *Gastroenterology* 2024 Apr; 166:690
2. Khedr A, Mahmoud EE, Attallah N, Mir M, Boike S, Rauf I, Jama AB, Mushtaq H, Surani S, Khan SA. Role of octreotide in small bowel bleeding. World J Clin Cases 2022; 10(26): 9192-9206
3. Holleran G, Hall B, Breslin N, McNamara D. Long-acting somatostatin analogues provide significant beneficial effect in patients with refractory small bowel angiodysplasia: Results from a proof of concept open label mono-centre trial. United European Gastroenterol J. 2016 Feb;4(1):70-6
4. Scaglione G, Pietrini L, Russo F, Franco MR, Sorrentini I. Long-acting octreotide as rescue therapy in chronic bleeding from gastrointestinal angiodysplasia. Aliment Pharmacol Ther. 2007 Sep 15;26(6):935-42
5. Molina Infante J, Pérez Gallardo B, Hernández Alonso M, Mateos Rodríguez JM, Dueñas Sadornil C, Fernández Bermejo M. Octreotide long acting release for severe obscure gastrointestinal haemorrhage in elderly patients with serious comorbidities. Med Clin (Barc). 2009 Nov 7;133(17):667-70



MANAGEMENT OF ANTICOAGULATION THERAPY IN THE CONTEXT OF ATRIAL CATHETER REMOVAL SECONDARY TO EXTENDING IN LOCO THROMBOSIS. DESCRIPTION OF A CASE.

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Background: Ventriculo-peritoneal and ventriculo-atrial shunts are the two most common techniques for draining cephalospinal fluid. There are some complications, the most common of which are malfunction and infection of the system. Thromboembolic events, superior vena cava obstruction, and cor pulmonale are the typical complications of ventriculoatrial shunt. If the embolic complication exists, it is possible that this, despite adequate anticoagulation, will be sustained by the presence of the catheter. In this case, removal is necessary. However, management of DOACs in case of atrial venous catheter removal in the derivative setting is not described in the literature to our knowledge.
Case description: We describe a case of a 34-year-old woman, suffering from neurofibromatosis I with optic tract glioma, secondary obstructive hydrocephalus undergoing five ventricle-peritoneal shunt surgeries since 1991 performed for malfunction of the respective previous ones. In 2010 performed conversion to atrial ventricle shunt for infection of previous system with ventricular catheter in left lateral ventricle and medium pressure Pudenz valve. In September 2021 she was admitted for PE, left jugular and brachiocephalic veins thrombosis near distal catheter of ventriculoatrial shunt. She was discharged with indication to apixaban at a dosage of 5 mg bid and radiological follow-up. In December 2021 she was admitted for postural instability and CT finding of supratentorial ventricular dimensional increase. CT was negative for PE, but found thrombosis of left subclavian vein, brachiocephalic vein and through paraspinal collateral circles, interesting the azygos vein, also of the superior vena cava. Placed then ventriculo-peritoneal shunt and, given high embolic risk, maintained ventriculo-atrial shunt in place. She was on subcutaneous heparin and discharged to our Thrombosis Outpatient Clinic, where apixaban was reinitiated, first at full dose, then to maintenance dose. Six months later she repeated angioTC with persistence and thrombotic extension in both caudal and cranial directions, so she underwent removal of the DVA catheter in late 2022. Management of anticoagulation therapy was discussed with hemostasis expert and neurosurgeons. It was decided to discontinue apixaban 24 hours before and reintroduce anticoagulation therapy 48 hours after surgery preceded by intermediate-dose heparin. We observed no thrombotic or hemorrhagic complications in the peri- and postoperative period.
Conclusions: According to EHRA guidelines, neurosurgical procedures, toutcourt, are procedures with a high risk of bleeding. Therefore, the planned withdrawal of anticoagulant therapy for apixaban is at least 48 hours before the procedure. The atrial catheter is generally inserted, at the neck level, into the jugular vein and then advanced to the right cardiac atrium. Removal of the atrial catheter alone is done by making a cut at the neck level and pulling the catheter out; however, it is not considered a high-risk bleeding procedure from a surgical point of view. In this case, we opted for suspension of anticoagulation therapy 24 hours before the procedure. Apixaban therapy can then be reintroduced 48 hours after the procedure, but in this case, it was preceded by intermediate-dose EBPM due to high thrombotic risk. We observed no complications. At a following CT scan, we observed complete recanalization of subclavian and jugular thrombosis. In conclusion, we suggest that managing anticaogulation therapy is complex and although guidelines trace a path, we always need to identify and quantify the thrombotic and hemorrhagic burden in order to tailor the best choice for every single patient.

CARDIORESPIRATORY FITNESS AND PHYSICAL FUNCTION IN ADULT PATIENTS WITH FABRY DISEASE: A CROSS-SECTIONAL MULTICENTER STUDY

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Background: Fabry Disease (FD) is a rare, X-linked lysosomal storage disorder that affects multiple organ systems, including the musculoskeletal system. However, physical status in FD patients remains poorly characterized. Therefore, this cross-sectional multicenter study aims to evaluate physical fitness and physical function in FD patients and to investigate their relationship with sex, FD phenotype, and enzyme replacement therapy (ERT) or chaperone treatment.
Methods: Adult patients (age >18 years) with a genetic diagnosis of FD were screened. Demographic and laboratory data were collected. Cardiorespiratory fitness, measured by peak oxygen uptake (VO_2 peak), was assessed using cardiopulmonary exercise testing (CPET). Body composition was assessed by multi-frequency bioelectrical impedance analysis (BIA), including Fat-Free Mass Index (FFMI), Fat Mass Index (FMI), and Phase Angle (PA). Physical function was evaluated through the 6-minute walk test, handgrip strength, chair-stand test, and the Short Physical Performance Battery. Perceived fatigue was also assessed using self-report questionnaires. Statistical analyses were performed, grouping patients by sex (male or female), phenotype (classic or late-onset/VUS), and treatment status (ERT/chaperone-treated or untreated).
Results: A total of 42 FD patients (13 males; mean age 46 years [SD 13.9]) were enrolled. CPET revealed sex- and phenotype-specific differences. A significantly higher prevalence of predicted VO_2 peak <85% was observed in classic phenotype patients (53.8%) compared to late-onset/VUS patients (11.5%; $p < 0.01$). Body composition analysis indicated lower FFMI in classic phenotype patients compared to late-onset/VUS (mean 16.8 kg/m² [SD 1.0] vs 18.6 kg/m² [SD 2.1]; $p = 0.01$). Furthermore, PA was significantly lower in treated males

(mean 4.8° [SD 1.0]) than in untreated ones (mean 7.6° [SD 0.9]) (p = 0.04), and significantly higher in those with greater VO_2 peak values (r = 0.879, p = 0.01). Compared to reference values in the general population, physical function tests in classic phenotype males showed that 74.3% scored below the 50th percentile in handgrip strength (mean 26.1 kg [SD 7.8]), and 60.9% performed below predicted chair-stand test values (mean 12.4 repetitions [SD 4.3]). Fatigue self-reported scores were higher in classic and treated patients compared to late-onset/VUS (p = 0.05) and untreated ones (p = 0.02), respectively.
Conclusions: Our findings show that patients with classic phenotype, particularly males, were associated with reduced maximum exercise capacity and physical performance. These results highlight the need to integrate CPET, functional tests, bioelectrical impedance analysis, and self-report fatigue tools into the routine evaluation of FD patients.

LOOKS LIKE A NEOPLASM, BELONGS TO AMYLOIDOSIS, BUT IS USUALLY BENIGN: LOCALIZED AMYLOIDOSIS. A LONG-TERM RETROSPECTIVE MONOCENTRIC STUDY

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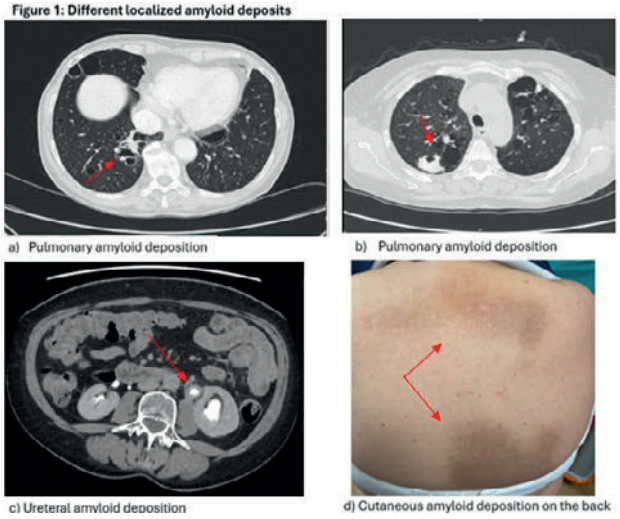
Unlike systemic amyloidosis, localized amyloidosis is certainly rarer, under-reported and less studied. In this form, the deposition of amyloid is confined to a specific site, with no evidence of systemic tissue infiltrations. In the majority of cases, it is a solid lesion with absent contrast enhancement.
However, its pathogenesis and evolution remain poorly understood. We report our experience, analyzing its localization, risk factors, progression, relapses and outcomes.
We retrospectively analyzed traceable patient medical records referred to our regional amyloidosis center in the Tuscany region, selecting those with localized amyloidosis, defined by histological confirmation of amyloid deposits confined in one organ, made by positive Congo red stains showing an apple-green refraction under polarized light, in the absence of any evidence of vital organ involvement, through evaluation of specific markers, including NT-proBNP, Troponins, Alkaline phosphatase, and creatinine and 24-hour urine protein to assess for cardiac, hepatic, and renal involvement. Typing was performed by immunogold on elecronmicroscopy.
31 patients were diagnosed with localized amyloidosis. The organ involved are reported in Table 1 with the respiratory system (n = 17, 55%), the skin (n=5 , 16%) and the genitourinary system (n=3, 10%) as the most frequenting sites. In 11 out 31 patients typing reveal an AL amyloidosis with 8 λ and 3 k amyloid deposit. Smoking was the major risk factor (17 of 31), of whom 12 in the respiratory tract, while the remaining cases showed localization in the bladder (n=1), breast (n=1), lymph node (n=1), tongue (n=1), and stomach (n=1).
The association with autoimmune diseases was also notable and the correlation with Interferon (IFN) therapy was suggestive (Table1). Amyloid deposits often appeared as solid lesions, (Figure 1) and produced symptoms due to their mass effect. Subsequently, a differential diagnosis was essential through histological confirmation. None of the 31 patients demonstrated evidence of systemic amyloidosis at the time of diagnosis (Table 1). Only one patient had nephrotic proteinuria and underwent renal biopsy and genetic testing, leading to a diagnosis of Fabry disease. A monoclonal gammopathy was identified in 3 out of 31 patients at diagnosis, characterized by IgA Lambda, IgM Lambda, and IgG Lambda components, respectively. In these 3 patients, the search for a systemic form was conducted in a extensive manner, including a biopsy of the periumbilical abdominal fat, which resulted negative for amyloid deposit in all cases.
Eleven of the 31 patients underwent surgical excision of the deposits following diagnosis, of whom 5 experienced local recurrences during follow-up, all occurring at the original sites of disease. The mean time between surgery and recurrence was 7.8 years (SD ± 5.9). In no patient the localized amyloidosis progressed to systemic disease. Among patients without a monoclonal component at diagnosis, none developed a detectable serum or urinary monoclonal protein up to the last available follow-up. Survival data were available for 27 of the 31 patients, showing a current mean age of 64.5 years (SD ± 9.8), with a mean survival time from diagnosis to last follow-up of 9.5 years (SD ± 9.3). The longest ongoing survival recorded was 32 years. Two patients died, at 64 and 77 years, 12 and 6 months after the diagnosis, respectively. The first due to a squamous lung carcinoma in the same site affected by amyloidosis; the second due to recurrence of urothelial carcinoma and was one of the patients with serum monoclonal component (IgA Lambda). Two patients were lost to follow-up, and survival data for these individuals remain unknown.
Localized amyloidosis is an uncommon disease, showing an excellent prognosis with long median overall survival. In the majority of patients the primary indication was local symptom control. No patients required radiation therapy or systemic chemotherapy . Furthermore, the likelihood of recurrence of localized disease appears to be low and progression to systemic disease absent. In all cases where typing was performed the deposits showed AL type amyloidosis with a preponderance of λ vs k type. According to the literature, most cases of localized amyloidosis have been associated with smoking or autoimmune diseases. The potential link with IFN therapy appears to be at least suggestive. Given the incomplete understanding of the disease's pathogenesis, it is plausible that a persistent inflammatory stimulus may contribute to the localized abnormal production of immunoglobulins and their products by a minimal B clone in the involved sites. Localized amyloidosis is an unexpected diagnosis in the context of a suspected malignancy and is essential to refer patients to a specialized center for a diagnosis and to exclude systemic disease. Despite the favorable prognosis, these cases must be carefully monitored to identify any local recurrence or systemic transformation.

Figure 1: Different localized amyloid deposits



N° of Patients: 31
Sex: 13 M; 18 F

Mean age at diagnosis:
58,4 years (SD 12,2)

Risk factors:
- **Smoke:**
17 Patients yes (54.8%)
8 Patients no
6 Patients unknown

- **Autoimmune diseases:**
1 Celiac disease;
2 multiple sclerosis;
1 Common Variable Immunodeficiency on Ig therapy;
3 SLE;
3 Hypothyroidism under treatment
2 Sjogren disease;
1 Psoriatic Arthritis

Other concomitant comorbidities:
4 COPD; 1 kidney cancer; 2 HCV; 1 Fabry disease; 1 Tuberculosis; 1 alcoholic; 2 Lymphoma

- **Unknown:** 5

- **IFN therapies:**
3 Patients

Some had an overlap of more than one of these risk factors.

Symptoms at diagnosis 18 Patients

Systemic involvement at diagnosis:
None

Monoclonal component at diagnosis:
3 Patients
-1 IgA Lambda
-1 IgG Lambda
-1 IgM Lambda

Congo Red staining positive on biopsy:
31 out of 31 (100%)

Typing by electron microscopy and immunogold:
11 out of 31, of which in 100% of cases it was light chain (27.3% kappa, 72.7% lambda)

Clinical markers at diagnosis:
Serum free light chains
- Kappa: 22.7 mg/L (SD 16.6)
- Lambda: 20.4 mg/L (SD 12.6)
- K/L: 1.19 (SD 0.47)
- Bence Jones: none

ALP: 69.5 U/l. (SD 14.5)
OGT: 31.6 U/l. (SD 33.1)
NT Pro BNP: 266.6 pg/ml. (SD 388.9)
eGr. 0.82 ml/s/1,4 (SD 0.19)
24-hour Proteinuria: < 300 mg in 30 out of 31 Patients

Localization:
19 respiratory tract:
- 11 lungs;
- 2 bronchi;
- 3 trachea;
- 2 larynx;
- 1 nasal turbinate;

5 cutaneous:
- 2 back;
- 1 anterior chest;
- 1 eyelid;
- 1 lower limb

1 breast
1 lymph node
1 bladder
1 ureter
1 prostate
1 tongue
1 gastric

Surgical removal of amyloid deposits:
11 yes (6 lungs, 1 bladder, 1 eyelid, 1 tongue, 2 larynx)
- 18 no;
- 2 unknown

Recurrences:
- 5 out of 11 operated (1 bladder, 1 eyelid, 1 tongue, 2 larynx) (mean age between diagnosis and first recurrence 7,8 years (SD 5.9)

- Localization of recurrence: all at the same site as the initial disease

Positive follow up for serum and/or urinary monoclonal component: None

Progression to systemic disease: None

Survival:
2/ yes
Current mean age 64,5 years (SD 9,8);
- Years of survival from diagnosis to last follow-up: 9.5 years (SD 9.3), with maximum survival of 32 years (ongoing)

- 2 deceased (at 64 and 77 years) causes:
- Lung cancer in the same site as amyloidosis (1 year after amyloidosis diagnosis)
- Recurrence of urothelial cancer (6 months after amyloidosis diagnosis)

2 unknown

ORGANIZATION OF INTENSIVE SHORT OBSERVATION INSIDE THE U.O.C. M.C.A.U. OF THE PAPARDO HOSPITAL

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U.O.C. M.C.A.U. Ospedale Papardo

The Intensive Short Observation Units inside the Emergency, Urgency and Acceptance Departments were introduced in Anglo-Saxon countries starting from the 60s. In Italy there have been various national regulatory references to define the organizational methods of Intensive Short Observation. In August 2019, the Ministry of Health issued the "National Guidelines on Intensive Short Observation-OBI" for the diffusion of these U.O.S. in the DEA and in the ER in order to reduce inappropriate hospitalizations, increase the safety of discharges and improve the patient care process. : The sector studies carried out have immediately demonstrated an undoubted benefit brought by the Short Observation Units in relation to the improvement of the quality of care and the

appropriateness of hospitalizations and discharges. According to the definition of the Ministry of Health, "OBI is a method of managing emergencies-urgencies for patients with acute clinical problems with a high degree of criticality but low risk of evolution, or low criticality but with potential risk of evolution, with a high probability of reversibility, with the need for a diagnostic and therapeutic process that cannot be postponed and/or managed in other healthcare contexts." The Short Intensive Observation Unit of the Papardo Hospital currently has an Open Space room of approximately 40 square meters in addition to a bathroom also for the disabled equipped with five beds, integrated inside the S.C. M.C.A.U.. All beds have oxygen and a suction system available. The beds are separated by curtains. If necessary, it is possible to use another three beds located in a new area of the S.C. M.C.A.U.. Also in this area equipped with toilets also for disabled people, the beds have oxygen and aspiration system available. The stations dedicated to OBI are 1 for every 5000 visits to the Emergency Room. Three of the five beds of the OBI of the Papardo Hospital are equipped with a multi-parameter monitoring system. Inside the OBI rooms there is an emergency trolley, devices for the administration of oxygen, an electrocardiograph, a defibrillator, a mechanical ventilator and an infusion pump. The blood gas analyzer and the ultrasound are shared with the Emergency Room. According to the table of minimum staffing of the OBI drawn up by the Ministry of Health in the National Guidelines on Brief Intensive Observation, for a unit of 5 to 8 stations, a doctor with a commitment of 60 minutes per day per station, a nurse for 24 hours and an OSS for 12 hours of the day are foreseen, shared during the night hours. During the night, since it is not possible to guarantee a doctor dedicated to the OBI, health care will be provided by the doctors of the Emergency Department.

Admission criteria in OBI

- The patient must have a prominent problem to be defined in terms of diagnostic evaluation with a high possibility of stabilization.
- Instrumental clinical approach of medium complexity also with monitoring.
- Intensive clinical observation and therapeutic interventions limited in time.

Criteria for non-admission to OBI

- Instability of vital parameters with serious clinical conditions (red code and in some cases orange code at admission)
- Infectious risk
- Psychomotor agitation with harmful behaviors for oneself or others
- Multi-pathological patients
- Conditions requiring emergency hospitalization

-Scheduled hospitalizations

The OBI doctor takes charge of the patient transferred from the ER through the computerized medical record and examines him. Based on what has already been done by the colleague from the ER, he defines the further diagnostic and therapeutic path, activates the necessary procedures and carries out the subsequent re-evaluations of the patient. He also provides instructions to the OBI nurse on the therapies to be administered and on the methods of observation to be carried out. At the end of the Short Observation period, which must last no less than six hours and no more than forty-four hours from the time of taking charge at Triage, the doctor decides whether to admit the patient to a hospital ward or to discharge him or her home or to be entrusted to territorial or residential facilities. In any case the OBI doctor issues to the patient, or to the hospitalization facility, a paper copy of the medical record and a copy of the report of the tests performed and the specialist visits performed.

LATE PRESENTATION OF ADULT STILL'S DISEASE

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Introduction: We describe the case of a 57-year-old male patient whose clinical history began at the beginning of December 2023 with the onset of fever (max 39.5 °C) and pain on the anterior aspect of the thighs with hyperesthesia. The patient initially took paracetamol. The tests performed at home excluded SarsCov2 infection (negative nasopharyngeal swab) and showed an increase in inflammation indices (ESR: 110 mm, CRP: 1.75 mg/dl (vn: 0-0.5), alpha2 globulins: 13.4%, fibrinogen: 655 mg/dl). The symptoms progressively worsened over the following weeks with the onset of migratory arthralgias so much so that the patient was unable to walk during the feverish episodes. In the absence of fever, the pain was bearable even if it limited daily activity. On December 20, 2023, the patient went to the emergency room at the San Bartolomeo hospital in Sarzana where he was admitted and transferred to internal medicine. The physical examination confirmed arthralgia without signs of arthritis and thigh pain with hyperesthesia. The patient reported pharyngodynia, but there were no signs of acute pharyngitis.

Methods: Laboratory tests confirmed the increase in inflammation indices (ESR: 125 mm, CRP: 1.85 mg/dl, alpha2 globulins: 12.8%, fibrinogen: 620 mg/dl, ferritin: 660 mcg/L, PLT: 555000/mm3), anemia (Hb: 8.1 g/dl, MCV: 88 Fl), increased transaminases (AST: 112 IU/L, ALT: 96 IU/L), LDH (638 IU/L) and leukocytosis with relative and absolute neutrophilia (GB: 22500/mm3-N: 70%-15750/mm3). ANA, ENA. rheumatoid factor, anti-citrulline antibodies, anti-thyroperoxidase and anti-thyroglobulin antibodies were negative and TSH was normal. An immunological consultation was requested at our UO. The anamnesis did not reveal any significant previous pathology including immunological and thrombophilic pathologies. The patient denied taking any drugs previously. We recommended performing a chest-abdominal CT and PET. The chest-abdominal CT showed multiple lymphadenopathy above and below the diaphragm, hepatosplenomegaly, a small collection in the right iliac fossa of doubtful significance and diverticulosis of the sigma. PET with 18F-FDG tracer demonstrated hyperuptake of multiple lymph nodes above and below the diaphragm, of the spleen, of the bone marrow, of the superficial and deep femoral vessels bilaterally and of the stomach. A bone marrow biopsy was scheduled which excluded a possible lymphoma. The suspicion of adult Still's disease was confirmed not only by the clinical findings and the tests performed, but also by the Yamaguchi criteria (at least 2 major criteria present: fever for more than 2 weeks > 39°C, neutrophilic leukocytosis, arthralgia for more than 2 weeks; all minor criteria: Pharyngodynia or pharyngitis - lymphadenopathy and/or splenomegaly - hypertransaminasemia - negative rheumatoid factor and antinuclear antibodies (ANA) (at least 3 required); exclusion criteria excluded: infections - neoplasms - inflammatory diseases of other origins. Diagnosis of adult Still's disease with late onset was made (the age groups most affected by the disease: one is between 15 and 25 years, the other between 36 and 46 years), the patient was treated with methylprednisolone 500 mg IV for 5 consecutive days with immediate response (apirexia after 48 hours and progressive decrease in pain) followed by prednisone 75 mg orally (1 mg/Kg) for 20 days. After 10 days the arthromyalgia was reduced allowing the patient to walk again. The inflammation indices decreased after 7 days of therapy (ESR: 65 mm, CRP: 0.95 mg/dl, alpha2 globulins: 11.3%, fibrinogen: 440 mg/dl, ferritin: 460 mcg/L, PLT: 450000/mm3). The tests confirmed the decrease in transaminases (AST: 55 IU/L, ALT: 50 IU/L) and LDH (255 IU/L). After 2 months all abnormal tests were normal except for mild neutrophilic leukocytosis attributable to prednisone therapy (GB: 10000/mm3; N: 55%). It was decided to start anakinra 100 mg subcutaneously daily.

Follow up: After approximately 1 month of therapy, the patient reported a clear improvement in the clinical picture, in particular no further fever episodes and almost complete remission of the arthromyalgia. Laboratory tests confirmed the improving trend in the following months with negative inflammation indices after 3 months of therapy with anakinra 100 mg subcutaneously per day and prednisone progressively reduced in dosage to 10 mg. The control PET was scheduled for October 2024 and confirmed the remission of the disease with complete metabolic response and resolution of splenomegaly. The tests were always normal with occasional increases in ESR that have not yet allowed the suspension of prednisone (5 mg/day from December 2024): last ESR value: 42 mm (March 2025). Anakinra 100 mg subcutaneously per day continues. The question of when to permanently discontinue prednisone and consider reducing the weekly dosage of anakinra remains open.

GPA: THE IMPORTANCE OF A MULTIDISCIPLINARY APPROACH IN RARE DISEASES

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Premises: Granulomatosis with polyangiitis (GPA), formerly called Wegener's granulomatosis, is a rare, potentially life-threatening systemic vasculitis of small vessels, mediated by the immune system, characterized by an inflammatory pattern with necrosis and granulomatous infiltration affecting the upper and lower airways and the kidneys. The diagnosis of GPA is made through clinical evaluation, laboratory tests for the detection of ANCA, and histological examination. Early recognition of the disease onset is essential for diagnosis and treatment, requiring a prompt diagnostic-therapeutic process involving a multidisciplinary team to ensure improved prognosis and quality of life for the patient. We describe the case of a patient who presented to our attention with an unspecific clinical picture, for whom the early detection of the disease allowed the initiation of effective targeted treatment, coordinated with a multidisciplinary team of specialists.

Description of the case report: 64-year-old female with hyperpyrexia, cough, and significant asthenia. She had been admitted to another hospital where a chest CT was performed, revealing multiple bilateral parenchymal consolidations with peri-hilar, peribronchovascular, perilymphatic, and subpleural distribution.

For diagnostic evaluation, the patient underwent bronchoalveolar lavage with cytological examination concluding with "amorphous material including bronchial epithelia without atypia, various granulocytes and histiocytes, some erythrocytes, and squamous cells." Microbiological tests and tumor markers were all negative, renal function was normal, but there was an increase in inflammatory indices and neutrophilic leukocytosis, leading to the initiation of empirical antibiotic and corticosteroid therapy with clinical improvement. During hospitalization, due to conjunctival hyperemia, an ophthalmological assessment was conducted, diagnosing superior temporal episcleritis in the right eye. After discharge, the patient developed evening fever and diarrhea, prompting a colonoscopy, which was negative. Due to the persistence of the described symptoms, the patient accessed the Emergency Department, where acute renal failure and elevated inflammatory indices were found, leading to hospitalization in the Internal Medicine ward for suspected infectious diarrhea, acute renal failure from dehydration, and septic state in a patient with non-specific lung lesions. Given the simultaneous pulmonary and renal involvement and excluding other etiologies (infectious, neoplastic), in suspicion of autoimmune vasculitis, an autoimmune study was performed, revealing an anti-proteinase 3 antibody titer greater than 500 CU/ml. Therefore, the patient underwent a renal biopsy, concluding with "necrotizing extracapillary glomerulonephritis, ANCA-associated, anti-PR3 positive." To complete the diagnostic process for the vasculitic picture, an ENT evaluation and facial CT were performed, revealing thickening of the mucous membrane lining the walls of the paranasal sinuses and signs of bilateral ethmoiditis, as well as a chest CT showing ubiquitous ground-glass areas. In light of these clinical, laboratory, and radiological findings and the histological examination, a diagnosis of Granulomatosis with Polyangiitis (GPA) was made. During hospitalization, hemodialysis sessions and non-invasive ventilation became necessary due to severe respiratory failure. According to EULAR guidelines, the patient was treated with boluses of methylprednisolone (1g/day for three consecutive days), plasma exchange sessions, and administration of cyclophosphamide intravenously (500mg the first week and the same dose after two weeks) in association with rituximab 375 mg/m2 (750 mg in one administration per week for four weeks). However, the immunosuppressive therapy was not without complications, as the patient presented with septic conditions, which were treated with appropriate antibiotic therapy, allowing for effective resumption of active treatment of the underlying condition with clinical, laboratory, and instrumental improvement at discharge. The patient was discharged home with spontaneous diuresis, without the need for home oxygen therapy, and with a prescription for corticosteroid and immunosuppressive therapy with azathioprine 2 mg/kg. This therapy was confirmed, with appropriate adjustments, during the outpatient follow-up at 30 days post-discharge, given the stability of the clinical picture in the hematochemical tests reviewed and the absence of side effects.

Conclusions: The diagnosis of GPA is complicated and often delayed due to the variety of its clinical manifestations and because it is a rare disease that is not well known. For this reason, GPA represents a diagnostic and therapeutic challenge that primarily involves internists due to the complexity and variety of the clinical picture, and therefore requires an interdisciplinary team composed of nephrologists, pulmonologists, ophthalmologists, and otolaryngologists; this is essential for the timely initiation of appropriate therapy in order to improve prognosis, both in terms of survival and organ damage.

51. UREA TO CREATININE RATIO (UCR): AN OVERLOOKED INEXPENSIVE AND RAPID MARKER OF ACUTE KIDNEY INJURY

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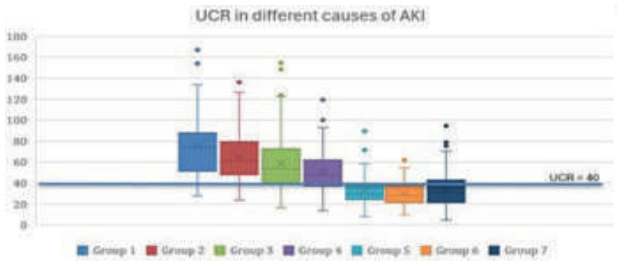
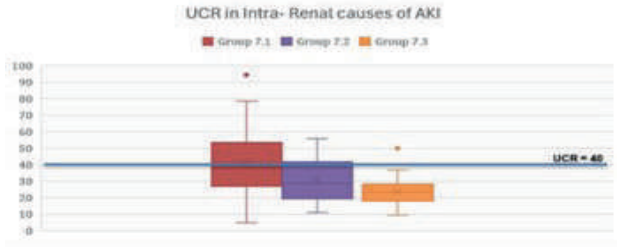
Background and aims: Acute kidney injury (AKI) is a common condition with multiple etiologies, requiring timely identification of the underlying cause for appropriate treatment. A simple and widely available marker is needed to aid clinicians in stratifying AKI causes. This article explores the role of the urine-to-creatinine ratio (UCR) as a potential marker for AKI stratification. While existing literature has associated a UCR > 40 with pre-renal causes of AKI or active gastrointestinal bleeding, no studies have stratified AKI based on the presence of chronic kidney disease (CKD) or examined the UCR in the context of all possible causes of AKI. Additionally, very few studies have addressed the UCR in intra-renal causes of AKI in patients with a biopsy diagnosis. We therefore aim to address these unresolved questions.

Methods: We conducted a retrospective observational study by searching the most common causes of AKI. The UCR was calculated. We analyzed 6036 patients; 5452 were subsequently excluded, and 584 were included. The patients were classified according to the cause of AKI into seven major groups: Pre-Renal AKI + Gastrointestinal Bleeding without CKD (39 Patients-Group 1), Pre-Renal AKI + Gastrointestinal Bleeding with CKD (52 Patients-Group 2), Pre-Renal AKI in Hypovolemic or Heart Failure conditions without CKD (128 Patients-Group 3), Pre-Renal AKI in Hypovolemic or Heart Failure conditions with CKD (100 Patients-Group 4), Post-Renal AKI without CKD (80 Patients-Group 5), Post-Renal AKI with CKD (57 Patients-Group 6), and Intra-Renal AKI (128 Patients-Group 7).Group 7 was then subdivided into three micro-groups, depending on whether the damage primarily affected the Glomerulus (65 Patients-Group 7.1), the Small Vessels (33 Patients-Group 7.2), or the Tubule- Interstitium (30 Patients-Group 7.3). Group 7.1 was further divided into Group 7.1.a - 31 Patients (Nephrotic Syndrome and Serum Albumin < 2.5 g/dL), Group 7.1.b – 9 Patients (presence of both Nephrotic Syndrome and Nephritic Syndrome) and Group 7.1.c – 25 Patients (Nephritic or Sub – Nephrotic Syndrome with Serum Albumin > 2.5 g/dL).

Results: Pre-renal AKI (Groups 3, 4) exhibited UCR values significantly above the 40 threshold [Group 3: mean UCR 58.5 (SD 25.6); Group 4: mean UCR 50.5 (SD 19.0)]. Moreover, pre-renal AKI with concomitant active gastrointestinal bleeding (Groups 1, 2) exhibited even higher UCR values [Group 1: mean UCR 75.3 (SD 32.9); Group 2: mean UCR 64.5 (SD 25.0)].Post-renal AKI (Groups 5, 6), on the other hand, showed UCR values < 40 [Group 5: mean UCR 32.6 (SD 13.6); Group 6: mean UCR 30.5 (SD 11.7)]. Considering all intra-renal AKI cases collectively (Group 7), mean UCR was 34.2 (SD 16.3). Upon detailed analysis of the UCR in Group 7.1 [UCR medio 40.7 (SD 18.2), where the percentage of nephrotic syndromes with serum albumin < 2.5 g/dL was 47.7 %], the UCR was higher compared to Groups 7.2 and 7.3 [respectively Group 7.2 mean UCR 30.9 (SD 11.4) and Group 7.3 mean UCR 24.0 (SD 8.0] ; Furthermore, when subdividing subgroup 7.1, we found a mean UCR > 40 in Group 7.1.a [mean UCR 46.7 (SD 18.1)] compared to Group 7.1.b [mean UCR 38.3 (SD 17.4)] e 7.1.c [mean UCR 33.9 (SD 15.7)].

Discussion: This study investigates the UCR across different types of AKI. In pre-renal AKI (Groups 3 and 4), UCR tends to exceed 40 due to hemodynamic instability, with elevated antidiuretic hormone (ADH) levels increasing both water and urea reabsorption. This results in higher plasma urea concentrations, while creatinine increases mainly due to reduced glomerular filtration rate (GFR). In contrast, in active bleeding or gastrointestinal absorption due to blood breakdown products (Groups 1 and 2), urea levels rise without significant changes in serum creatinine. Obstructive AKI (Groups 5 and 6) is associated with UCR values under 40, linked to decreased in the net hydraulic pressure gradient across glomerular capillaries resulting in a decline in GFR and decreased reabsorbation of solutes and water due to abnormalities in tubular function. In intra-renal AKI (Group 7), UCR presents an intermediate value. Patients with glomerular involvement (Group 7.1) show elevated UCR due to the high percentage (47.7%) of patients with nephrotic syndrome and serum albumin levels < 2.5 g/dL (Group 7.1.a) activating compensatory mechanisms that retain water, salt, and urea. Nephritic and Sub- nephrotic syndrome (7.1.c) shows less pronounced alterations in oncotic pressure and urea retention, leading to lower UCR values. Tubulointerstitial (Group 7.2) and small vessel damage (Group 7.3) replicate post-renal AKI patterns with UCR <40. In conclusion, the urea-to-creatinine ratio offers greater diagnostic efficiency compared to individual values of Creatinine or Urea. Its use could also be valuable in specific renal disease that has heterogeneous physiopathological mechanisms (e.g., monoclonal gammopathy, with damage localized at the tubular rather than glomerular level).





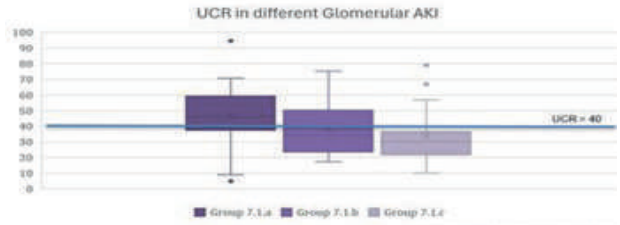


Figure 1: UCR in different AKI

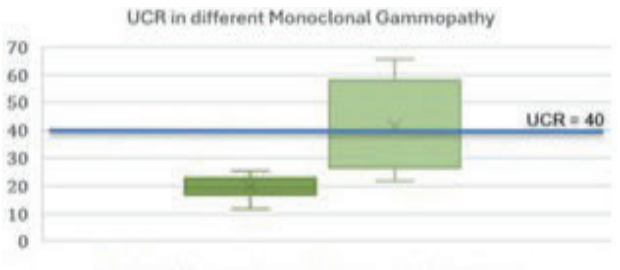


Figure 2: UCR in different Monoclonal G

CLINICAL FEATURES AND OUTCOMES OF PATIENTS WITH FULL SPECTRUM OF COVID-19 SEVERITY AND CONCOMITANT HERPESVIRUS REACTIVATION

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Background: and aims: Some studies suggested a high incidence of human herpesvirus (HHV) reactivation in severe acute respiratory syndrome coronavirus 2 (SARSCoV2) infection. However, the specific evidence accumulated to date is still rather scanty, posing a not yet solved dilemma for clinicians in terms of their diagnostic and clinical relevance. Based on these premises, our aim was to evaluate the prevalence of HHV reactivations in a large population with various severity degrees of coronavirus disease 2019 (COVID-19).
Methods: We conducted a single center, retrospective and observational study, and analyzed 102 individuals consecutively admitted in Novara University Hospital for COVID-19 from January to July 2022 (corresponding to the fifth wave of the pandemic) and representing the full spectrum of this disease severity (i.e., asymptomatic, mild-to-moderate, and severe-to-critical). These subjects were compared with 51 SARS-CoV-2-negative subjects which had been hospitalized for acute respiratory failure in the same time frame and were comparable in terms of clinical and demographic characteristics.
Results: Positivity was found in 76% of subjects for at least one HHV, and in 46% for ≥2 HHV. These proportions were more prevalent in SARS-CoV-2-positive than in negative patients (83% vs. 61%; 56% vs. 27%, respectively). The most common found HHV was HHV-7 both in the whole population (51%) and in SARS-CoV-2-positive and negative subjects (57% and 39%, respectively). Human cytomegalovirus (HMCV), herpes simplex virus (HSV)-1, Epstein-Barr virus (EBV) and HHV-6 were more represented in SARSCoV2-positive individuals, while no reactivations for HSV-2 and varicella-zoster virus were observed in this study. No single or combined HHV reactivation was associated with the 60-day mortality rate. However, HCMV as a single reactivation was a strong independent predictor of COVID-19 severity, need for admission to intensive care unit (ICU), and longer hospitalizations. Anyway, all other detected HHV, expect EBV, were more frequently activated in the symptomatic forms of COVID-19, explaining why they were generally associated to median longer hospitalizations and lymphocytopenia. Moreover, HSV-1 and HHV-7 were significantly more represented in ICU-admitted patients. When considering multiple (i.e., > 1) HHV reactivations. the above reported evidence was not only confirmed but, indeed, reinforced. First of all, they appeared to be more represented in SARS-CoV-2-positive subjects compared to negative ones, and with a strong linear trend as the severity of COVID-19 increased. Moreover, the same phenomena were elicited as the number of concomitant reactivations rose. Even more importantly, when considering only SARS-CoV-2-positive individuals, ≥ 3 reactivations were more represented in the subjects suffering from the most severe forms of COVID-19, requiring ventilatory support, or needing longer lengths of hospitalization. HHV reactivations also proved to be independent predictors of some clinically relevant hard endpoints, such as the occurrence of hospitalized severe/critical COVID-19 forms (with consequent ICU admission), or the need for long (> 14 days) hospital stays.
Conclusions: In this study, the prevalence of HHV reactivation in SARS-CoV-2-positive patients was significantly higher compared to negative subjects; these data confirmed that SARS-CoV-2 favors their reactivation. When focusing on the more severe COVID-19 infections, there seemed to be an increased HCMV reactivation rate, which could unfavorably affect the prognosis. These phenomena were elicited when multiple HHV reactivation were co-existing in the same subjects. Taken together, our data suggest that, in patients symptomatic for moderate-to-severe COVID-19, the diagnosis of HHV coinfections could have a clinical utility, in that it would help to predict a possible worsening of the clinical conditions. Moreover, it is reasonable to suggest that HCMV reactivation should be systematically searched in COVID-19 cases admitted to ICU. Our experience ultimately indicates a need for further investigations on viral reactivations and coinfections among COVID-19 patients.

PHYLOGENETIC AND GENOMIC CHARACTERIZATION OF WHOLE GENOME SEQUENCES OF A HERPES SIMPLEX VIRUS TYPE 1 ISOLATE IDENTIFIED POSSIBLE VIRULENCE DETERMINANTS IN A HUMAN SUBJECT WITH FULMINANT HEPATITIS

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Background: and aims: Herpes simplex virus 1 (HSV-1) is a rare cause of acute hepatitis in patients with chronic immunosuppression. HSV-1 hepatitis has the propensity to cause acute liver failure and death. The presenting signs and symptoms can be nonspecific, thereby causing the diagnosis to go overlooked with inadequate management, leading to a high mortality rate.
Methods: We performed whole-genome sequencing (WGS) of HSV-1 on available peripheral blood samples from a case of fatal acute liver failure, using a metagenomics approach (GenBank accession number: NC_001806.2). The 85.7% of raw reads passed the quality filter and were assembled -post host-removal- to obtain whole-genome of HSV-1. Phylogenetic analysis was then performed, with sequential assessment of the robustness of branches and the impact of variant effect.
Results: A 49-year-old female on adjuvant chemotherapy (paclitaxel plus carboplatin) for endometrial cancer with complete response and in apparent good health unexpectedly died from fulminant hepatitis within one week; no are relevant comorbidities were evident in her medical history. Molecular virology ultimately showed as the cause of death a hepatitis from a robust reactivation of HSV-1 (circulating DNA: 1,129,900,000 copies/mL). As soon as the molecular biology results were available (that is, a few hours before her untimely death), a rescue therapy with intravenous acyclovir was started, with no noticeable change in her clinical course at this point. Phylogenetic analysis was performed after death. Multiple sequence alignment of HSV-1 sequences retrieved from

NCBI databases was performed, selecting a final dataset of 182 whole-genome HSV-1 sequences with associated metadata. The sequenced HSV-1 strain belonged to USA phylogenetic clade. In detail, the Italian HSV-1 strain clustered in a specific branch with a strains isolated in Florida in 2002 (OQ724868.1). In addition to the American clade, the phylogeny revealed the Kenya clade that contains sequences isolated in the period 2006-2016. A characterization of single nucleotide polymorphisms (SNPs) and insertions/deletions (indels) was carried out to determine their effects on the viral genome. The impact of variant effect was then evaluated with a classification in four categories (high, moderate, modifier, low). The great majority of the variants (n=2,316) were reported as modifiers, 221 were classified as low impact, and 105 at moderate effect. Only one variant, classified as insertion-deletion (indel), was detected with a high impact effect (c.905_906ins, GTTTTàGTTTT). Usually, the insertion of additional nucleotides is assumed to have high (disruptive) impact in the protein, probably causing truncation, loss of function or triggering nonsense-mediated decay. The variant c.905_906ins was previously detected at position 105483 in the UL49A gene and functional classified as 'frameshift and splice region variant'. The UL49A gene in HSV-1 is known to encode a small membrane protein that has counterparts in other herpesviruses and appears to function in virion morphogenesis, replication and assembly, after interaction with the glycoprotein M, another known modulator of virus-induced membrane fusion. In addition to this gene, the study also analyzed genetic variants in other important genes, such as US7, UL36, and UL30. These latter ones are involved in other crucial steps of the HSV-1 life cycle, including alpha-regulation, capsid transport, and viral polymerase function. More in detail, the US7 gene, which has an alpha-regulatory function, exhibited the highest number of variants (n=54), followed by UL36 and UL30, which are involved in capsid transport and replication, respectively. However, the untimely death of the infected patient precluded our ability to detect whether or how these variants may have impacted virus functions in the viral population in vivo.
Conclusions: Although a rare complication, HSV hepatitis should always be kept in mind as a fatal complication in patients with acute hepatitis and chronic immunosuppression, as in the case reported here. The results of this variant analysis revealed an indel in the UL49A gene, which caused a frameshift mutation and disrupted the gene coding sequence, suggesting a substantial impact on viral replication. Moreover, the aforementioned high number of other variants in genes such as US7, UL36, and UL30 suggested that these regions may be hotspots for adaptive mutations that allow the virus to escape immune recognition or become resistant to treatment. Ultimately, it is reasonable to speculate that a better understanding of these mutations could, among other things, help in the development of more targeted antiviral therapies or vaccines that account for the diversity of HSV-1 strains circulating in the Italian population.

IMPACT OF AGE AND SEX ON VIRAL LOAD IN HEPATITIS C VIRUS INFECTION

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Premises and purpose of the study: The determinants of hepatitis C virus (HCV) viral load remain incompletely understood, and may differ in females, who are relatively protected from the consequences of HCV infection during their reproductive years. We aimed to evaluate how age affects the relationship between sex and viral load.
Material and methods: We studied a consecutive series of 922 naïve patients (males n = 497, median age 62 years) which had been referred to our Center for the treatment of chronic hepatitis C.
Results: Females were older (median age 68 vs. 57, $p < 0.001$) and had a higher prevalence of HCV genotype 2 (33% vs. 20%, $p < 0.001$) than males; there was no difference between sexes regarding the METAVIR fibrosis stage. The median HCV RNA concentration was 1.017 × 106 IU/mL (interquartile range, 0.286–2.400), with no differences between males and females in the whole study population, but with significantly higher geometric means of circulating HCV RNA in the males below 55 years. Among males, the METAVIR stage was the strongest independent predictor of a high viral load (defined as the highest two quartiles), with advanced stages inversely associated with viral load ($p = 0.008$). In females, age was the only independent predictor, with women aged ≥55 years exhibiting higher HCV viremias ($p = 0.009$).
Conclusions: These findings are consistent with data showing that estrogens exert an antiviral effect in in vitro models of HCV. Their declining levels after the menopause may explain the "catch-up" phase of HCV-related liver disease, observed in older women.

CEREBROSPINAL FLUID ASCITES AS A LATE COMPLICATION OF VENTRICULOPERITONEAL SHUNT PLACEMENT

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Background: Accumulation of fluid within the peritoneal cavity results in ascites, which main cause is portal hypertension from liver cirrhosis. Amongst the other possible causes, ventriculoperitoneal shunts (VPS) have rarely been described.
Clinical case description: A 36-year-old male, with a history of craniopharyngioma-associated obstructive hydrocephalus deserving of a VPS placement in 2014, was evaluated in our Liver Clinic for new-onset ascites from April 2024. Abdominal ultrasound confirmed the clinical suspicion of peritoneal effusion. He started a diuretic treatment to which there was little to no response and, ultimately, required multiple paracenteses. New-onset ascites workup included peritoneal fluid analyses (including cytologic and flow cytometry evaluations), in addition to laboratory tests and imaging (computed tomography). All the main causes could reasonably be excluded (including systemic or localized inflammations/infections, advanced liver disease from most viral or non-viral causes, central nervous system or splanchnic cancers, heart or kidney failure, pancreatitis, and peritoneal tuberculosis), and clinically significant portal hypertension could not be confirmed (serum ascites albumin gradient: 1.1 g/dL). So ultimately, a diagnosis of VPS-associated refractory ascites was made, requiring a VPS externalization. Two months after the procedure, only minimal residual ascites is evident.
Conclusions: It is important to recognize the association between VPS placement and the potential development of non-infectious non-malignant ascites, even years later.

EVALUATION OF GLYCEMIC STATUS AND SUBCLINICAL ATHEROSCLEROSIS IN FAMILIAL HYPERCHOLESTEROLEMIA SUBJECTS WITH OR WITHOUT LDL RECEPTOR MUTATION

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Background: Familial hypercholesterolemia (FH) is a genetic condition characterized by elevated LDL-C and increased cardiovascular risk. Beyond LDL-C levels, the impact of genotype on glucose homeostasis has not been well evaluated. We aimed to evaluate the impact of genotype on glycemic status and on atherosclerotic injury in FH subjects.
Methods: We conducted a cross-sectional study on 322 FH subjects not on lipid-lowering therapy (LLT) and without history of cardiovascular disease. Biochemical and genetic analyses as well as vascular profile assessment were obtained from all subjects. The study population was divided into two groups according to genotype: LDL receptor (LDLR) group and non-LDLR (NLDLR) group.
Results: The LDLR group exhibited a higher prevalence of low glycemic status (LGS) than the NLDLR group (44.1% vs. 26%, $p < 0.01$), whereas a high glycemic status (HGS) was more prevalent in the NLDLR group compared with LDLR group (74% vs. 55.9%, $p < 0.01$). The NLDLR group exhibited a higher prevalence of peripheral atherosclerotic plaques than the LDLR group (93.4% vs. 73%, $p < 0.05$), while coronary artery calcification (CAC) presence was more prevalent in the LDLR group compared with the NLDLR group (74.7% vs. 48%, $p < 0.01$). In a secondary analysis the study population was stratified into three groups based on LDLR genotype: NLDLR, LDLR defective, LDLR null groups. The prevalence of LGS progressively increased from the NLDLR to the LDLR null group, while HGS showed an inverse trend (p for trend < 0.05). Peripheral atherosclerotic plaque prevalence decreased from the NLDLR to the LDLR null group (p for trend < 0.05), while CAC prevalence increased progressively in the three groups (p for trend < 0.01). Logistic regression analysis showed that FH groups with an LDLR mutation were inversely associated with HGS (p for both < 0.01) and the LDLR null group exhibited the strongest association.
Conclusions: FH subjects with NLDLR mutations exhibited a worse glycemic

profile, while null LDLR mutations showed the strongest inverse association with HGS. The integrations of genetic, lipid and glucose data could be useful to better identify the metabolic profile and the atherosclerosis distribution in FH subjects.

IMPACT OF ENDOVASCULAR TREATMENT ON FUNCTIONAL OUTCOME IN ISCHEMIC STROKE: A REAL-WORLD RETROSPECTIVE STUDY

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Background: and AimIschemic stroke (IS) remains a significant cause of death and disability worldwide. Over recent decades, management has evolved from supportive care to active reperfusion strategies, including intravenous thrombolysis (IVT) with recombinant tissue plasminogen activator (rt-PA) and mechanical thrombectomy (MT). While IVT is the first-line treatment, its limited efficacy in large vessel occlusion (LVO), narrow therapeutic window, and bleeding risk have driven the development of endovascular approaches. This study evaluated clinical and procedural predictors of functional outcomes at discharge and 90 days in patients with LVO IS treated with MT, with or without IVT, in a real-world setting.
Methods: We conducted a retrospective, single-center study at the Stroke Unit of Perugia Hospital, Italy, including all patients with anterior or posterior circulation LVO strokes treated with MT between January 2021 and December 2023. Demographics, vascular risk factors, stroke severity (National Institutes of Health Stroke Scale, NIHSS), neuroimaging findings, procedural variables, and outcomes were collected. Poor functional outcome was defined as modified Rankin Scale (mRS) ≥3 at discharge and at 90 days. Procedural success was defined as a modified Thrombolysis in Cerebral Infarction (mTICI) score of 2b–3. Patients with mRS ≤2 were compared to those with mRS ≥3 at both timepoints.
Results: A total of 127 patients were included. The mean age was 71.7(± 12.3)years; 73% had hypertension, 41.6% dyslipidemia, and 37.3% atrial fibrillation. 23(18%) patients reached a mRS ≤ 2; 104(82%) a mRS ≥ 3 at discharge. At 90-day, 41(32%) patients vs 86(68%) had a mRS ≤ 2 and ≥ 3, respectively. In-hospital mortality was 17.3%, with 3 additional deaths at 90-day(19.4%). Patients with poor outcomes were significantly older, more often affected by systemic hypertension, had higher NIHSS scores on admission, and had an IS due to a tandem occlusion (respectively, p=0.02, 0.01, 0.007, 0.003).At univariate analysis at discharge: older age(OR 1.04, 95% CI 1.00-1.08, p=0.03), systemic hypertension(OR 3.19, 95% CI 1.24-8.24, p=0.02), higher NIHSS scores on admission(OR 1.26, 95% CI 1.11-1.47, p=0.001), tandem occlusion(OR 4.50, 95% CI 1.65-14.50, p=0.006), stenting(OR 11, 95% CI 2.16-201.24, p=0.02), general anesthesia(OR 5.44, 95% CI 2.03-14.78, p=0.001); IVT (OR 0.29, 95% CI 0.08-0.85, p=0.04), local anesthesia (OR 0.22, 95% CI 0.08-0.6, p=0.003), mTICI (OR 0.44, 95% CI 0.19-0.75, p=0.02).At univariate analysis at 90-days: higher NIHSS scores on admission(OR 1.19, 95% CI 1.07-1.34, p=0.002), tandem occlusion(OR 2.40, 95% CI 1.12-5.32, p=0.03), stenting(OR 10.67, 95% CI 2.97-68.39, p=0.002), groin-to-recanalization time(OR 1.01, 95% CI 1.00-1.03, p=0.01), general anesthesia(OR 4.05, 95% CI 1.71-9.92, p=0.002); IVT(OR 0.36, 95% CI 0.15-0.82, p=0.02), local anesthesia(OR 0.28, 95% CI 0.11-0.66, p=0.004), mTICI(OR 0.51, 95% CI 0.31-0.74, p=0.002).At multivariate analysis, mRS ≥3 at discharge was associated with baseline NIHSS(OR 1.25, 95% CI 1.07-1.51, p=0.01), general anesthesia(OR 7.11, 95% CI 1.72-33.55, p=0.01) and stenting(OR 10.01, 95% CI 1.35-223.19, p=0.05). At 90-day, mRS ≥3 was significantly associated with higher baseline NIHSS(OR 1.22, 95% CI 1.05-1.44, p=0.02), stenting(OR 5.63, 95% CI 1.20-41.73, p=0.05) and groin-to-recanalization time(OR 1.01, 95% CI 1-1.03, p=0.05). IVT before MT was inversely associated with 90-day mRS ≥3(OR 0.26, 95% CI 0.06-0.92, p=0.05).
Discussion: This study highlights the complex interplay of clinical and procedural factors influencing outcomes after MT. While randomized trials demonstrate MT efficacy in selected patients, real-world application reveals additional challenges. Stroke severity at admission remained a strong predictor of poor outcome, while general anesthesia, stenting, and tandem occlusion were linked to worse prognosis.Longer groin-to-recanalization times correlated with unfavorable results, emphasizing the importance of minimizing procedural delays. The type of sedation plays a role in this context. General anesthesia may increase time to reperfusion and cause perioperative hypotension, negatively affecting neurological recovery. Local or conscious sedation may reduce delays and allow for intraoperative neurological assessment. Strategies favoring local sedation, guided by a multidisciplinary consensus, could improve outcomes by aligning procedural efficiency with patient safety.Despite its limitations, IVT before MT was independently associated with favorable outcomes, supporting its continued use in eligible patients. These findings reinforce the value of a combined therapeutic approach in acute IS care.
Conclusion: Predictors of poor functional outcome in IS patients treated with MT include higher stroke severity, use of general anesthesia, need for stenting, and longer procedural times. Bridging IVT appears to improve recovery. Although randomized trials support MT, individualized selection remains essential in real-world settings. Prospective multicenter studies are warranted to validate these findings and refine protocols for optimal stroke care.

POTENTIAL TOLERABILITY OF TRITICUM MONOCOCCUM IN PATIENTS WITH NON-CELIAC WHEAT SENSITIVITY. AN ONGOING CLINICAL TRIAL TO UNRAVEL PATHOPHYSIOLOGICAL 'SINGULARITY' OF WHEAT SENSITIVITY

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Background: patients suffering from wheat-related troubles, in absence of celiac disease or wheat allergy diagnosis, can suffer from non-celiac wheat sensitivity (NCWS). This is characterized by both gastrointestinal and extra-intestinal symptoms, which improve with the elimination of wheat intake (WFD). To date no definitive explanation of pathogenetic mechanisms of NCWS has been proved, and no specific non-invasive diagnostic biomarker has been recognized. NCWS prevalence is estimated to be in a wide range, world-wide, between 0.6% and 13%, and its clinical presentation overlaps with the irritable bowel syndrome (IBS). To identify NCWS patients among those with IBS-like clinical presentation can permit to cure this critical condition and to reduce the social costs. However, a real need for strict adherence to WFD in NCWS has never been demonstrated. In this context, research is actively trying to find wheat varieties with absent or low immune reactivity to be used for the treatment of NCWS patients. Preliminary evidence supports the assumption that diploid wheat species, such as Triticum monococcum (TM), compared to common ones (Triticum aestivum (TA)), could possess a lower immunogenic potential in NCWS patients.
Aims: the first objective of our study is to verify whether the use of a diploid wheat (TM), with a lower concentrations and bioactivity of Amylase-Tripsyn-Inhibitors (ATIs) and with gliadin proteins with a better digestibility, compared to a hexaploid one (TA) could improve both symptoms and quality of life (QoL) of NCWS subjects. The second objective is the identification of non-invasive serological biomarkers for NCWS diagnosis. The third objective is to identify T cell lymphocytes able to recognize cognate peptides from wheat proteins to better classify and monitor patients affected by NCWS.
Methods: we planned a prospective, double-blind clinical trial with crossover, in which patients already diagnosed with NCWS (according to international criteria and with a double-blind placebo-controlled wheat challenge), following a strict WFD, will be exposed to a double-blind wheat challenge (DBWC) with both TM and TA. The experimental plan is divided into 4 work packages (WPs):
WP1 - Evaluation of clinical response to TM compared to TA by a DBWC with crossover: 1) evaluation of GI symptoms by the Gastrointestinal Symptom Rating Scale; 2) evaluation of extraintestinal symptoms by an extraintestinal symptoms rating scale; 3) evaluation of quality of life (QoL) by the IBS-QoL questionnaire.
WP2 - Evaluation of intestinal permeability and damage biomarkers during WFD, TM and TA challenge: 1) in vivo evaluation of intestinal permeability by the Lactulose/Mannitol (La/Ma) ratio test; 2) analysis of serological indexes of intestinal damage and permeability (zonulin, occludin and claudin 1, i-FABP, LPS, LBP, F-actin, ASCA IgA and IgG anti-Bacteroides IgA and IgG), by ELISA assays.
WP3 - Evaluation of immunological, inflammatory, and visceral hypersensitivity response during WFD, TM and TA challenge: 1) Analysis of fecal and plasmatic biomarkers of visceral hypersensitivity by ELISA assays (fecal calprotectin, ECP, tryptase, s substance P, somatostatin, serotonin and VIP); 2) analysis of the humoral immune response to gluten by ELISA assays (anti-deamidated gliadin peptides IgA and IgG); 3) analysis of serological inflammatory biomarkers by simultaneous high sensitivity microsphere-based Luminex technology and ELISA assays (G-CSF, GM-CSF, IFN-γ, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-9, IL-10, IL-12 (p40), IL-13, IL-15, IL-17, IL-21,IL-22, IL-33, IFN-γ- IP-10, MIP-1α, MIP-1β, TNF-α, TGF-β, visfatin, CCL2 and resistin, histamine, AZU1 and BMP7); 4) immunophenotyping of whole blood for quantification of immune cell subpopulations and their activation status, evaluation of gut homing biomarkers and identification of specific cell population involved in the systemic

immune response to wheat; 5) Identification, through SC transcriptome and TCR sequencing, of T cell lymphocytes able to recognize cognate peptides from wheat proteins, in the rectal mucosa of NCWS subjects.
WP4 - Evaluation of gut microbiota during WFD, TM and TA challenge by in vitro amplification of bacterial genetic materials from fecal samples by PCR methods and identification of gut microbiota composition.
Study progress: to date (April 2025), 39 out of the 68 patients planned have been enrolled. All patients have undergone the scheduled analyses during the DBWC, including proctoscopy with biopsy samples for the analysis of T cell lymphocytes, by means of SC transcriptome and TCR sequencing (12 patients out of 10 planned). It is worth noting the high number of dropouts that has slowed down recruitment.
Impact: if successful we will prove that a dietary regimen with TM would be a suitable and a less expensive alternative to a WFD in NCWS subjects, significantly impacting their QoL, and we could also unravel the pathophysiological basis of this condition, identifying, at the same time, a potential non-invasive biomarker.
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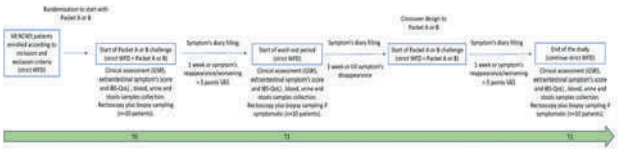

EFFECT OF SEASONAL EXPOSURE IN AEROALLERGEN-SENSITIZED PATIENTS WITH IRRITABLE BOWEL SYNDROME-DIARRHOEA

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Background: Irritable bowel syndrome (IBS) is a chronic and multifactorial disorder with a notable impact on patients' quality of life. Among its subtypes, diarrhea-predominant IBS (IBS-D) has been increasingly associated with immune dysregulation and mast cell activity. Recent literature suggests a potential correlation between IBS and atopic diseases, particularly allergic rhinitis and asthma. In this context, seasonal variations in airborne allergen exposure,especially pollens, could influence gastrointestinal symptoms, although clinical evidence remains sparse.
Objectives: To assess the seasonal variability of gastrointestinal symptoms in atopic patients with IBS-D, comparing symptom burden during off-season periods versus peak pollen season.
Methods: We conducted a retrospective, monocentric observational study at the Fondazione IRCCS San Matteo Hospital in Pavia, Italy, including adult patients with IBS diagnosed according to Rome IV criteria between 2021 and 2024. All participants underwent allergologic testing (skin prick tests and/or serum-specific IgE) to assess sensitization to seasonal (e.g., Grass pollens) and perennial (e.g., house dust mites, HDM) aeroallergens. Patients undergoing allergen specific immunotherapy, following exclusion diets, or with incomplete data were excluded. Symptom burden was assessed with the Gastrointestinal Symptom Rating Scale (GSRS) and a Visual Analog Scale (VAS) for abdominal pain/distension, recorded at two time points: off-season (T0) and during pollen season (T1). Factors associated with symptoms variability were analysed in bivariate analysis.
Results: A total of61patients were included (median age34years [IQR25–50]; female-to-male ratio3.6:1), of whom38(62.2%) had IBS-D. Respiratory atopy was more prevalent in IBS-D patients, with allergic rhinitis as the dominant phenotype. Sensitization to inhalant allergens was found in approximately half of the cohort. In the overall sample, GSRS and VAS scores did not significantly differ between T0and T1. However, among IBS-D patients sensitized to grass pollens (n=18), a significant increase in gastrointestinal symptom scores was observed during the pollen season. GSRS total scores rose from25.3±7.4(T0) to28.7±8.2(T1; p =0.04), with lower GI subscale scores increasing from15.9±5.9to18.8±7.1(p =0.01). VAS scores for abdominal pain/distension also increased significantly (from2.6±3.0 to 3.9±3.5; p =0.03). No significant variations were found in patients sensitized to HDM or in non-sensitized individuals. Bivariate analysis revealed male sex as a predictor of greater symptom variability (coefficient1.69;95% CI:0.04–3.34; p =0.04).
Conclusions: This study demonstrates a significant seasonal exacerbation of intestinal symptoms in IBS-D patients sensitized to Grass pollens, supporting the hypothesis of an immune-allergic contribution to symptom variability. The findings underscore the relevance of mast cell–mediated mechanisms and systemic allergic responses in the pathophysiology of IBS-D. The absence of similar symptom changes in patients sensitized to perennial allergens suggests that seasonal exposure plays a critical role. These results encourage the integration of allergologic assessment in the diagnostic workup of IBS-D and advocate for a personalized, multidisciplinary approach in the management of IBS-D patients, especially during pollen season. Further prospective studies are warranted to confirm these observations and to explore targeted therapeutic interventions.

SLEEP QUALITY AND ITS CLINICAL CORRELATES IN ELDERLY PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Introduction: Type 2 Diabetes Mellitus (T2DM) is a complex condition associated with numerous comorbidities. Recently, factors previously ignored, such as sleep disturbances, have been shown to play a much more significant role. Indeed, growing evidence has demonstrated that both qualitative and quantitative sleep alterations are associated with an increased risk of cardiovascular events, obesity, anxiety-depressive disorders, and poorer glycemic control in diabetic patients. The aim of our study was to evaluate the relationship between sleep disturbances, anxiety-depressive disorders, and quality of life in elderly patients with T2DM.
Material and methods: Elderly patients with T2DM aged over 65 years attending the Internal Medicine division of ARNAS Garibaldi-Nesima Hospital in Catania were recruited. Patients with obstructive sleep apnea syndrome, those receiving treatment for anxiety-depressive disorders, or those with known sleep disorders were excluded. Each patient underwent collection of anthropometric, laboratory, medical history data and completion of three questionnaires: the Pittsburgh Sleep Quality Index (PSQI), the Geriatric Depression Scale (GDS), and the WHO-QoL-BREF to investigate sleep quality, depression, and quality of life, respectively.
Results: A total of 93 patients were recruited and divided based on their PSQI score into a PSQI ≥ 8 group (n=31) and Controls (PSQI < 8, n=62). Patients in the PSQI ≥ 8 group showed a higher prevalence of depressive disorders (4.77 ± 3.81 vs 2.44 ± 2.02, p < 0.001) and a poorer quality of life in the physical (61.4 ± 19.1 vs 72.4 ± 13.2, p = 0.002), psychological (59.2 ± 15.2 vs 73.3 ± 13.7, p < 0.001), and social (62.1 ± 19.7 vs 76.1 ± 15.5, p < 0.001) health domains of the WHO-QoL BREF. Patients in the PSQI ≥ 8 group also seems to had a longer duration of diabetes (15.3 ± 10.5 vs 12.5 ± 9.83 years, p=0.220), a worst renal function (eGFR sec CKD-epi 67.1 ± 20.5 vs 76.3 ± 17.7, p=0.042), and had a higher prevalence of retinopathy compared to controls (19.4% vs 7.3%, p=0.093).
Discussion: Sleep disorders are increasingly prevalent in the general population, likely due to stressors related to modern lifestyles. Sleep plays a vital role in regulating physiological processes, including glucose metabolism. A bidirectional relationship between sleep and diabetes has been established: sleep disturbances increase the risk of developing diabetes, while individuals with diabetes often experience poor sleep due to symptoms like nocturia, polydipsia, and hypoglycemia. Our results confirm that poor sleep quality (PSQI ≥8) in patients with type 2 diabetes mellitus (T2DM) is associated with a significantly higher burden of depressive symptoms and a worse quality of life in the physical, psychological, and social domains of the WHO-QoL BREF. These findings align with previous studies that highlight how poor sleep is linked to reduced well-being and increased emotional distress in diabetic populations. Furthermore, we observed a significantly lower estimated glomerular filtration rate (eGFR) in the PSQI ≥8 group, suggesting a potential relationship between poor sleep and impaired renal function. This observation is supported by emerging evidence that links sleep disturbances—particularly short sleep duration and fragmentation—with faster kidney function decline, possibly due to chronic inflammation and sympathetic overactivation. Although differences in diabetes duration and retinopathy prevalence did not reach statistical significance, trends suggest that patients with poor sleep may have a more severe disease profile and be at greater risk of complications. These findings underscore the importance of comprehensive assessment in diabetic care, including sleep quality evaluation.
Conclusion: This study confirms that poor sleep quality in T2DM patients is strongly associated with higher depressive symptoms, poorer quality of life, and worse renal function. These results reinforce the need for routine sleep assessment in diabetic management. Identifying sleep disturbances early may help clinicians intervene to prevent further psychological and organ-related

complications, supporting a more integrated and patient-centered care approach.

	PSQI ≥ 8 (n=31)	PSQI < 8 (n=62)	p value
Diabetes duration (year)	15.3±10.5	12.5±9.83	0.220
Diabetic retinopathy	19.4%	7.3%	0.093
eGFR sec CKD-epi (ml/min/1.73m²)	67.1 ± 20.5	76.3 ± 17.7	0.042
Geriatric Depression Scale	4.77±3.81	2.44±2.02	<0.001
WHO-QoL BREF – physical	61.4 ± 19.1	72.4 ± 13.2	0.002
WHO-QoL BREF – psychological	59.2±15.2	73.3±13.7	<0.001
WHO-QoL BREF – social	62.1±19.7	76.1±15.5	<0.001
WHO-QoL BREF – ambient	67.7 ± 11.9	71.2 ± 13.5	0.231

	PSQI ≥ 8 (n=31)	PSQI < 8 (n=62)	p value
Age (year)	71.6 ± 7.21	69.4 ± 7.62	0.190
Female	14/31 = 45.2%	18/62 = 29%	0.123
Male	17/31 = 54.8%	44/62 = 71%	0.123
BMI (Kg/m2)	27.3 ± 4.15	28.6 ± 4.46	0.210
Waist circumference (cm)	104 ± 11.6	106 ± 10	0.465
Systolic Blood Pressure (mmHg)	132 ± 13.5	135 ± 10.7	0.238
Dyastolic Blood Pressure (mmHg)	74 ± 10.9	79.5 ± 10.2	0.024
Smokers	6/30 = 20%	21/62 = 33.9%	0.171
Ex Smokers	15/30 = 50%	12/62 = 20%	0.003
Coffee users	27/30 = 90%	47/61 = 77%	0.136

	PSQI ≥ 8 (n=31)	PSQI < 8 (n=62)	p value
Basal Glucose (mg/dl)	128 ± 35.4	133 ± 30.4	0.582
HbA1c (%)	6.87 ± 0.896	6.75 ± 0.951	0.575
LDL colesterol (mg/dl)	80.8 ± 51.3	77.6 ± 27.7	0.714
Metformine	24/31 = 77.4%	41/55 = 74.5%	0.766
Insuline use	8/31 = 25.8%	13/55 = 23.6%	0.822
GLP1-RA	10/31 = 32.3%	24/55 = 43.6%	0.300
SGLT2i	6/31 = 19.4%	17/55 = 30.9%	0.245
DPP4-I	3/31 = 9.7%	5/55 = 9.1%	0.928
Statina	23/31 = 74.2%	44/56 = 78.6%	0.642
Ezetimibe	11/31 = 35.5 %	24/56 = 42.9%	0.502

SUBPHENOTYPING APPROACH IN INDIVIDUALS AT ELEVATED RISK OF DIABETES IDENTIFIES PERSONS WITH INCREASED ARTERIAL STIFFNESS, IRRESPECTIVE OF THE CLASSICAL CLASSIFICATION OF GLUCOSE TOLERANCE.

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Background: and aims: Prediabetes is associated with increased cardiovascular (CV) risk and incidence of diabetes. However, this condition is quite heterogeneous and a new subphenotyping approach for persons at elevated risk of diabetes was proposed to improve the stratification of the risk of diabetes onset and its complications. This study aimed to evaluate arterial stiffness across these subtypes.
Methods: 377 persons without prior diagnosis of diabetes and CV events underwent (1) physical examination and review of clinical history, smoking status, and medications; (2) classical glucose tolerance assessment through oral glucose tolerance test (OGTT), fasting glucose and HbA1c dosage; (3) CV risk assessment through tonometry measured arterial stiffness (i.e. pulse wave velocity – PWV –, augmentation index – AugI –, and subendocardial viability ratio – SEVR) and intima-media thickness (IMT) evaluation. Participants with incident diabetes (n=61) and with missing data for subphenotyping (n=57) were excluded. Thus, 259 participants were assigned to one of the following subtypes according to sex, body mass index, waist circumference (WC), fasting glucose, fasting insulin, glucose and insulin 2h-post-OGTT, triglycerides, and HDL cholesterol: (1) Low-risk; (2) Very-low-risk; (3) Beta-cell-failure; (4) Low-risk/obese; (5) High-risk/insulin-resistant/fatty-liver; (6) High-risk/visceral-fat/nephropathy. A multiple regression analysis adjusting for major confounders was performed to evaluate the association between subptypes and PWV.
Results: The overall study population showed a mean age of47.88±11.03years and148individuals (57.1%) were females. The20% and75.5% of individuals in subtypes5and6, respectively, were normal glucose tolerant (NGT) when the classical definition was applied. Subtype5(8.88±1.83m/s) showed higher PWV in comparison to subtypes1(7.29±1.69m/s),2(7.14±2.49m/s), and4(7.49±1.47m/s) (all P<0.05). Subtype6(8.07±1.67m/s) showed nominally higher PWV in comparison to subtypes1,2, and4and a lower SEVR than subtype3(145.47±28.08vs165.62±35.50%, P =0.033). No differences were identified for AugI. After adjusting for age, sex, BMI, WC, antihypertensive therapy, systolic blood pressure, LDL cholesterol, active smoking, and HbA1c, subtype5(β =1.79[0.70-2.88], P =0.001) and6(β =1.09[0.02-2.16], P =0.047) were associated with higher PWV.
Conclusions: Subtypes 5 (High-risk/insulin-resistant/fatty-liver) and 6 (High-risk/visceral-fat/nephropathy) of prediabetic metabolism exhibit subclinical vascular damage and higher CV risk. Early screening for CV disease, as well as personalized clinical interventions, in these subtypes, irrespective of classical glucose tolerance classification, could be important to mitigate adverse CV outcomes.

NATURAL KILLER T CELLS LINK STRESS HYPERGLYCEMIA TO COGNITIVE DECLINE IN HFPEF

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Background: Heart failure with preserved ejection fraction (HFpEF) is prevalent among patients with multiple comorbidities, particularly older adults, and is associated with an increased risk of frailty. Since frail older adults with HFpEF often experience multiple chronic conditions and are at risk for major complications, we reasoned that SHR may serve as a valuable prognostic marker in this vulnerable population. On these grounds, we investigated the relationship between SHR and cognitive impairment in a population of frail older adults with HFpEF.
Methods: We conducted a prospective observational study enrolling consecutive frail older adults with a prior diagnosis of HFpEF admitted to the local health unit of the Italian Ministry of Health (ASL) in Avellino, Southern Italy, between March 2021 and March 2022. Inclusion criteria were: age >65 years, confirmed diagnoses of frailty and HFpEF, and a Montreal Cognitive Assessment (MoCA) score <26
Results: We screened 295 patients, of whom 70 did not meet the inclusion criteria and 21 declined to provide clinical information. A total of 204 patients successfully completed the study. Participants were categorized into two groups based on SHR values: ≤1 or >1. Notably, patients in the SHR >1 group exhibited significantly lower global cognitive function compared to those in the SHR ≤1 group (MoCA in SHR ≤1: 21.06 ± 2.8 vs. MoCA in SHR >1: 19.52 ± 3.9; p = 0.0014). Through peripheral blood immunophenotyping, we detected significantly higher levels of Natural Killer T (NKT) cells in patients with SHR≤1 compared to SHR>1; in contrast, (PD-1, Programmed cell Death Protein 1), a key regulator of NKT cell activity,5 was more expressed in the SHR>1 group.
Discussion: Our findings suggest that SHR may serve as a new marker of cognitive impairment in this population, independent of diabetes status, as our cohort included individuals with diabetes, prediabetes, and normal glycemia. Additionally, NKT cells in patients with SHR≤1 might be associated with controlled immune responses, while the higher PD-1 expression in SHR>1 could be involved in the regulation of inflammation in the settings of HFpEF and its associated complications.

AN UNRECOGNIZED CASE OF GLANZMANN'S THROMBASTHENIA ASSOCIATED WITH GASTROINTESTINAL BLEEDING

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Background: Glanzmann's thrombasthenia (GT) is a rare autosomal recessive disorder caused by a deficiency or dysfunction of the glycoprotein IIb/IIIa complex on platelets, leading to impaired aggregation and a predisposition to

mucocutaneous bleeding. GT may be associated with gastrointestinal angiodysplasia (GIADs).1

Case report: A 22- year-old Egyptian male with an unspecified bleeding diathesis presented to ER for atraumatic left-sided submammary chest pain started four days earlier and worsened with inspiration. The patient also reported episodes of nausea and "coffee ground" vomiting. Initial findings included severe microcytic anemia with hemoglobin levels at 3.7 g/dL. Endoscopic evaluation revealed only edematous gastropathy and hyperemia of the bulb, with biopsies performed and worsening of gastrointestinal bleeding (GIB). Diagnostic workup excluded common hereditary and acquired coagulopathies (PT, aPTT, Factor VIII, vWF, CMV, EBV, Parvovirus B19 and malaria screening). However, platelet function testing (PFA-100) was prolonged and Born platelet aggregation test showed absent response to ADP, collagen and arachidonic acid with weak response to ristocetin, suggesting GT, which was confirmed by cytofluorimetry that showed glycoprotein IIb/IIIa deficiency.

Management included recombinant activated Factor VII (rFVIIa) , tranexamic acid and supportive care. Capsule endoscopy revealed ongoing gastric bleeding near the biopsy site, previously treated with endoclips placement but the blood-painted mucosa obscured potential GIADs identification. Platelet transfusion was avoided to prevent alloimmunization. The patient improved with rising hemoglobin levels and no further GIB episodes, leading to discharge with antifibrinolytic prophylaxis and follow-up care.

Discussion: GT is a rare autosomal recessive disorder caused by a deficiency or dysfunction of the glycoprotein IIb/IIIa complex on platelets. The global incidence is 1:1,000,000, with higher prevalence in regions with high consanguinity. It accounts for approximately 9% of all platelet function disorders and the number of reported cases has increased in recent years.1

The hallmark of GT is mucocutaneous bleeding such as purpura, epistaxis, gum bleeding and menorrhagia. GIB may also occur. Clinical manifestations of GIB in GT often resemble more common gastrointestinal disorders, which can lead to delayed or incorrect diagnoses. Many patients with spontaneous GIB also present with coexisting gastrointestinal conditions such as peptic ulcers, polyps, Helicobacter pylori infection or GIADs.1

In this reported case, the patient presented with GIB without any clear underlying cause. The only lesion found was a small bleeding ulcer at the site of a previous biopsy, which worsened the preexisting bleeding.

Diagnosis of GT requires a thorough clinical evaluation, including the patient's personal and family medical history. GT should be considered in individuals with recurrent bleeding since childhood. Laboratory evaluation typically shows normal platelet count, size, and granularity. Platelet aggregometry reveals absent or diminished responses to ADP, collagen, and arachidonic acid, with a weak response to ristocetin. Flow cytometry confirms the diagnosis by demonstrating reduced or absent expression of CD41 (GPIIb) and CD61 (GPIIIa), and genetic testing can provide further confirmation.1

Management of GT is mainly supportive, focusing on controlling both acute and chronic bleeding and minimizing risks during invasive procedures. Platelet transfusion remains the standard therapy but is limited due to the potential risk for alloimmunization.2 rFVIIa is commonly used for mild to moderate bleeding, with transfusions reserved for emergencies.3 Additional therapies, particularly effective for gastrointestinal bleeding, include fibrin sealants, autologous platelet-rich clots, octreotide and bevacizumab.3The only definitive cure for GT is hematopoietic stem cell transplantation, performed in only a few patients cases.

Conclusion:

In young patients with a history of mucocutaneous bleeding and severe microcytic anemia with a normal coagulation profile, it is recommended to perform, alongside the endoscopic diagnostic work-up, tests for platelet disorders.

INACTIVE HBV CARRIER AND LATENT TB INFECTION AND ATRIAL FLUTTER: A SPECIAL CASE OF BULLOUS PEMPHIGOID

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Introduction: Bullous pemphigoid is a rare autoimmune bullous skin disease characterized by subepidermal blisters that appear on portions of normal or inflamed skin, usually in a diffuse manner (on the flexor regions of the proximal portion of the arms and legs, in the axillary area, in the groin and abdomen), often in association with itching. The disease mostly affects the elderly. It is characterized by the production of autoantibodies directed against two structural proteins found in the dermal-epidermal junction and which ensure its cohesion, namely the BP 1 antigen (BPAG1 or AgBP230) and the BP 2 antigen (BPAG2, AgBP180 or collagen XVII) which determine the separation between the dermis and the epidermis and the formation of vesicles. It is generally an idiopathic pathology but some drugs are associated with the onset of the disease (diuretics, antiarrhythmics, neuroleptics, gliptins, immunotherapeutics). Systemic corticosteroids (methylprednisolone: 0.5-1 mg/kg/day) are indicated as standard treatment, however, there are refractory forms treated with immunosuppressants (methotrexate, mycophenolate mofetil, rituximab).

Case report: S.O. an 84-year-old man with chronic ischemic cardiomyopathy, type 2 diabetes and chronic renal failure came to clinical observation for the appearance of widespread pemphigoid lesions on erythematous skin complicated by skin superinfection on the entire body except the scalp. No new medications were reported in the last six months. At home he was undergoing corticosteroid and antihistamine therapy without benefit. Blood tests showed a picture of neutrophilic leukocytosis in the absence of a marked increase in inflammation indices. The peripheral smear showed rare hypergranulated neutrophils and small granulated lymphocytes without atypia, as per leukocyte activation, in particular of B lymphocytes. The autoimmune panel was negative. To exclude the paraneoplastic nature of the pemphigoid, a total body CT was performed which was normal. Intravenous corticosteroid therapy (Methylprednsione 1 mg/kg/day) and antihistamine therapy were confirmed without benefit. Skin biopsy was performed confirming bullous pemphigoid. The hospital stay was characterized by a stable skin condition with the appearance of widespread crusted lesions. The patient developed an episode of atrial flutter with high ventricular response for which antihistamine therapy was suspended. In consideration of the therapeutic refractoriness to cortisone, it was decided to start the patient on immunosuppressive therapy. The infectious disease screening for research was negative for acute infection but showed latent HBV infection (inactive carrier), while the quantiferon was positive for latent M. tuberculosis infection. After specific antibiotic and antiviral treatment, the first cycle of Rituximab was administered during hospitalization.

Conclusion: Healing times for bullous pemphigoid are generally long, in fact only after several months of drug therapy, about half of patients experience complete remission; however, a maintenance regimen is often necessary to keep the disease under control. A correct anamnesis is a fundamental phase of the medical visit, today unfortunately neglected due to the lack of time, excessive reliance on instrumental and laboratory tests and the increasingly cumbersome role that information technology and bureaucratic urgency have assumed in our daily work. A personalized diagnosis is needed on a case-by-case basis and its management, which often requires a multidisciplinary approach, remains among the most challenging clinical problems. To date, there are still no specific and shared guidelines; therefore, it is strongly recommended to operate a hypothetical-deductive diagnostic approach scheme.

EVALUATIONS OF METABOLIC AND INNATE IMMUNITY PROFILES IN SUBJECTS WITH FAMILIAL HYPERCHOLESTEROLEMIA WITH OR WITHOUT SUBCLINICAL ATHEROSCLEROSIS

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Background: Familial hypercholesterolemia (FH) is a genetic condition characterized by high low-density lipoprotein cholesterol (LDL-C). The presence of risk modifiers could promote the atherosclerotic injury beyond LDL-C. Our aim was to evaluate metabolic and innate immunity profiles in FH subjects with or without subclinical atherosclerosis.

Methods: In this cross-sectional observational study, we evaluated 211 genetically confirmed FH subjects on LDL-C target and without cardiovascular diseases. Biochemical analyses, LDL-C burden (LCB) calculation and vascular profile evaluation were obtained from all subjects. Study population was divided into two groups according to subclinical atherosclerosis: the subclinical atherosclerosis (SA) group and non-subclinical atherosclerosis (NSA) group.

Results: SA group had higher LDL-C at diagnosis (288.35 ± 24.52 vs 267.92 ± 23.86, $p < 0.05$) and LCB (13,465.84 ± 3617.46 vs 10,872.63 ± 3594.7, $p < 0.001$) than NSA group. SA group had higher white blood cell count (WBCC, 6.9 ± 1.66 vs 6.1 ± 1.16), neutrophil count (NC, 4.2 ± 1.3 vs 3.6 ± 1.11), monocyte count (MC, 0.8 ± 0.2 vs 0.4 ± 0.1), triglyceride to high-density lipoprotein ratio (TG/HDL, 1.73 ± 0.72 vs 1.45 ± 0.69), triglyceride-glucose index (TyG, 8.29 ± 0.35 vs 8.01 ± 0.33) than NSA group (p value for all < 0.01). Multivariate logistic regression analysis showed that LCB ($p < 0.01$), WBCC ($p < 0.01$), NC ($p < 0.05$), MC ($p < 0.05$) were associated with subclinical atherosclerosis. Simple linear regression analyses showed that LCB was associated with WBCC, NC, MC (p value for all < 0.01).

Conclusion: An increased LCB and an impaired innate immunity profile were found in FH subjects with subclinical atherosclerosis and they were independently associated with atherosclerotic injury. LCB could modulate the innate immunity profile.

SURGERY IN PATIENTS WITH FACTOR VII DEFICIENCY MANAGED WITH PD-FVII.

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Background: Congenital factor VII (FVII) deficiency is the most common among the rare hemorrhagic disorders, inherited in an autosomal recessive pattern. FVII deficiency is classified as: severe, FVII <10% (greatest risk for major spontaneous bleeding); moderate, 10%-20% (at risk for mild spontaneous or triggered bleeding); and mild, 20%-50% (usually asymptomatic). Acquired FVII deficiency can be isolated or combined with other decreased factor levels. Only a few cases of isolated acquired FVII deficiency are reported in the literature. The ideal replacement therapy for patients with congenital FVII deficiency is plasma derived FVII (pd-FVII) or recombinant FVII concentrate (rVFIIa). FFP can also be used if FVII concentrates are not accessible, but with the concern of volume overload. Another option is a 4-factor PCC. The dosE/duration of the treatment with FVII concentrates depends on the severity of the deficiency, and on the patient's clinical condition.
Aim: The aim of this study is to assess the efficacy /safety of non-activated pd-FVII for perioperative hemostatic treatment in patients with congenital/ acquired FVII deficiency.
Patients and methods: Patients with congenital or acquired factor VII deficiency treated with pd-FVII for perioperative hemostasis in 3 university hospitals.
Results: We report 10 procedures in 9 patients, 2 with acquired deficiency (vitamin K deficiency, warfarin overdosage) and 7 with congenital deficiency. The pd-FVII was used at a dose of 20 to 30 IU/kg/dose.
Discussion: In the post-operative period only one patient presented hematuria (after surgery for prostate hypertrophy), resolved with pd-FII concentrate.

Table 1.

No. procedure	Gender	Age (yrs)	Body weight (Kg)	FVII:C	Type of surgery	pd-FVII IU/Kg	FVII:C POST-TREATMENT	Total consumption	OUTCOME	NOTES
1	M	59	74	49%	LUNG BIOPSY	20 IU/Kg/ 6 hr	70%	2400 IU	ABSENCE OF COMPLICATIONS	
2	M	62	80	20%	AORTOCORONARY BYPASS	20 IU/Kg/ 6 hr	70%	4200 IU	ABSENCE OF COMPLICATIONS	
3	M	15	42	35%	AORTIC VALVE REPAIR	20 IU/Kg/ 6 hr	80%	2400 IU	ABSENCE OF COMPLICATIONS	
4	M	71	75	6%	POST-SURGICAL BLEEDING	20 IU/Kg/ 6 hr	82%	4200 IU	ABSENCE OF COMPLICATIONS	Vit k deficiency
5	M	65	75	22%	NEPHRECTOMY FOR UROTHELIAL CANCER	25 IU/Kg/ 8 hr	NA	24000 IU	ABSENCE OF COMPLICATIONS	
6	M	33	80	NA	PERICARDIOCENTESIS	20 IU/Kg	NA	1200 IU	ABSENCE OF COMPLICATIONS	WARFARIN OVERDOSAGE
7	F	26	50	19%	REMOVAL OF LEFT BRACHIAL CYST	30 IU/Kg	110%	1800 IU	ABSENCE OF COMPLICATIONS	
8	F	26	50	19%	THYROIDECTOMY FOR PAPILLARY CANCER	30 IU/Kg	120%	1800 IU	ABSENCE OF COMPLICATIONS	
9	M	76	70	40%	PROSTATIC HYPERPLASIA	20 IU/Kg/ 6 hr	130%	4200 IU	HAEMATURIA	
10	M	42	130	41%	BARIATRIC SURGERY	30 IU/kg/ 6 hr	NA	14400 IU	ABSENCE OF COMPLICATIONS	

PROGNOSTIC IMPACT OF HEART FAILURE IN PATIENTS WITH FRAGILITY HIP FRACTURES

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Background: Heart failure (HF) is a chronic condition associated with high morbidity and mortality, and its incidence is expected to rise due to the progressive aging of the population. Similarly, osteoporosis and fragility fractures—particularly hip fractures—are becoming increasingly common in the elderly and represent a major cause of disability and mortality. The relationship between HF and bone fragility is of particular interest, as both conditions are typical of aging but also share several risk factors and pathophysiological mechanisms. The coexistence of HF may synergistically worsen patient prognosis; however, evidence in this area remains limited. The aim of this study was to evaluate the prognostic impact of HF in patients hospitalized for fragility-related hip fractures, with a specific focus on mortality, rehospitalization, and incident fractures during the 12 months following the index event.
Methods: We enrolled patients aged ≥50 years who were hospitalized for fragility-related hip fractures and managed within the Fracture Liaison Service (FLS) program between March 2023 and January 2024 at the Azienda Ospedale–Università di Padova. Within this cohort, we conducted a nested case-control study including 117 patients with a history of HF and 117 age- and sex-matched controls without HF. Data collection included clinical, echocardiographic, and biochemical parameters, as well as the assessment of in-hospital complications and 12-month outcomes.
Results: A total of 508 patients were included, 23% of whom had a history of HF. Patients with HF were older (86.0 vs. 82.7 years, p<0.001) and exhibited a higher burden of individual comorbidities, including arterial hypertension, prior myocardial infarction, atrial fibrillation, chronic obstructive pulmonary disease, and advanced chronic kidney disease. They also had a significantly greater overall comorbidity burden, as measured by the Cumulative Illness Rating Scale–Comorbidity Index (CIRS-CI) (5 vs. 3, p<0.001). To reduce potential bias due to demographic differences, we performed a nested case-control study using propensity score matching for age and sex. With regard to in-hospital complications, patients with HF had a significantly higher incidence of acute decompensated heart failure (30% vs. 4%, p<0.001), acute myocardial injury (21% vs. 5%, p=0.02), and acute kidney injury (13% vs. 1%, p=0.003). However, these complications were not associated with increased 30-day mortality (p=0.811). Regarding 12-month mortality, we observed a non-significant trend toward reduced survival in patients with HF (HR 1.68, 95% CI: 0.96–2.93, p=0.067). From a skeletal perspective, there was no significant difference in the incidence of new fragility fractures between the two groups (p=0.170).
Conclusion: Even in the context of osteoporotic hip fractures, patients with HF represent a clinically vulnerable population, at increased risk for in-hospital complications and potentially poorer long-term outcomes. Timely recognition and management of heart failure—even when it is not the primary reason for admission—may help optimize clinical outcomes and reduce the burden of systemic complications in this high-risk group.

SEX-RELATED DIFFERENCES IN LIPID PROFILES AND CARDIOVASCULAR OUTCOMES IN A HIGH-RISK DIABETIC COHORT: FOCUS ON MACE, MALE, AND COMPOSITE EVENTS

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Background: Sex-related disparities in cardiovascular outcomes are of increasing interest in high-risk diabetic populations, where residual risk remains substantial despite optimal therapy. Lipoprotein(a) [Lp(a)] is an emerging atherothrombotic factor whose role may vary across sexes and clinical phenotypes. This study investigated sex-based differences in lipid profiles and outcomes, including major adverse cardiovascular events (MACE), major adverse limb events (MALE), and their composite, in a real-world diabetic cohort.
Methods: We analyzed data from 158 diabetic patients (mean age 81.6±7.8 years, 61% male) with established or high-risk atherosclerotic disease. Baseline variables included age, sex, diabetes status, lipid profile [LDL-C, HDL-C, Lp(a)], renal function, and cardiometabolic medications. Outcomes were prospectively collected and included: (1) MACE, (2) MALE, and (3) the composite endpoint (MACE+MALE). Logistic regression models were fitted for each outcome including sex (male), age, diabetes, LDL-C, and Lp(a) as covariates. Kaplan-Meier analysis and Cox regression were considered for time-to-event outcomes using follow-up time and event indicator.
Results: The study population included 158 diabetic patients with high cardiovascular risk, with a mean age of 81.6 ± 7.8 years and a male predominance (61%). Female patients were significantly older than their male counterparts (84.2 ± 6.8 vs. 80.1 ± 8.1 years, p=0.02), but no significant sex differences were observed in body mass index, waist-to-hip ratio, or smoking history. Lipid profiles, however, revealed notable differences: women had lower median LDL-C levels (77.1 mg/dL) compared to men (95.4 mg/dL, p=0.009), while HDL-C was significantly higher in females (47.0 mg/dL vs. 41.2 mg/dL, p=0.041). In contrast, lipoprotein(a) [Lp(a)] levels did not differ significantly

by sex (28.6 mg/dL in women vs. 34.2 mg/dL in men, p=0.177).

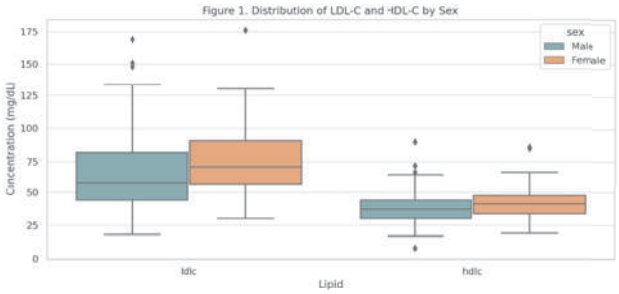

Figure 1. Boxplots showing the distribution of low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) levels stratified by sex. Female patients exhibited significantly lower LDL-C and higher HDL-C compared to male patients (p=0.009 and p=0.041, respectively), consistent with known sex-specific lipid patterns. Median and interquartile ranges are displayed.

During follow-up, MACE occurred in 52 of 158 patients. Event rates were extremely high in both sexes, with 15/15 women and 37/38 men experiencing events, which substantially limited survival analysis. In multivariate logistic regression, advancing age (p=0.016) and elevated LDL-C levels (p=0.007) were independently associated with MACE, while sex and Lp(a) were not significant predictors. For MALE, 45 events were recorded among 148 patients with available data. Age remained a borderline significant predictor (p=0.048), but neither male sex nor Lp(a) levels were independently associated with MALE occurrence. When considering the composite endpoint of MACE plus MALE, a total of 100 events occurred among the 158 patients. In this analysis, both age (p=0.008) and LDL-C (p=0.001) emerged as strong and consistent predictors, whereas sex and Lp(a) remained non-significant.

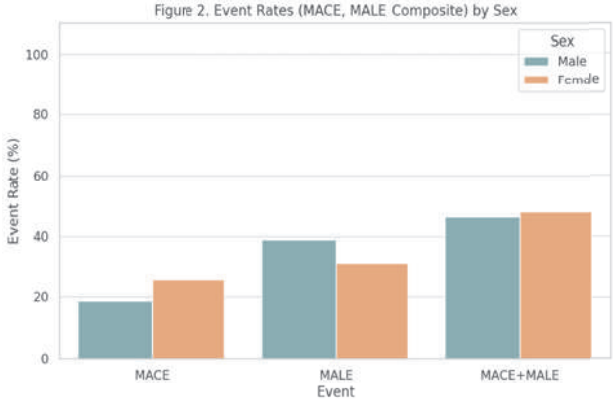

Figure 2. Event Rates (MACE, MALE, Composite) by Sex. Bar chart illustrating the percentage of patients experiencing major adverse cardiovascular events (MACE), major adverse limb events (MALE), and the composite endpoint (MACE+MALE), stratified by sex. Event rates were consistently high in both men and women, with minimal sex-based differences observed across all endpoints. The composite event rate exceeded 60% in both sexes, highlighting the extreme cardiovascular and limb risk in this high-risk diabetic cohort.

Kaplan-Meier survival curves stratified by sex showed minimal divergence, with median follow-up times of 98 days in women and 100 days in men. The exceedingly high event rate, particularly among women, limited the ability of time-to-event analysis to detect meaningful differences. As a result, Cox proportional hazards modeling was deemed inappropriate due to violation of proportional hazards assumptions in this context.

Conclusions: In this real-world cohort of elderly diabetic patients with high cardiovascular risk, we found significant sex-based differences in lipid profiles but not in Lp(a) levels or event incidence. LDL-C and age emerged consistently as independent predictors across MACE, MALE, and composite outcomes, while sex and Lp(a) did not. These findings suggest that Lp(a) may not confer differential risk by sex in advanced disease settings, and reinforce the need for aggressive LDL-C lowering in both men and women. Further prospective studies are warranted to validate these observations and to refine individualized risk stratification.

PRE-PROCEDURAL ADHERENCE TO SECONDARY PREVENTION THERAPY AND LONG-TERM RISK OF CARDIOVASCULAR AND LIMB EVENTS AFTER LOWER EXTREMITY REVASCULARIZATION IN PATIENTS WITH PERIPHERAL ARTERY DISEASE: A PROSPECTIVE REAL-WORLD COHORT STUDY

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Background: Peripheral artery disease (PAD) is a major atherosclerotic condition associated with high rates of cardiovascular morbidity and mortality. Among patients undergoing lower extremity revascularization (LER), the residual risk of major adverse cardiovascular events (MACE) and major adverse limb events (MALE) remains unacceptably high, despite procedural success. International guidelines recommend comprehensive secondary prevention therapies—including antiplatelet agents, statins, ezetimibe, and renin-angiotensin system inhibitors—for risk reduction. However, the real-world impact of adherence to these medications prior to revascularization is poorly characterized. This study aimed to evaluate whether adherence to guideline-recommended pharmacological therapy before LER independently predicts the occurrence of MACE and/or MALE during follow-up in a real-world PAD population.
Methods: We prospectively enrolled 126 consecutive patients undergoing LER for symptomatic PAD. At the time of revascularization, we collected detailed information on patient demographics, comorbidities, and ongoing pharmacological treatment. Adherence to secondary prevention therapy was defined as the prescription of at least 3 out of 5 key drug classes: aspirin, clopidogrel, statins, ezetimibe, and ACE inhibitors or angiotensin receptor blockers (ARBs). This definition was chosen to reflect a clinically meaningful degree of adherence in line with current practice guidelines. All patients were followed longitudinally for the occurrence of adverse events. The primary endpoint was a composite of MACE (nonfatal myocardial infarction, stroke, or cardiovascular death) and MALE (acute limb ischemia, major amputation, or clinically driven reintervention). Cox proportional hazards regression was used to assess the association between adherence status and outcomes, with multivariable adjustment for age, sex, diabetes mellitus, hypertension, coronary artery disease (CAD), and cerebrovascular disease (CVD).
Results: At baseline, 74 patients (58.7%) were considered adherent to secondary prevention therapy. The median age was 75 years (IQR 68–83), and 68% were male. Diabetes and hypertension were highly prevalent (82.5% and 81.7%, respectively), as were CAD (72%) and prior CVD (28%). During a median follow-up of 26 months, 52 patients (41%) experienced the composite endpoint (MACE or MALE). In multivariable Cox regression, non-adherence to medical therapy prior to LER was independently associated with a significantly increased risk of adverse events (hazard ratio [HR] 2.17, 95% confidence interval [CI] 1.31–3.60; p = 0.0026). When analyzed separately, non-adherence was associated with both, increased risk of MACE (HR 2.19, 95% CI 1.02–4.72; p = 0.045) and increased risk of MALE (HR 2.37, 95% CI 1.29–4.34; p = 0.005). Other variables including age, sex, diabetes, hypertension, CAD, and CVD were not significantly associated with the outcomes in adjusted models. Kaplan-Meier analysis demonstrated a significantly higher cumulative incidence of events in the non-adherent group (log-rank p < 0.01).

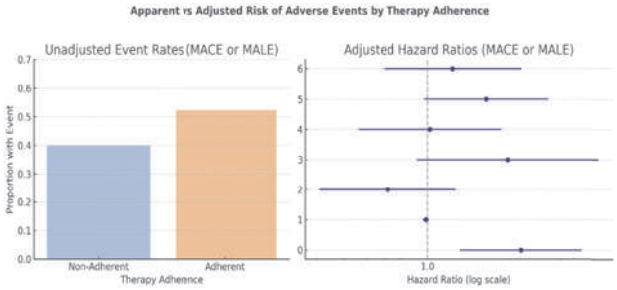

Figure 1. Apparent vs Adjusted Risk of Adverse Events by Therapy Adherence. Left panel: Bar plot showing the unadjusted incidence of the composite endpoint (MACE or MALE) stratified by adherence to secondary prevention therapy

before lower extremity revascularization (LER). Patients classified as "adherent" (receiving ≥3 of 5 recommended drug classes) showed a higher crude event rate (52.3%) compared to non-adherent patients (40.0%). This observation likely reflects differences in baseline clinical risk between groups.
Right panel: Forest plot displaying adjusted hazard ratios (HR) for the composite endpoint derived from a multivariable Cox regression model. After adjustment for age, sex, diabetes, hypertension, coronary artery disease, and cerebrovascular disease, adherence to therapy was independently associated with a significantly lower risk of MACE or MALE (HR 0.46, 95% CI 0.28–0.76). A vertical dashed line indicates the null effect (HR = 1.0). Hazard ratios are plotted on a logarithmic scale, with 95% confidence intervals shown as horizontal lines.

Conclusions: In this prospective real-world cohort of patients undergoing lower extremity revascularization for PAD, adherence to secondary prevention therapy prior to the procedure emerged as a strong and independent predictor of reduced long-term cardiovascular and limb-related complications. These findings underscore the importance of optimizing medical therapy not only postoperatively, but also before intervention, as part of a comprehensive vascular risk reduction strategy. Our results support the integration of structured pharmacological optimization programs before revascularization and suggest that failure to adhere to secondary prevention guidelines may represent a modifiable risk factor in PAD patients.

PREVALENCE AND CLINICAL CORRELATES OF ALCOHOL USE DISORDER IN PATIENTS WITH PERIPHERAL ARTERY DISEASE: INSIGHTS FROM A REAL-WORLD COHORT

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Background: Peripheral artery disease (PAD) is a manifestation of systemic atherosclerosis associated with high morbidity and cardiovascular risk. While lifestyle-related factors such as smoking and diabetes are well-established contributors to PAD, the role of alcohol use disorder (AUD) remains underexplored. Given the complex interactions between chronic alcohol consumption, metabolic derangements, vascular inflammation, and hepatic dysfunction, a deeper understanding of AUD in PAD populations is warranted.
ObjectivesThis study aimed to investigate the prevalence of AUD and at-risk alcohol consumption in a real-world PAD population, to describe the clinical and biochemical profile of patients with AUD, and to explore the association between alcohol-related behaviors and PAD severity.
Methods: We conducted a retrospective observational study including 103 patients with confirmed PAD across various Leriche-Fontaine / Rutherford stages. Alcohol consumption patterns were assessed through structured interviews and standardized screening tools, including the AUDIT-C. AUD was defined according to DSM-5 criteria, and patients were further stratified based on AUD severity (mild, moderate, severe). At-risk consumption was defined based on validated thresholds of alcohol units/week. PAD severity was classified using the Leriche-Fontaine/Rutherford system. Clinical, metabolic, and laboratory variables were compared across alcohol use categories using univariate (Wilcoxon, chi-square) and multivariate analyses (logistic regression with bootstrapped confidence intervals). A clustering analysis (k-means with PCA) was performed to identify phenotypic subgroups within the AUD population.
Results: AUD was identified in approximately 21% of the PAD cohort, while 17% reported at-risk alcohol consumption. A significant association emerged between PAD severity and AUD prevalence ($p = 0.02$), with the highest prevalence observed in Leriche-Fontaine / Rutherford stage IV-III6. AUD was strongly associated with male sex (100% vs 72%, $p = 0.01$) and current smoking (77% vs 22%, $p < 0.001$). Compared to patients without AUD, those with AUD had significantly lower HbA1c values (median 6.3% vs 6.6%, $p = 0.04$), while no differences were observed in BMI, lipid profile, renal function, or inflammatory markers. GGT levels showed a trend toward elevation with increasing AUD grade, though this did not reach statistical significance (Figure). Similarly, eGFR showed a trend toward reduction with higher AUD severity. Among patients with AUD, unsupervised clustering revealed two distinct phenotypes: one characterized by elevated GGT, ALT, and AST (suggestive of hepatic involvement), and another with more preserved hepatic parameters but greater metabolic derangement. Patients with at-risk alcohol use, despite not meeting AUD criteria, were older (median age 78 vs 71 years, $p = 0.001$) and had similar metabolic and vascular profiles compared to those without at-risk use.

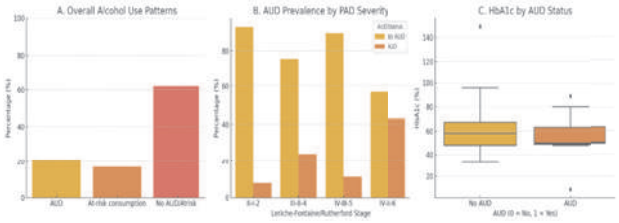

Figure. Panel A shows the distribution of alcohol-related behaviors in the PAD cohort, with 21% of patients having AUD, 17% reporting at-risk alcohol consumption, and 62% without either. Panel B illustrates the increasing prevalence of AUD with PAD severity, reaching its peak in Leriche-Fontaine / Rutherford stage IV / III6 ($p = 0.02$). Panel C compares HbA1c values, highlighting significantly lower levels among patients with AUD compared to those without ($p = 0.04$).

Conclusions: In this real-world PAD population, AUD and at-risk alcohol consumption were common and associated with distinct clinical patterns. AUD was linked to male sex, smoking, and more advanced PAD, whereas metabolic parameters were not consistently altered. Our findings suggest that systematic screening for alcohol use behaviors in PAD patients may reveal high-risk subgroups and guide multidisciplinary management strategies. Future studies should explore longitudinal outcomes and the potential role of tailored interventions for AUD in PAD care pathways.

URIC ACID AND CARDIOVASCULAR/LIMB RISK IN DIABETIC PATIENTS WITH CHRONIC LIMB-THREATENING ISCHEMIA (CLTI): EVIDENCE OF A NON-LINEAR ASSOCIATION

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Background: Uric acid (SUA) has been linked to endothelial dysfunction, inflammation, and cardiovascular risk, but its prognostic role in diabetic patients with chronic limb-threatening ischemia (CLTI) remains unclear. We investigated the association between SUA levels and major adverse events in a prospective cohort of CLTI patients.
Methods: We analyzed a prospective dataset of 158 patients with CLTI, including SUA levels, clinical and metabolic parameters, and longitudinal outcomes. Hyperuricemia was defined as SUA >7 mg/dL in men and >6 mg/dL in women. Outcomes included major adverse cardiovascular events (MACE), major adverse limb events (MALE), and a composite outcome. Logistic regression and non-linear models (SUA + SUA^2) were used to explore associations.
Results: SUA values were available in 92 out of 158 patients included in the study, with 58% of them classified as hyperuricemic according to sex-specific thresholds. Compared with normouricemic patients, those with hyperuricemia displayed significantly higher levels of glycated hemoglobin (HbA1c) (mean 7.64% vs. 6.95%, $p = 0.028$), suggesting a worse glycometabolic profile. There was also a trend toward reduced renal function among hyperuricemic patients, as reflected by lower estimated glomerular filtration rate (eGFR), although this did not reach statistical significance.

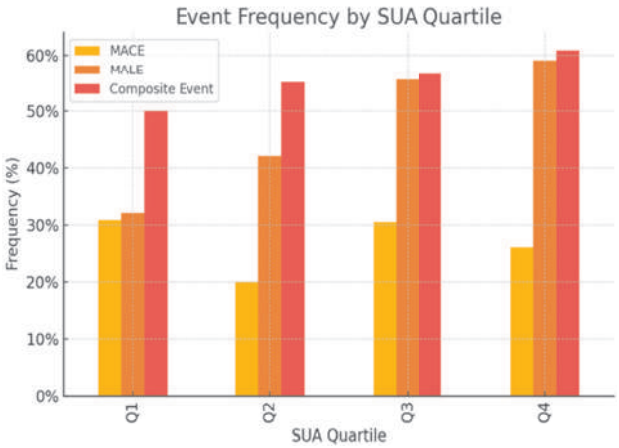

Figure 1. Event frequency by SUA quartile

In logistic regression models adjusted for age, body mass index (BMI), renal function, diabetes, and hypertension, hyperuricemia was not independently associated with the occurrence of MACE, MALE, or the composite endpoint. However, when a non-linear model including both SUA and SUA^2 was applied, a U-shaped relationship emerged between uric acid levels and the risk of MACE. In this model, both the linear term for SUA ($p = 0.066$) and the quadratic term SUA^2 ($p = 0.065$) approached statistical significance, suggesting that both low and high uric acid levels may be associated with an increased risk of cardiovascular events. Interestingly, in the same multivariable model, BMI was significantly and independently associated with MACE ($p = 0.020$), reinforcing the role of metabolic burden as a contributor to vascular risk in patients with CLTI. These findings were further supported by stratified analyses across SUA quartiles, which showed an increasing trend in adverse event rates in both the lowest and highest quartiles, particularly for the composite outcome.

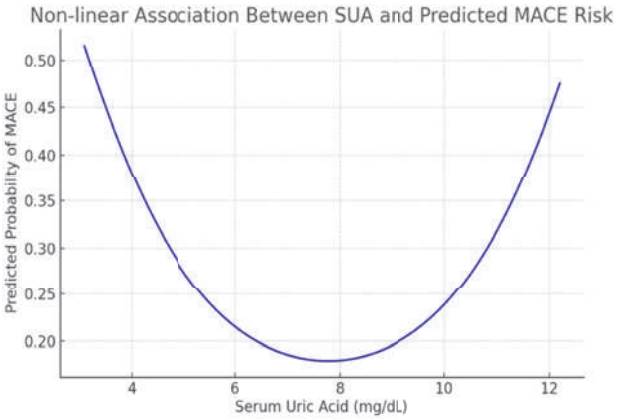

Figure 2. Non-linear association between serum uric acid and predicted MACE risk

Conclusions: In patients with CLTI, SUA does not show a linear association with adverse cardiovascular outcomes but may follow a non-linear (U-shaped) pattern. Uric acid may represent a non-traditional biomarker to enhance risk stratification in personalized vascular medicine.

HYPERFERRITINEMIA AS A MARKER OF RARE DISEASE: KNOWLEDGE FOR RECOGNITION

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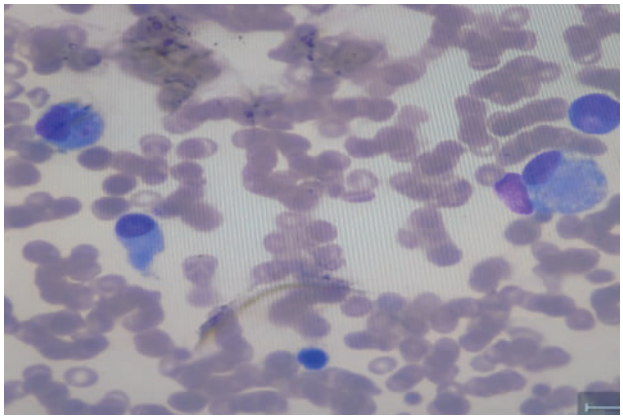
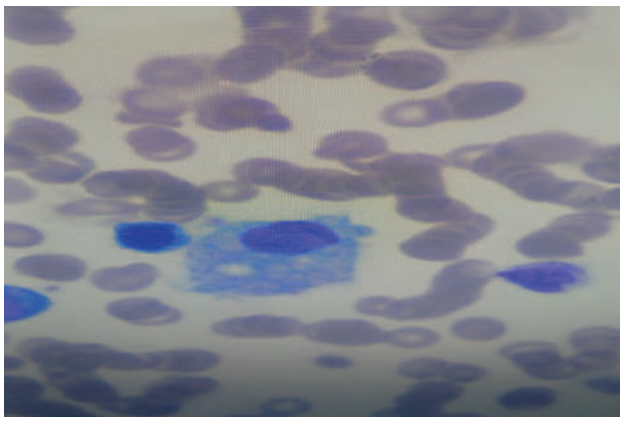
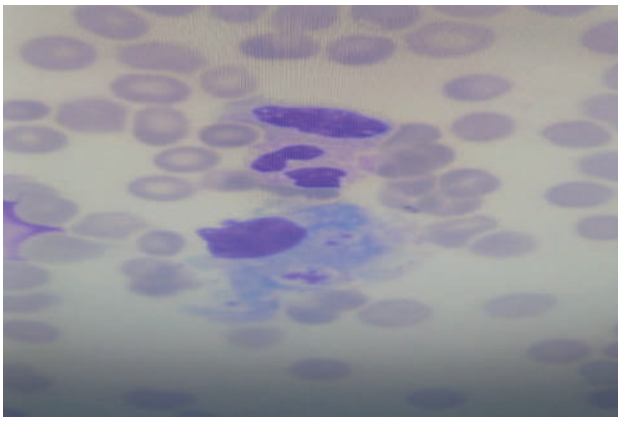
A 67-year-old male patient was admitted to the Internal Medicine department due to persistent fever, peaking at 39°C, with diarrhea from 20 days and asthenia. Blood exames showed elevated inflammatory markers (PCR 120 mg/dl), increased fecal calprotectin (6000 ug/g), ferritin (3000 ng/ML), D-dimers (3500), transaminases (65 U/L, ALT 87 U/L), LDH (600 U/L), prolonged PT INR (1.7). Tumor markers, autoimmunity, stool culture and parasitological examinations were negative. Empirical antibiotic therapy was started. Viral screening was negative except for CMV IgM positivity. A total-body CT scan revealed ascites, splenomegaly (130 mm) and periaortic lymphadenopathy. Peripheral blood cytological exame and lymphocyte immunophenotyping were inconclusive.
An EGDS showed erosive gastritis with active bleeding. Colonoscopy was not performed due to the patient's critical condition. Valganciclovir therapy was initiated, but no clinical improvement was observed. On the eighth day of hospitalization, the patient developed severe pancytopenia, worsening liver function, and further coagulation abnormalities (PT, aPTT, fibrinogen, and AT III). Leishmaniasis or hemophagocytic syndrome were suspected, a bone marrow biopsy (BOM) was performed. Histological analysis revealed macrophages exhibiting hemophagocytosis, leading to a diagnosis of hemophagocitosys.
Discussion: Hemophagocytic Syndrome (HS) is a condition characterized by macrophage hyperactivation, resulting in the phagocytosis of red, white blood cells and platelets, usually triggered by viral or several bacterious infections or rheumatic diseases (MAS) in genetically predisposed individuals. Diagnosis is based on the presence of at least five out of eight major criteria, including cytopenia of at least two cell lines, ferritin levels >500, hypertriglyceridemia, splenomegaly, and evidence of hemophagocytosis in the bone marrow biopsy. The patient was treted with high-dose corticosteroid therapy without response. He was transferred to the intensive care unit, where he died a few days later.
Conclusion: Early diagnosis of HS remains challenging due to the absence of specific hematochemical markers. The clinical picture often mimics sepsis or disseminated intravascular coagulation (DIC), leading to underdiagnosis. Hemophagocytosis detected on a bone marrow biopsy remains a key diagnostic finding, but the prognosis is poor.
In the context of viral infections—particularly CMV—the presence of elevated inflammatory markers, ferritin levels >500, fever, and splenomegaly should always prompt consideration of HS and warrant a bone marrow biopsy. Early recognition and timely treatment initiation are crucial, although mortality remains high.







UNRAVELING THE RISK FACTORS FOR TYPE II DIABETES IN SEVERE OBESE PATIENTS WITH INDICATION FOR BARIATRIC SURGERY: RETROSPECTIVE ANALYSIS

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Questo studio indaga i fattori di rischio per il diabete mellito di tipo II (T2DM) in pazienti gravemente obesi sottoposti a valutazione per chirurgia bariatrica. Abbiamo condotto un'analisi retrospettiva di 734 individui, valutando le associazioni tra T2DM e variabili clinico-demografiche tra cui età, sesso, ipertensione, dislipidemia, abitudine al fumo e indice di massa corporea (BMI). La regressione logistica e il test esatto di Fisher sono stati utilizzati per identificare i predittori significativi.
La coorte aveva un'età media di 39 anni (DS = 11,5) e un BMI medio di 41,92 kg/m² (DS = 5,16). La prevalenza di T2DM era del 9,5%, con tassi più elevati tra i pazienti con ipertensione, dislipidemia e anamnesi di fumo. Il sesso non ha mostrato alcuna associazione significativa con il T2DM (p = 0,4818). Al contrario, ipertensione (p = 0,0098; OR = 2,344), dislipidemia (p = 0,0009; OR = 2,467) e fumo (p = 0,00097; OR = 2,367) erano significativamente più frequenti nei pazienti diabetici.
La regressione logistica multivariata, raffinata secondo il criterio informativo di Akaike (AIC), ha identificato età (OR = 1,0245), ipertensione (OR = 1,9083), dislipidemia (OR = 2,0851) e fumo (OR = 2,259) come fattori predittivi indipendenti del diabete di tipo 2. Il modello ha dimostrato un'eccellente sensibilità (0,98) ma una bassa specificità (0,116), con un elevato valore predittivo negativo (0,987), a supporto del suo utilizzo nell'esclusione del diabete di tipo 2 tra i soggetti a basso rischio.
I nostri risultati sottolineano la natura multifattoriale del diabete di tipo 2 nell'obesità grave. Fattori modificabili come fumo, ipertensione e dislipidemia offrono obiettivi concreti per un intervento precoce. Una stratificazione completa del rischio può migliorare la valutazione preoperatoria e orientare le strategie preventive nelle popolazioni obese ad alto rischio.

Punteggio di Rischio Clinico per la valutazione del rischio di DM di tipo II nei pazienti Obesi

Il modello di regressione logistica può consentire di assegnare la probabilità di presenza di DM di tipo 2 in funzione del valore di predittori statisticamente significativi (Fumo, Età, Dislipidemia, Ipertensione) utilizzando la seguente equazione per calcolare un punteggio clinico:

$$y = a_0 + a_1F + a_2E + a_3D + a_4I$$

e la funzione logistica standard per valutare la probabilità di accadimento del diabete mellito di tipo 2:

$$P(T2DM|F,E,D,I) = p = \frac{1}{1+e^{-y}}$$

dove:

- F: Fumatori, fattore binario, codificato come Vero=1 e Falso=0
- E: Età in anni, codificata come valore intero
- D: Dislipidemia, fattore binario, codificato come Vero=1 e Falso=0
- I: Ipertensione, fattore binario, codificato come Vero=1 e Falso=0

e

Parametro	Valore	Errore standard	p-value
a_0	-4.37	0.56	$< 10^{-6}$
a_1	0.815	0.26	0.0023
a_2	0.0242	0.012	0.0484
a_3	0.735	0.285	0.0099
a_4	0.646	0.27	0.0185

Considerando l'intervallo della variabile "Età", da 16 a 70 anni, il punteggio clinico y è stato normalizzato nell'intervallo 0-10 e i pazienti sono stati raggruppati in quattro classi, in base al loro punteggio clinico e alla sensibilità (0,986) e specificità (0,116) scelte:

- Rischio basso, da 0 a 2,5
- Rischio moderato, da 2,5 a 5
- Rischio elevato da 5 a 10

Abbiamo eseguito un test χ^2 test per verificare l'esistenza di un'associazione tra la presenza di DM di tipo 2 e la classe di rischio. Il valore di probabilità dei risultati ($\chi^2 = 28.2, df = 2, pvalue < 10^{-6}$) mostra una relazione statisticamente significativa tra la classe di rischio e l'insorgenza di diabete di tipo 2.

BEYOND THE JOINTS: A RARE CASE OF SUBCORNEAL PUSTULAR DERMATOSIS IN RHEUMATOID ARTHRITIS

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A 68-years-old woman with an 11-year history of rheumatoid arthritis (RA) presented to our Rheumatology Clinic due to the acute exacerbation of a vesiculopustular rash that had been evolving over the past 3 months. The lesions, ranging from 1 to 7 millimeters, involved both elbows, the left axillary region and the left hip. Notably, they exhibited the hypopyon sign. The eruption followed a Herpes Zoster virus infection, which had been successfully treated with antiviral therapy. The patient denied taking any new medications, except for Talavir, and reported a family history of psoriasis. Initially, cutaneous manifestations were not associated with systemic symptoms. Thus, the patient underwent dermatological evaluation; a skin biopsy was performed, due to the clinical suspicion of a bullous disorder; specifically, subcorneal pustular dermatosis was the primary diagnostic consideration. While waiting the histopathological report, the patient's clinical condition deteriorated, marked by the emergence of systemic manifestations, including chills in the absence of fever, dizziness, hypotension, and a burning sensation in the involved areas. Thus, she was admitted to our department for close monitoring and further diagnostic workup. Given the acute progression, the differential diagnosis remained broad, with subcorneal pustular dermatosis, pustular psoriasis, and IgA pemphigus as possible aetiologies. A therapeutic agent with efficacy across all three conditions was selected, and treatment with acitretin was initiated. Following an initial clinical improvement, the patient's condition worsened abruptly, characterized by recurrence of fever, dissemination of pustules, and secondary impetiginization. Consequently, systemic corticosteroids and doxycycline were initiated; however, no significant clinical response was observed. Consequently, second-line therapy with the anti-tumor necrosis factor-α (TNFα) agent infliximab was started. In the following days, histopathological examination confirmed the suspicion of subcorneal pustular dermatosis. The patient then exhibited marked clinical improvement, evidenced by resolution of pustular eruption, desquamation of previously affected areas, and defervescence. Ultimately, she was discharged with a close outpatient follow-up plan and continued periodic administration of infliximab, which has successfully controlled both her cutaneous manifestations and underlying RA.
Subcorneal pustular dermatosis (SPD), also known as Sneddon Wilkinson disease, is a rare neutrophilic dermatosis, predominantly affecting middle-aged women, with a reported female-to-male ratio of 4:1. Clinically, SPD is characterized by recurrent episodes of flaccid pustules and superficial blisters, typically distributed on the trunk, intertriginous zones, and flexural regions of the extremities, while sparing the face and mucosal surfaces. SPD's diagnosis can be challenging due to its clinical and histopathological overlap with other pustular disorders, including pustular psoriasis, IgA pemphigus, and acute generalized exanthematous pustulosis. A distinguishing clinical feature is its usual confinement to the skin, without systemic involvement. Therefore, the presence of systemic symptoms often favors alternative diagnoses. Moreover, SPD typically exhibits a gradual onset. The morphology and distribution of the lesions, along with the presence of the characteristic hypopyon sign, are valuable diagnostic clues supporting SPD's diagnosis. However, diagnosis cannot rely solely on clinical history and physical examination. Histopathological evaluation is not only beneficial but essential for diagnostic confirmation. Characteristic findings include a neutrophilic infiltrate within the subcorneal layer of the epidermis, accompanied by an unremarkable dermis. Definitive diagnosis is supported by negative direct and indirect immunofluorescence studies, which also serve to exclude pemphigus and other immunobullous disorders. Once the diagnosis is established, prompt initiation of therapy is crucial. Dapsone is the first-line treatment due to its anti-neutrophilic properties. In cases of intolerance or contraindication, acitretin may be employed as an effective alternative. Systemic corticosteroids have also demonstrated efficacy, either as monotherapy or in combination with standard treatments. In refractory cases, biologic agents targeting TNFα, such as infliximab, have shown promising results. When effective, treatment induces resolution within 1-4 weeks; however, disease relapse is common, often necessitating long-term therapy.
This case depicts an exceptionally rare dermatological condition that is often misdiagnosed due to its clinical resemblance to other pustular dermatoses. Atypical features, such as systemic symptoms or an abrupt onset, can further complicate the diagnosis. In our case, the occurrence of fever, sudden clinical deterioration, and lack of response to initial therapies challenged the initial diagnostic hypothesis. Nevertheless, histopathological confirmation validated the suspected diagnosis. This case also underscores the critical importance of early and appropriate treatment, particularly in rapidly progressive forms.

76. CLINICAL CASE SERIES FROM AN ALLERGY AND IMMUNOLOGY CENTER IN EASTERN LIGURIA: A RETROSPECTIVE ANALYSIS OVER ONE YEAR

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Introduction: Chronic allergic and immunologic diseases represent a growing share of outpatient specialist consultations. Our Clinical Allergy and Immunology Center, located at San Bartolomeo Hospital in Sarzana, has, within its first year of activity, collected a significant number of cases, providing valuable insights into the clinical distribution and care demands of referred patients.
Materials and methods: A retrospective analysis was conducted on patients evaluated at our center between December 2023 and March 2025. Demographic, clinical, and diagnostic data were collected from individuals with suspected or confirmed allergic or immunologic disorders. Day Hospital activities were also assessed, including diagnostic workups and specialized treatments.
Results: A total of 1,116 patients were assessed, including 712 females (63.8%) and 404 males (36.2%), aged between 11 and 93 years. Among them, 779 patients were diagnosed with strictly immuno-allergological conditions.
Of these, **578 patients (74.2%)** presented **allergic diseases**, distributed as follows:
201 patients (25.8%) were affected by **immunologic diseases**, including:
During the study period, **34 Day Hospital admissions** were recorded for diagnostic evaluations and treatments, including provocation testing, therapeutic infusions, and multidisciplinary monitoring.
Conclusions: Our case series highlights the broad heterogeneity of conditions managed within an Allergy and Immunology Center. Allergic diseases accounted for the majority of outpatient consultations, yet the rise in complex immunologic disorders underscores the need for an increasingly integrated multidisciplinary approach. The Day Hospital setting has proven to be an essential tool for managing selected cases, ensuring early diagnosis, access to advanced testing, and personalized follow-up, ultimately improving clinical outcomes and patient quality of life.

IMPACT OF TREATMENT, COMORBIDITIES AND GENDER ON VACCINATION ADHERENCE IN PATIENTS WITH AUTOIMMUNE DISEASES

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Introduction: We conducted a multicentre, cross-sectional, observational study of 291 immunocompromised patients recruited from five Italian centres between January and December 2024.
Study Population: 291 immunocompromised patients consecutively recruited from four Italian clinical centres (Ancona, Bari, Cagliari and Messina) between January and December 2024 were enrolled. Inclusion criteria were: age ≥18 years, confirmed diagnosis of immunosuppression (autoimmune disease and/or ongoing immunosuppressive therapy), complete availability of clinical and anamnestic documentation.
Data Collection: The following parameters were collected for each subject: demographic data (age, sex), clinical profile (presence of respiratory and endocrinological co-morbidities, specific autoimmune diseases including rheumatoid arthritis [RA] and Sjögren's syndrome [SS]), vaccination history (flu vaccinations administered during 2020-2023, pneumococcal vaccination, type of anti-COVID-19 vaccination), year of autoimmune disease diagnosis, and current pharmacological treatment (with particular attention to iloprost, mycophenolate mofetil, alprostadil, methylprednisolone, methotrexate, prednisone, bosentan and ambrisentan). Chronic therapies for non-autoimmune diseases has also been documented.
Statistical Analysis: Analysis of determinants of vaccination uptake was performed using a probit regression model to estimate the marginal probability of receiving influenza vaccination in 2024. The dichotomous dependent variable was defined as receipt of flu vaccination (yes/no). Main covariates included: age (stratified into categories: <25, 25-40, 40-60, 60-70, >70 years), sex, presence of comorbidities (endocrinological and respiratory), current therapies (i.e., iloprost), autoimmune diseases, vaccination history (cumulative number of previous influenza vaccinations, range 0-4) and pneumococcal vaccination status.
Marginal effects were calculated to quantify the variation in the probability of influenza vaccination associated with a unit change in each covariate, holding all other variables constant.
Additional variables were tested in the model but did not reach statistical significance.
Analyses were performed using Python (version 3.11), employing statsmodels libraries for statistical modeling, pandas for data management, and numpy for mathematical operations. Statistical significance was defined as $p<0.05$ for all analyses conducted. The performance of the Probit model was evaluated using the area under the ROC curve (AUC = 0.83, 95% CI 0.78–0.88), indicating excellent discriminative capacity in classifying patients based on their propensity for influenza immunization.
Main Results: Iloprost therapy was significantly associated with reduced probability of adherence to influenza vaccination (mean marginal effect: -30%, $p<0.01$), with an age-dependent gradient showing a more pronounced effect in subjects under 40 years. Stratified analysis by clinical center revealed geographic heterogeneity in the magnitude of this effect, with probability reduction ranging from -26% in Ancona to -4% in Messina in patients of the upper age group.
Respiratory comorbidities showed a negative association with vaccination propensity (-26%, $p<0.05$), while endocrinological comorbidities exhibited a positive association (+29%, $p<0.01$). The protective effect of endocrinological comorbidities was attenuated in the presence of Iloprost therapy, with gender-specific modulation: in female patients with endocrinological comorbidities, the negative effect of Iloprost was quantified at -21.9%, while in women without such comorbidities, the negative effect increased to -27.8%.
Sjögren's syndrome (SS) was associated with a greater reduction in vaccination propensity compared to rheumatoid arthritis (RA), with a particularly marked effect in women with limited vaccination history (up to -50.8% versus -22.5% in males with endocrinological comorbidities, $p<0.01$). For both conditions, a higher number of previous influenza immunizations progressively mitigated the observed negative effect. Specifically, in patients with SS and no previous vaccinations, the reduction in vaccination propensity reached -76% in women under 25 years of age, subsequently reducing to -3.0% in patients with identical characteristics but with 4 previous influenza vaccinations.
The additional variables tested in the model did not show statistically significant associations with vaccination propensity (all $p>0.05$).
Conclusion: : The results of our study would demonstrate the importance of awareness of one's own clinical condition and multiple pathologies in adhering to vaccination recommendations. In confirmation, even chronic treatments can enhance adherence to vaccination recommendations. All this would confirm the importance of adequate information by doctors at specialist centers.

ACTORS ASSOCIATED WITH THE USE OF ANTIARRHYTHMIC DRUGS IN VERY ELDERLY (≥80 YEARS) PATIENTS WITH ATRIAL FIBRILLATION AND RISK OF MORTALITY AND CARDIOVASCULAR EVENTS: DATA FROM THE NATIONWIDE ITALIAN START REGISTRY

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Background: There is limited evidence on the use of antiarrhythmic drugs (AADs) in elderly and very elderly patients with atrial fibrillation (AF). We investigated clinical characteristics of AF patients on AADs and its association with mortality and cardiovascular events (CVEs).
Methods: 4,244 very elderly (age ≥80 years) patients with AF from the nationwide START registry were included for this analysis. Patients were divided into 3 groups: no AADs (n=3,573), class 1c-AAD (n=207), Amiodarone (n=464). The risk of all-cause mortality and CVEs was analysed according to AAD use.
Results: Mean age was 84.8±3.8 years and 54.9% were women. Overall, 15.8% were treated with AADs, mainly amiodarone (10.9%) and Class 1c agents (4.9%). Patients receiving AADs exhibited distinct clinical and demographic profiles. Compared to no AAD, those on Class 1c agents were younger, more often female, and more likely to have paroxysmal AF (62.7% vs. 27.3%; p<0.001), with lower prevalence of heart failure (9.2% vs. 26.4%) and coronary artery disease (9.7% vs. 16.5%). In contrast, patients treated with amiodarone had higher rates of hypertension (88.4%), chronic kidney disease (13.1%), and greater use of diuretics (55.4%) and proton pump inhibitors (58.0%).
Multivariable logistic regression confirmed that use of Class 1c AADs was independently associated with younger age (OR 0.903; p<0.001), female sex (OR 1.457; p=0.016), paroxysmal AF (OR 3.434; p<0.001), and absence of diabetes, coronary artery disease, and heart failure. Other factors negatively associated with Class 1c use included digoxin (OR 0.193; p=0.005), COPD/OSAS (OR 0.533; p=0.037), and lack of family/social support (OR 0.539; p=0.001). Amiodarone use was similarly associated with younger age (OR 0.929; p<0.001), paroxysmal AF (OR 1.891; p<0.001), coronary artery disease (OR 1.351; p=0.016), wheelchair use (OR 1.540; p=0.034), and inversely associated with peripheral artery disease (OR 0.488; p=0.005), living alone (OR 0.527; p=0.021), digoxin use (OR 0.425; p<0.001), and lack of social support (OR 0.534; p<0.001).
During a mean follow up of 685,6±537.7 days, 492 all-cause deaths, 548 CV events. In univariable Cox regression, Class 1c AADs were significantly associated with reduced all-cause mortality (HR 0.371; p=0.003) and cardiovascular events (HR 0.443; p=0.005). Amiodarone showed no significant associations. However, these protective associations of Class 1c drugs were not confirmed in multivariable analysis.
Multivariable Cox regression identified the following independent predictors of all-cause mortality: Age (HR 1.117; p<0.001), Female sex (HR 0.697; p<0.001), Coronary artery disease (HR 1.391; p=0.007), Peripheral artery disease (HR 1.545; p=0.008), Anemia (HR 1.287; p=0.009), COPD/OSAS (HR 1.675; p<0.001), Chronic kidney disease (CKD) (HR 0.690; p=0.008), Wheelchair use (HR 1.670; p=0.004), Use of DOACs (HR 0.348; p<0.001), Lipid-lowering therapy (HR 0.679; p=0.001), RAAS inhibitors (HR 0.796; p=0.020).
Similarly, for CVEs, significant predictors included Age (HR 1.100; p<0.001), Female sex (HR 0.689; p<0.001), Coronary artery disease (HR 1.350; p=0.011), Peripheral artery disease (HR 1.639; p=0.001), Anemia (HR 1.260; p=0.012), Previous cerebrovascular disease (HR 1.297; p=0.017), COPD/OSAS (HR 1.658; p<0.001), CKD (HR 0.624; p<0.001), Wheelchair use (HR 1.575; p=0.008), Social/familial support (HR 0.781; p=0.020), DOAC use (HR 0.460; p<0.001), Lipid-lowering therapy (HR 0.713; p=0.002), RAAS inhibitors (HR 0.794; p=0.013).
Conclusions: . Among very elderly AF patients, AAD use—especially Class 1c agents—was selectively prescribed in patients with fewer comorbidities and better functional and social status. These results indicate that frailty elements affect the choice of AADs in elderly AF patients. While Class 1c agents were associated with favorable outcomes in unadjusted models, these effects did not persist after adjustment for comorbidities.

NEWS ON DYSPEPSIA MANAGEMENT: IS ROUTINE BIOPSY MAPPING WARRANTED IN H. PYLORI-NEGATIVE PATIENTS?

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Introduction: Dyspeptic symptoms are common, affecting about20% of the general population. While Helicobacter pylori (H. pylori) infection is a known cause of chronic gastritis and dyspepsia, it has become less prevalent in Western countries, leading to questions about the value of routine endoscopic biopsies in dyspeptic patients without H. pylori. This study examines the prevalence and severity of precancerous gastric lesions in dyspeptic patients with and without H. pylori infection to determine the need for endoscopic biopsies.
Materials and methods: This retrospective study enrolled2,171dyspeptic patients who underwent upper gastrointestinal endoscopy (UGIE) and biopsy mapping between January2022and August2024. Patients were divided based on H. pylori status using a composite reference method (CRM). Biopsy samples were collected and analyzed according to OLGA and OLGIM staging systems to assess the presence of precancerous lesions.
Results: Out of 2,171patients,646(29.8%) were H. pylori positive. In these patients, chronic active gastritis was prevalent, and a significant percentage reached OLGA/OLGIM stages III and IV, indicating higher cancer risk. Conversely, H. pylori-negative patients showed minimal gastritis, with most remaining at stage0in both staging systems. A risk factor analysis revealed that advanced age and male gender were associated with an increase in lesion severity, with patients in the oldest age quartile (67-89years) more likely to reach advanced OLGA/OLGIM stages. Among younger patients (18-46years), precancerous lesions were rare and predominantly at stage0.
Conclusions: Our findings suggest that routine biopsy sampling may not be necessary in dyspeptic patients without H. pylori infection, as these individuals rarely exhibit precancerous lesions. Biopsy guidelines may be reconsidered to target higher-risk populations, such as older males, to improve clinical efficiency and resource allocation.

ATOPY AND OTHER (FOOD) HYPERSENSITIVITIES IN NON-CELIAC WHEAT SENSITIVITY: SHOULD WE RECLASSIFY THESE PATIENTS AS 'ALLERGIC'? A RETROSPECTIVE CASE-CONTROL STUDY

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Background: recent advances in understanding non-celiac wheat sensitivity (NCWS) have proved that it should be considered a protean condition in which several potential triggers [e.g. gluten, wheat amylase-trypsin inhibitors (ATIs), etc.] might be responsible for intestinal mucosal damage, leading to an increase in intestinal permeability (IP) and exposure of foods/microbial peptides to immune cells, resulting in both a local and systemic inflammatory response, which can determine its gastrointestinal and extraintestinal clinical manifestations. Up to 75% of NCWS subjects complain of multiple foods hypersensitivities (MFH). These patients usually have clinical, immunological and histological features similar to wheat allergy patients, although without positive gluten/wheat IgE assays, allowing to hypothesize the existence of a non-IgE mediated hypersensitivity able to justify this complex framework. In addition, several studies have reported a certain association between atopic diseases (i.e. allergic oculorhinitis, allergic asthma, and atopic dermatitis) and NCWS.
Aims: in this study we aimed to define the presence and features of atopic diseases and other hypersensitivities (primarily food allergies/intolerances different from gluten/wheat) in NCWS compared with celiac disease (CD) and irritable bowel syndrome/functional dyspepsia (IBS/FD) and to analyze a possible correlation between these diseases and the other clinical manifestations characterizing NCWS patients.
Methods: this retrospective, multicenter study included NCWS patients consecutively diagnosed by double-blind placebo-controlled challenge with wheat, between January 2010 and December 2023. Their clinical, laboratory and histology data at diagnosis, thus before the start of a wheat-free diet, were retrospectively analyzed and compared to control subjects with CD and IBS/FD, diagnosed in the same period and in the same centers. According to the aims of the study, in addition to the clinical/laboratory features typical of NCWS, data were collected and analyzed regarding the family and personal history of atopy, the type of allergens responsible for the manifestations, and the positivity of prick tests, patch tests and total and food-specific IgE.
Results: atopic disease prevalence was higher in the NCWS patients (32.8%) than in those with CD (19.3%) and IBS/FD (21.5%) (P = 0.001 for both). Similarly, NCWS subjects reported a higher frequency of MFH (39.8%) and self-reported milk intolerance (SRMI) (65.9%) compared to the control groups (P < 0.001 for both). Allergic asthma, either alone (P=0.03) or in association with allergic rhinitis (P=0.005), was more frequently reported by NCWS patients compared to IBS/FD ones, who, on the contrary, usually complain more often of allergic conjunctivitis (P=0.004) or allergic rhinitis alone (P=0.02). Graminaceae hypersensitivity and nickel allergic contact dermatitis were more frequently reported in patients with NCWS (70.1% and 17.8%, respectively) vs both CD (48.7% and 9.4%, P=0.03 and P=0.01, respectively) and IBS/FD (50.8% and 6.7%, P=0.01 and P<0.001, respectively). On multiple logistic regression analysis, a coexistent atopic disease (OR 1.481), MFH (OR 3.882)

and SRMI (OR 2.259) proved to be variables associated with the NCWS diagnosis. In a subgroup analysis of the NCWS patients, subjects with atopy compared to those without more frequently showed nickel allergic contact dermatitis (P<0.001) and SRMI (P=0.03), positive patch test (P<0.001), skin prick test for foods (P=0.001), food-specific serum IgE (P=0.002), and elevated total serum IgE (P=0.02). On multiple logistic regression analysis, patch test positivity (OR 2.955), skin prick test for foods (OR 5.799), and food-specific serum IgE (OR 3.101) were confirmed as the main variables differentiating the 2 subgroups.
Conclusion: NCWS subjects have a higher frequency of atopic disease, MFH and SRMI when compared to both CD and IBS/FD patients. All these conditions could be considered as an expression of an underlying hypersensitivity milieu characterizing NCWS. In our opinion, this evidence could be of support in the differential diagnosis between NCWS and functional gastrointestinal disorders, especially if inserted into a broader diagnostic panel, including clinical, laboratory and microbiological data, which we hope will be developed as soon as possible through the collaboration of the various international research groups.
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ACCURACY OF A NEW INNOVATIVE COLUMN-FREE MINIATURIZED GAS-MASS SPECTROMETER (GMS) COMPARED TO A CLASSIC GMS TO DIAGNOSE AND MONITORING HELICOBACTER PYLORI INFECTION: A PROSPECTIVE SINGLE BLIND STUDY

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Background and aim: Helicobacter pylori (Hp) is a gram-negative, spiral-shaped microaerophilic bacterium, and its infection is one of the most common among humans, leading to chronic gastritis, peptic ulcer, gastric cancer, and MALT lymphoma. The gold standard for Hp infection diagnosis is the Composite Reference Method (CRM), including the ^{13}C Urea Breath Test (^{13}C-UBT), histological examination, rapid urease test (RUT) on antral biopsy, and culture examination on antral biopsy. Routinely, a mass spectrometer is used to detect and measure $^{13}CO^2$ in breath; however, this device implies very high performing costs. Therefore, new instruments have been considered, such as nondispersive isotope-selective infrared spectrophotometer (NDIRS) and, more recently, column-free portable gas mass spectrometer (MS) equipped with an original nanopore gas sampling system, which possesses unique features. The aim of this study is to compare the sensitivity and specificity of the first diagnosis and post-treatment control of Hp infection between the standard MS and the innovative column-free miniaturized gas MS based on nanotechnology.
Material and methods: Consecutive patients never treated for H. pylori infection and referred to our unit to perform an UGE between April and November 2024 were evaluated for this blind prospective trial. Patients' samples were analysed with both methods and data were compared.
Results: During the period of the study 328 consecutive patients were tested for Hp infection and 92 (28.0%) were positive. The ROC curve indicated 9.1 as best cut-off value. The comparison between the two analysis methods showed a sensitivity of 98.0% (CI95%, 92.0-99.0) and a specificity of 99.0% (CI95%, 97.00-100.0), no statistically significant differences were observed (p value= 0.572).
Conclusions: Our experience highlights the potential for introducing new diagnostic tools that are less demanding in terms of cost and labour, without compromising diagnostic accuracy. To our knowledge, this is the first time that an innovative diagnostic tool proves to be as compact and as reliable, for this reason it deserves to be implemented in clinical practice.

PROGNOSTIC ROLE OF MINI NUTRITIONAL ASSESSMENT IN SEPSIS-RELATED MORTALITY

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Prognostic Role of Mini Nutritional Assessment in Sepsis-Related Mortality, a Retrospective Cohort study
Background: The nutritional status plays a crucial role in the outcomes of critically ill patients, yet its prognostic value in sepsis remains underexplored. The Mini Nutritional Assessment (MNA) is a validated tool for evaluating nutritional status, but its predictive ability in sepsis-related mortality has not been well established. This study aims to assess the prognostic value of MNA in predicting mortality among septic patients and to evaluate its contribution to established prognostic scores.
Methods: A retrospective cohort study was conducted on patients diagnosed with sepsis. The MNA score at admission (MNA-T0) was analysed alongside traditional severity scores, including qSOFA, NEWS, and Apache II, in logistic regression models predicting overall and time-specific mortality (30-day and 90-day). The discriminatory ability of these models was assessed using receiver operating characteristic (ROC) curves.
Results: The logistic regression model incorporating MNA-T0 and qSOFA demonstrate a significant association between nutritional status and mortality (OR=0.847 per unit increase in MNA, p=0.0068). Lower MNA scores were associated with higher mortality risk. The addition of MNA to traditional prognostic scores resulted in enhanced predictive accuracy, as evidenced by an augmented area under the ROC curve (AUC). Analogous findings were observed for 30-day and 90-day mortality predictions, thereby reinforcing the role of MNA as an independent prognostic factor.
Conclusions: The findings indicate that poor nutritional status, as evaluated by MNA-T0, is significantly associated with elevated mortality risk in sepsis patients. The incorporation of MNA into established prognostic models has been demonstrated to enhance their predictive power, suggesting that routine nutritional assessment should be integrated into sepsis management strategies. Further prospective studies are required to confirm these findings and to explore targeted nutritional interventions in sepsis care.
Keywords: Sepsis, Mini Nutritional Assessment, Prognosis, Mortality, qSOFA, Nutritional Status

ATRIAL FIBRILLATION, HEART FAILURE PHENOTYPES AND ALL-CAUSE MORTALITY: INSIGHTS FROM THE NATIONWIDE START REGISTRY

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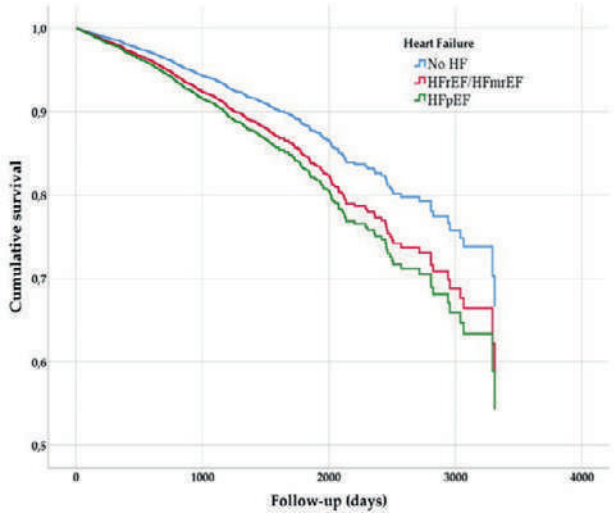
Background: Data on atrial fibrillation (AF) and heart failure (HF), especially with preserved ejection fraction (HFpEF), are scarce. Aim of our study eas to evaluate clinical characteristics of AF patients with HFpEF or reduced/mildly reduced ejection fraction (HFrEF/HFmrEF) and their association with all-cause mortality.
Methods: We included patients with AF on treatment with oral anticoagulant from the nationwide ongoing START registry. Patients were divided into three groups: 1) no HF, 2) HFrEF/HFmrEF (EF ≤50%), and HFpEF (EF >50%). Patients with HF should have had a clinical diagnosis or a history of hospitalization for HF. The association between HF types and all-cause mortality was investigated by Cox proportional hazards regression analysis to estimate hazard ratio (HR) and 95% confidence interval (95%CI) for each factor.
Results: We enrolled 10,369 AF patients on oral anticoagulants. Mean age was 76.4±9.4 years and 45.8% were women. Overall, 2,309 (22.2%) patients had HF (47.4% had HFpEF). During 720±576 days of follow-up (20,747 patients/year), 727 deaths occurred (3.5 per 100 patient-years). Both HFrEF/HFmrEF (HR 1.269, p=0.036) and HFpEF (HR 1.417, p=0.001) were associated with all-cause mortality. HFpEF was associated with mortality in men (HR 1.654, p=0.001) but not in women.
In HFpEF, age ≥75 years (HR 2.247, p=0.003), chronic respiratory disease (HR 2.109, p<0.001), anaemia (HR 1.482, p=0.035), paroxysmal AF (HR 0.528, p=0.012), severe chronic kidney disease with creatinine clearance <30 ml/min (HR 1.791, p=0.018), direct oral anticoagulants (HR 0.575, p=0.005), renin-an-

giotensin-aldosterone inhibitors (HR 0.670, p=0.033) were associated with all-cause mortality.
Conclusion: HFpEF is frequent in AF patients and was associated with an increased mortality, especially in men. Comorbidities and treatments were associated differently with mortality according to HF phenotype.



HFrEF/HFmrEF: Heart failure with reduced/mildly reduced ejection fraction, HFpEF: Heart failure with preserved ejection fraction

DIRECT ORAL ANTICOAGULANTS IN PATIENTS WITH ATRIAL FIBRILLATION AND MODERATE-TO-SEVERE CHRONIC KIDNEY DISEASE: INSIGHTS FROM THE START REGISTRY.

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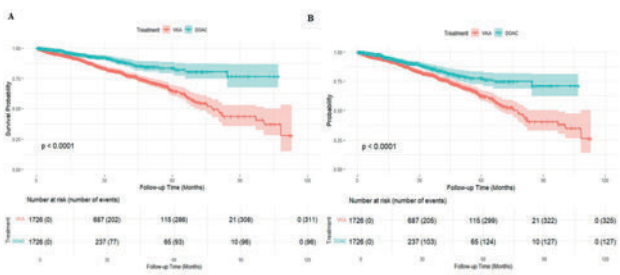
Background: Chronic kidney disease (CKD) and atrial fibrillation (AF) were comorbidities that often coexist, worsening patients' prognosis. Furthermore, vitamin K antagonists (VKAs), commonly used in AF patients with CKD had several side effects on the kidney function. Direct oral anticoagulants (DOACs) are increasingly used also in patients with AF and CKD, but limited evidence exists regarding outcomes in advanced CKD.
Methods: Patients with AF and CKD enrolled in the Italian prospective multicenter START registry were included in the analysis. Patients were divided into 3 groups based on the estimated glomerular filtration rate (eGFR): 1) eGFR 59-46 ml/min/1.73 m², 2) 45-30 ml/min/1.73 m², 3) 29-15 ml/min/1.73 m². The association of DOACs or VKAs use with all-cause mortality and cardiovascular events (CVEs) was assessed using Cox regression and Fine-Gray competing risk models. Propensity Score Matching (PSM) was used to confirm robustness of the analysis.
Results: Among 4,849 patients with AF and CKD, the mean age was 81.5±6.7 years, 57.9% were women, and 55.8% were on DOACs. after PSM, VKA and DOAC groups were balanced for all baseline clinical variables. At Kaplan-Meier curves, DOAC group showed a lower risk of all-cause of death (Log-rank test p<0.001) and CVEs (Log-rank test p<0.001) compared to VKA one (Panel A and B of the figure, respectively)
DOAC (vs VKAs) use was inversely associated with all-cause mortality in group 1 (HR 0.49, 95%CI 0.36-0.67, p<0.001), group 2 (HR 0.42, 95%CI 0.31-0.58, p<0.001) and group 3 (HR 0.20, 95%CI 0.10-0.39, p<0.001). Similar results were obtained for CVEs (HR 0.64, 95%CI 0.49-0.85, p=0.002, for group 1, HR 0.56, 95%CI 0.42-0.75, p<0.001 for group 2, HR 0.31, 95%CI 0.17-0.55, p<0.001, for group 3). No significant differences were observed among DOACs.
Conclusions: The benefit of DOAC therapy over VKAs increases by the severity of CKD. DOACs may be preferred over VKAs across CKD stages in elderly AF patients.

Figure. Kaplan-Meier curve evaluating all-cause mortality (Panel A) and cardiovascular events (Panel B) in patients with atrial fibrillation and chronic kidney disease treated with direct oral anticoagulants or vitamin K antagonist on propensity score-matched cohorts.



ANTICOAGULATION TREATMENT AND MORTALITY RISK IN ELDERLY PATIENTS WITH ATRIAL FIBRILLATION: A SUBGROUP ANALYSIS OF THE NATIONWIDE ITALIAN START REGISTRY

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Background: Anticoagulation may be challenging in very elderly atrial fibrillation (AF) patients due to their pharmacokinetic peculiarities and their frailty.
Objective: To estimate clinical factors associated with direct oral anticoagulants (DOACs) use and the risk of all-cause and cardiovascular (CV) deaths, CV events (CVEs) and any bleeding according to anticoagulants.
Design: Prospective multicentre cohort study
Setting: Patients with AF from the Nationwide ongoing START registry
Partecipants: 4244 patients with AF aged ≥80 years (533 aged ≥90 years)
Exposure: DOACs vs vitamin K antagonist (VKA)
Main Outcomes and Measures: Outcomes were all-cause mortality, CV death and CVEs.Univariable and multivariable Cox proportional hazards regression analysis was used to calculate the adjusted relative hazard ratios (HRs) and 95% confidence interval (95%CI). The number needed to treat (NNT) was calculated at 12 and 24 months.
Results: Mean age was 84.8 years, 54.9% were women. Frailty elements as tendency to falls (Odds ratio [OR] 0.659, p=0.030), living alone (OR 0.735, p=0.027) and lack of familial/social support (OR 0.743, p<0.001) were inversely associated with DOACs use. Conversely, mobility reduction (ie. wheelchair users) associated with DOAC use (OR 1.572, p=0.014).
During a mean follow-up of 685.6±537.7 days, DOAC inversely associated with all-cause mortality (Hazard Ratio [HR] 0.351, p<0.001), CV death (HR 0.379, p<0.001), CVEs (HR 0.459, p<0.001) but not with bleeding (Table 1). At 24 months, the NNT for all-cause death was 10.98, for CV death 40.15, and for CV events 13.38 (Table 2).
In ≥90 years patients, the NNT for all-cause death, CV events and CV death was 4.20, 4.48 and 11.96 at 24 months, respectively.
Conclusions: In conclusion, frailty elements influence the choice of oral anticoagulants. DOACs show a favourable profile especially in the eldest patients with longer follow-up.

Table 1. Clinical characteristics	Total cohort (n: 4,244)	VKA (n: 1,528)	DOAC (n: 2,716)	p-value
Age (Years)	84.8±3.8	84.1±3.2	85.1±4.0	<0.001
Women (%)	2,331 (54.9)	845 (55.3)	1,486 (54.7)	0.712
Paroxysmal AF (%)	1,300 (30.9)	407 (27.4)	893 (32.9)	<0.001
Arterial hypertension (%)	3,572 (84.2)	1,270 (83.1)	2,302 (84.8)	0.160
Diabetes (%)	814 (19.2)	287 (18.8)	527 (19.4)	0.622
Previous CAD (%)	720 (17.0)	316 (20.7)	404 (14.9)	<0.001
Previous cerebrovascular disease (%)	736 (17.3)	257 (16.8)	479 (17.6)	0.500
Obesity* (%)	623 (14.7)	207 (13.5)	416 (15.3)	0.118
Anaemia (%)	1,475 (34.8)	547 (35.8)	928 (34.2)	0.284
Heart failure (%)	1,101 (25.9)	439 (28.7)	662 (24.4)	0.002
Cancer (%)	699 (16.5)	257 (16.8)	442 (16.3)	0.646
Peripheral artery disease (%)	264 (6.2)	119 (7.8)	145 (5.3)	0.002
COPD/OSAS (%)	543 (12.8)	200 (13.1)	343 (12.6)	0.667
CKD** (%)	1000 (23.6)	301 (19.7)	699 (25.8)	<0.001
Alcohol use (%)	201 (4.7)	107 (7.0)	94 (3.5)	<0.001
CHA_2DS_2-VASc (mean)	4.3±1.2	4.4±1.2	4.3±1.2	0.127
HAS-BLED (mean)	2.3±0.7	2.3±0.8	2.2±0.7	0.001
Frailty elements				
Dementia (%)	241 (5.7)	64 (4.2)	177 (6.5)	0.007
Immobilization syndrome (%)	60 (1.4)	13 (0.9)	47 (1.7)	<0.001
Wheelchair users (%)	207 (4.9)	54 (3.5)	153 (5.6)	0.009
Tendency to fall (%)	148 (3.5)	65 (4.3)	83 (3.1)	0.122
Living alone (%)	260 (6.1)	117 (7.7)	143 (5.3)	0.008
Social/familial support (%)	3,059 (72.1)	1,058 (69.2)	2,001 (73.7)	0.001
Therapy				
Type of DOAC (%)				
Apixaban	949 (22.4)	-	949 (34.9)	
Rivaroxaban	645 (15.2)	-	645 (23.7)	
Edoxaban	615 (14.5)	-	615 (22.7)	
Dabigatran	506 (11.9)	-	507 (18.7)	
Concomitant Aspirin (%)	493 (11.6)	219 (14.3)	274 (10.1)	<0.001
Class 1c antiarrhythmics (%)	207 (4.9)	53 (3.5)	154 (5.7)	0.002
Amiodarone (%)	464 (10.9)	178 (11.6)	286 (10.5)	0.262
Lipid lowering therapy (%)	1,351 (31.8)	472 (30.9)	879 (32.4)	0.323
RAAS inhibitors (%)	2,353 (55.4)	832 (54.5)	1,521 (56.0)	0.329
Beta blockers (%)	1,932 (45.5)	834 (54.6)	1,098 (40.4)	<0.001
Calcium channel blockers (%)	972 (22.9)	364 (23.8)	608 (22.4)	0.285
Diuretics (%)	2,021 (47.6)	752 (49.2)	1,269 (46.7)	0.119
Digoxin (%)	427 (10.1)	176 (11.5)	251 (9.2)	0.018
Proton pump inhibitors (%)	1,602 (37.7)	628 (41.1)	974 (35.9)	0.001
Antipsychotic drugs (%)	439 (10.3)	123 (8.0)	316 (11.6)	0.001
Anxiolytic drugs (%)	463 (10.9)	168 (11.0)	295 (10.9)	0.961
Antiepileptic drugs (%)	103 (2.4)	38 (2.5)	65 (2.4)	0.982

Table 2. Association between DOAC use and clinical endpoints

DOAC *(vs VKA)**	Hazard Ratio	95% confidence interval	P-value
All-cause death (n:492)	0.35	0.29-0.43	<0.001
CV death (n: 110)	0.38	0.25-0.57	<0.001
CV events (n: 548)	0.46	0.38-0.55	<0.001
Any bleeding (n: 221)	1.17	0.88-1.56	0.283

**adjusted for each baseline clinical characteristic*

A. Overall population	NNT (12 months)	p-value	NNT (24 months)	p-value
All-cause mortality	23.50	<0.001	10.98	<0.001
CV mortality	81.91	0.002	40.15	<0.001
CV events	26.68	<0.001	13.38	<0.001
B. Patients aged ≥90 years				
All-cause mortality	7.99	0.002	4.20	0.001
CV mortality	51.31	0.163	11.96	0.018
CV events	8.32	0.002	4.48	0.001

ORAL ANTICOAGULANTS AND RISK OF MYOCARDIAL INFARCTION IN PATIENTS WITH ATRIAL FIBRILLATION: A SYSTEMATIC REVIEW AND META-ANALYSIS.

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Background: Atrial fibrillation (AF) require long-term therapy with anticoagulants and had also an increased risk of myocardial infarction (MI). However, there were no data about better choice among direct oral anticoagulants (DOACs) and vitamin K antagonist (VKA) in these patients. The aim of our study is to analyse the efficacy of each anticoagulant, in patients with AF alone or undergoing concomitant percutaneous coronary intervention (PCI)
Methods: Systematic review and network meta-analysis including AF patients on anticoagulants. Endpoints were major adverse cardiovascular event (MACE) and myocardial infarction (MI). Rankograms and SUCRA were also performed.
Results: 44 studies were included (Table 1) in the network meta-analysis including 1.794.583 patients, (85.3% on DOACs and 40.6% females) with an average age between 63.2 and 88.6 years.
About MACE, in AF patients, apixaban, dabigatran, edoxaban and rivaroxaban were associated with lower risk of MI compared to VKA (hazard ratio [HR] 0.73, 9%% confidence interval [95%CI] 0.10 – 0.91, HR 0.83, 95%CI 0.70-1.00, HR 0.87, 95%CI 0.68-0.99, and HR 0.85, 95%CI 0.73-1.00, respectively). SUCRA showed dabigatran and apixaban as first choice in patients with AF+PCI and AF alone, respectively.
Apixaban, dabigatran, edoxaban and rivaroxaban (HR 0.83, 95%CI 0.72 – 0.96, HR 0.84, 95%CI 0.74-0.96), HR 0.68, 95%CI 0.53-0.86 and HR 0.83, 95%CI 0.73-0.94, respectively) were associated with a lower risk of MI compared to VKA. Analysis of SUCRA showed edoxaban as first choice.
Conclusions: DOACs were associated with lower risk of MI compared to warfarin. Among DOACs, edoxaban and apixaban seems to be the first choice in these patients.
PROSPERO registration number. CRD42023407778

Year	First Author	Design	Clinical Setting	Total Cohort	DOAC (%)	Female (%)	Age (mean)	CHA2DS 2-VASC	HAS BLED
2013	Ortogiano (ENGAGE-AF TIMI 48)	PostH	NVAF	21105	66.7	38.1	72.0		
2021	A. Briasoulis	R	NVAF	28011	52.1	10.5	67.1		
2021	R. D. Lopes	R	NVAF + CAD/PAD	155038	94.0	45.9	78.7	4.3	3.6
2021	A. Elis	R	NVAF	252	38.5	46.8	78.7	4.9	2.5
2021	E. Crocetti	R	NVAF	8543	87.1	48.7	77.0	4.4	
2022	P. Liu	R	NVAF	1246	63.2	41.3	71.0		
2022	G. Y. H. Lip (GLORIA-AF)	PostH	NVAF	12359	100.0	45.2	71.7	3.2	1.3
2022	L. Boivin-Proulx	R	NVAF	1656	24.3	55.8	72.6	2.6	3.4
2022	L. Boivin-Proulx	R	NVAF	1792	30.1	56.1	74.2	2.7	3.4
2022	Q. Yu	R	NVAF + lower-extremity revascularisation	319	55.8	47.0	80.0	5.1	2.3
2022	A. Jaksa	R	NVAF	5022	55.8	36.9	77.0	3.4	
2023	Y. Talmor-Barkan	R	NVAF	56553	100.0	51.3	77.3	4.2	3.0
2021	A. B. Jonasson	R	NVAF	4670	100.0	40.4	72.0	2.6	
2023	M. Oymonyez	R	NVAF	254478	75.8	47.4	75.0	3.5	2.4
2021	R. D. Lopes	R	NVAF + CAD/PAD	155038	57.2	45.9	78.7	4.3	3.6
2020	Chan	R	NVAF and diabetes	26779	78.3	46.3	74.5	4.4	3.1
2019	Pratt	R	NVAF	4836	71.8	48.0	81.9	2.2	
2019	Amin	R	NVAF	198171	58.9	50.1	78.2	4.6	3.3
2019	Russo	P	NVAF	899	43.3	43.0	71.2	3.8	2.7
2018	Yu	R	NVAF	11712	50.0	42.3	70.5	4.5	
2018	Lun Lai	R	NVAF	4722	68.3	52.0	88.6	3.8	
2018	Ji-Young Lee	R	NVAF	31739	72.0	46.3	73.8	2.3	
2018	Barnett (ROCKET AF)	PostH	NVAF	14236	49.9	40.0	73.0	3.5	
2020	Coleman	R	NVAF + PAD	8303	39.2	36.0	74.0	3.0	2.0
2019	Baker	R	NVAF	24646	43.3	36.5	70.0	4.0	
2018	Själander	R	NVAF	64382	42.2	41.4	74.0	3.1	
2018	Briasoulis	R	NVAF	85596	32.5	53.0	77.0	4.4	1.7
2018	Han-Pu Lee	R	NVAF	42000	61.9	48.0	78.0	4.0	3.0
2016	Gibson (PIONER-AF)	R	NVAF + PCI	2124	66.6	25.5	70.1	3.8	3.0
2018	Mueller	R	NVAF	14577	100.0	45.3	74.0	2.9	2.0
2020	Vranckx (ENTRUST-AF PCI trial)	RCT	NVAF + PCI	1506	49.9	25.5	69.7	4.0	3.0
2019	Oldgren (RE-DUAL PCI trial)	RCT	NVAF + PCI	2725	64.0	24.0	70.8	3.6	2.7
2012	Hohnloser (RE-LY)	PostH	NVAF	18113	66.8	36.4	71.5		
2013	Bahit (ARISTOTLE)	PostH	NVAF	18184	50.2	35.2	70.0		
2014	Larsen	R	NVAF	13914	36.0	42.5	70.3		
2015	Graham	R	NVAF	134414	50.0	51.5			
2015	Lauffenburger	R	NVAF	64935	32.5	39.9	69.9	2.7	
2015	Seeger - MARKETSCAN	R	NVAF	31058	50.0	37.8	68.5	3.1	2.2
2015	Seeger - Clinformatics	R	NVAF	7320	50.0	30.2	63.2	2.8	2.2
2015	Chan	R	NVAF - Asian	19853	50.1	42.0	75.5	4.1	2.6
2015	Villines	R	NVAF	25586	50.0	41.2	73.9	3.9	3.4

HEPATIC INJURY RISK ASSESSMENT IN ELDERLY PATIENTS WITH ATRIAL FIBRILLATION: ANALYSIS FROM THE NATIONWIDE ITALIAN START REGISTRY.

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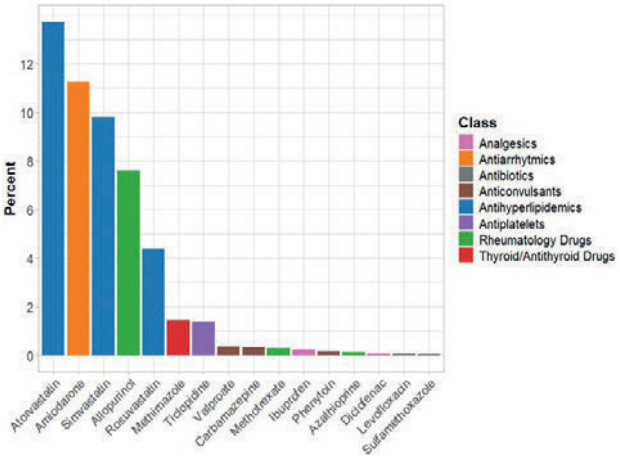
Background: Atrial fibrillation (AF) had an increasing risk of drug-drug interactions and hepatotoxicity due to polipharmacy. We analyzed the use of potentially hepatotoxic drugs in anticoagulated AF patients.
Methods: Using the LiverTox classification, we categorized AF patients from the START registry based on LiverTox A drug use (high hepatotoxicity risk). Logistic regression estimated odds ratios (ORs) and 95% confidence intervals (95%CIs) for factors associated with these drugs, and their impact on liver function tests (LFTs).
Results: Median age was 81 years (46% women). Among 8,215 AF patients, 40,355 distinct drugs were prescribed, with a median of 5 per patient (IQR 3-7). A total of 3,416 (41.6%) received at least one LiverTox A drug; these patients were more often male, overweight, smokers, hypertensive, diabetic, or had prior cardiovascular/cerebrovascular events. They were also more likely to be on polypharmacy (74% taking ≥5 drugs, with 8.4% taking ≥10 drugs) and more frequently used LiverTox A [HD] or B drugs. Statins, amiodarone, and allopurinol were the most prescribed LiverTox A drugs (Figure 1), both overall and across all cardiovascular subgroups. In multivariable analysis, among

LiverTox A drugs, amiodarone (OR 1.61, 95%CI 1.29–2.00) and methimazole (OR 1.83, 95%CI 1.04–3.03) were associated with elevated LFTs. Other frequently prescribed drugs—warfarin, furosemide, ramipril, lansoprazole, and canrenone—were also associated with increased LFTs. Direct oral anticoagulants (DOACs) had a lower risk of LFT elevation than warfarin after adjustment for confounders.
Conclusion: Many AF patients are treated with drugs at high risk of hepatotoxicity, an accurate choice of drugs could reduce hepatotoxicity risk.



CONTINUOUS GLUCOSE MONITORING (CGM) AND PSYCHOLOGICAL ASSESSMENT IN ADULTS WITH INHERITED METABOLIC DISORDERS (IMDS) PRONE TO HYPOGLYCEMIA

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Background: Glycogen storage diseases (GSDs) and congenital hyperinsulinism (CH) are inborn metabolic diseases (IMDs) that predispose individuals to hypoglycemia, potentially affecting cognitive function, psychological well-being, sleep quality, and quality of life. Continuous glucose monitoring (CGM) allows for a detailed evaluation of glycemic patterns and may uncover associations with neurocognitive and psychological outcomes, especially in IMDs prone to hypoglycemia, where data remain scarce.
Methods: A cross-sectional study was conducted at the Division of Metabolic Diseases, University Hospital of Padua. CGM data (Freestyle Libre 2, Abbott) were analyzed over 24 hours and during nighttime (00:00–07:00), assessing: Time in Range (TIR: 70–140 mg/dL), Time Below Range 1 (TBR1: <70 mg/dL), Time Below Range 2 (TBR2: <54 mg/dL), and Time Above Range (TAR: >140 mg/dL), based on disease-specific thresholds. Hypoglycemia-related awareness and fear were investigated using the Clarke Hypoglycemia Awareness Questionnaire and the Hypoglycemia Fear Survey (HFS-Behavior and HFS-Worry subscales). Neurocognitive and psychological assessments included the Montreal Cognitive Assessment (MoCA), Frontal Assessment Battery (FAB), Generalized Anxiety Disorder-7 (GAD-7), Patient Health Questionnaire-9 (PHQ-9), Pittsburgh Sleep Quality Index (PSQI), and the 12-item Short Form Health Survey (SF-12).
Results: Eleven adults were enrolled (9 GSDIa, 1 GSDXI, 1 CH; mean age 35.6 ± 8.8 years).
CGM results showed: TIR = 83.3 ± 15.1% (night = 83.8 ± 21.2%), TBR1 = 6.6 ± 10.2% (night = 9.3 ± 17.4%), TBR2 = 0.4 ± 1.0% (night = 0.9 ± 1.7%), TAR = 9.9 ± 12.6% (night = 6.0 ± 14.1%), mean glycemia over 24h = 103.4 ± 22.6 mg/dL (night = 96.7 ± 17.5 mg/dL).
The average MoCA score was within the normal range (equivalent score = 3.55 ± 0.7/4). FAB scores indicated mild impairment (equivalent score = 2.09 ± 1.3/4), particularly in executive functions (4.55 ± 0.8/6). A higher FAB total adapted score (14.7 ± 2.0/18) was correlated with higher mean glycemia over 24h ($p < 0.05$).
GAD-7 (8.82 ± 5.1) and PHQ-9 (7.73 ± 4.8) scores indicated mild anxiety and depressive symptoms. PSQI scores (8.09 ± 3.8) suggested poor sleep quality. SF-12 scores (PCS = 45.6 ± 7.8; MCS = 43.4 ± 12.8) were below the Italian population average.
HFS-Worry scores (16.4 ± 13.3) were negatively associated with TAR over 24h, TAR at night, and mean glycemia over 24h ($p < 0.05$). HFS-Behavior scores (8.0 ± 3.5) were positively associated with nocturnal TBR1 ($p < 0.05$). Clarke scores indicated preserved hypoglycemia awareness (2.8 ± 1.3), with higher scores correlating with increased TAR over 24h ($p < 0.05$).
Discussion: In this population, mild anxiety and depressive symptoms were present alongside generally preserved cognitive performance. Better frontal function was associated with higher mean glycemia over 24h, suggesting that more stable glucose levels may support executive functioning. Nocturnal hypoglycemia was linked to increased behavioral responses, possibly reflecting heightened vigilance or reactive management during nighttime glucose dips. The correlation between impaired hypoglycemia awareness and increased TAR may reflect a dysfunctional long-term compensatory strategy. These findings underscore the importance of an integrated assessment in adults with IMDs prone to hypoglycemia, combining CGM data with neuropsychological and health evaluations.

PASH SYNDROME: WHEN HIDRADENITIS SUPPURATIVA AND PYODERMA GANGRENOSUM MEET

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Introduction: Pyoderma gangrenosum (PG) and **hidradenitis suppurativa (HS)** are both inflammatory skin conditions classified as **neutrophilic hypodermic dermatoses**. These conditions share connections with other autoinflammatory disorders driven by immune responses. Their pathogenesis is complex, rooted in significant imbalances within the innate and adaptive immune systems, especially elevated levels of **tumor necrosis factor-α (TNF-α)**, **interleukin (IL)-1**, **IL-8**, **IL-17**, and **IL-23**.
Although the association between PG and HS is rare, it is increasingly recognized in scientific literature. This clinical case describes a patient with chronic HS complicated by ulcerative lesions compatible with PG, emphasizing the diagnostic and therapeutic challenges.
PASH Syndrome: PASH syndrome is a rare autoinflammatory syndrome (AIS) characterized by a combination of **pyoderma gangrenosum (PG)**, **acne conglobata**, and **hidradenitis suppurativa (HS)**. While no standard treatment has been established, clinical cases have reported promising results with systemic antibiotics, immunosuppressants, and biological therapies.
Clinical Case
Patient
Medical History
Clinical Presentation
Diagnostic Tests
Blood tests
Skin biopsy
Cultures and serological tests
Diagnosis: Pyoderma gangrenosum associated with hidradenitis suppurativa.
Treatment and Follow-Up: The patient was initially treated with **prednisone (1 mg/kg)**, followed by the introduction of a TNF-α inhibitor (**adalimumab**). Progressive improvement in ulcers and inflammatory lesions associated with HS was observed. After 6 months of follow-up, partial remission was achieved, with significant reduction in pain and ulcerative recurrences.
Discussion: The association between PG and HS represents a complex diagnostic challenge, due to the potential clinical overlap with cutaneous infections or vasculitis. Optimal treatment requires a multidisciplinary approach involving **dermatologists**, **rheumatologists**, and **surgeons**. Biological agents, particularly TNF-α inhibitors, offer a promising therapeutic option in resistant cases.
Conclusions: This clinical case emphasizes the importance of considering **pyoderma gangrenosum** in patients with severe **hidradenitis suppurativa**, especially in the presence of atypical ulcers. Prompt treatment with immunosuppressants can significantly improve the prognosis and quality of life of affected patients.
Bibliografia: Pyoderma gangrenosum, acne, and hidradenitis suppurativa (PASH) syndrome: A case report and review of the literature M. Braun-Falco, M. Kovnerystyy, M. Lohse, G. Ruzicka Journal of the American Academy of Dermatology, 2011PASH syndrome: a novel surgical approach A. S. Santos, M. M. Santos, A. P. Santos, et al. Anais Brasileiros de Dermatologia, 2017Hidradenitis Suppurativa (HS) Acne InversaNational Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

FIB-4 AS A PREDICTOR OF CLINICAL OUTCOMES IN NON-CRITICAL INPATIENTS

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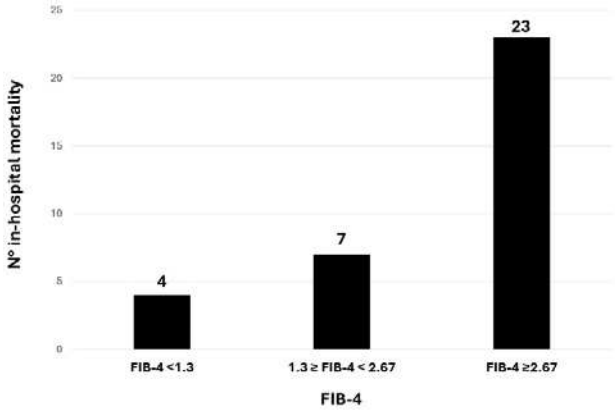
Introduction and Aim: The fibrosis-4 index (FIB-4), a non-invasive liver fibrosis score, is widely used for assessing liver fibrosis in patients with chronic liver diseases. However, its role in predicting clinical outcomes remains underexplored, particularly in non-critical hospital settings. This study aims to evaluate the association between the FIB-4 score and clinical features and outcomes in multimorbid elderly patients hospitalised in the Internal Medicine department enrolled in the Clinical Outcomes in HOspitalized patients Receiving Treatment at San Andrea Hospital (COHORTS) study.
Methods: A total of 217 individuals (113 men, 104 women), aged 65 or older, admitted to the internal medicine department were included in the study and divided into three groups according to FIB-4 cut-off: lowest risk of fibrosis (<1.3); moderate risk of fibrosis (≥1.3 to < 2.67); high risk of fibrosis (≥2.67). The FIB-4 index was calculated by age, Aspartate Aminotransferase (AST), platelets count and Alanine Aminotransferase (ALT). Classical Charlson Comorbidity Index was calculated as index of multimorbidity. The association between FIB-4 index and clinical variables was analysed using univariate analysis. A logistic regression model was performed to verify the association between liver fibrosis and mortality.
Results: Patients with high risk of liver fibrosis were more likely to be male, older, and exhibited higher AST and acid uric levels and lower platelet counts and estimated Glomerular Filtration Rate (eGFR) compared to those in the lowest risk category. Notably, patients with high risk of liver fibrosis had a 3.2-fold increased risk of in-hospital death compared to those with lower risk (OR 3.2, 95% CI 1.01 – 10.88), independently of confounders including Charlson Comorbidity Index, sex and age.
Conclusion: The FIB-4 index may serve as a valuable predictor of adverse outcomes in hospitalized elderly multimorbid patients. Those at higher risk of liver fibrosis are more likely to experience in-hospital mortality. Further studies are needed to better understand the role of these scores as predictors of clinical outcomes in hospital settings.



ASSOCIATION BETWEEN IGF-1 AND CLINICAL FEATURES AND OUTCOMES IN HOSPITALISED PATIENTS

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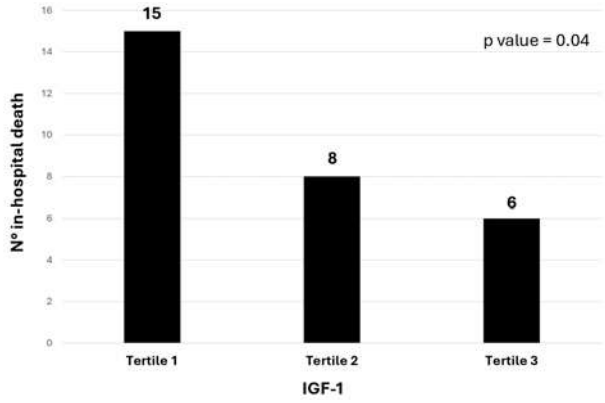
Introduction and Aim: Aging is a complex physiological process that involves several changes in clinical parameters and physiological responses. Among these factors, Insulin-like Growth Factor 1 (IGF-1) plays a crucial role in regulating metabolism and maintaining muscle mass. This study explored the correlation of IGF-1 with several clinical features and outcomes in multimorbid elderly patients hospitalized in the Internal Medicine department enrolled in the Clinical Outcomes in Hospitalized Patients Receiving Treatment at San Andrea Hospital (COHORTS) study.
Methods: The study enrolled 150 individuals (75 men, 75 women) aged 65 or older admitted to the Internal Medicine department. The population was categorized into three groups according to IGF-1 tertile levels. Classical Charlson Comorbidity Index was calculated as an index of multimorbidity. Univariate analyses and a logistic regression model analysed the association between IGF-1 and clinical variables and outcomes.
Results: Patients in the lower tertile of IGF-1 were more likely to be female and older. They exhibited elevated levels of C-reactive protein (CRP) and reduced levels of albumin compared to those in the highest tertile. Furthermore, in the lower tertiles of IGF-1, in-hospital mortality was higher than in the third tertile (p=0.04). Univariate analysis revealed an inverse association between IGF-1 levels and the length of recovery (p=0.03). Notably, patients in the lower IGF-1 tertiles had a 3.1-fold increased risk of mortality (OR 3.1, 95%CI 1.1-8.9) compared to those in the highest tertile, independently of the Charlson Comorbidity Index.
Conclusion: IGF-1 could serve as a relevant biological marker for predicting recovery time and adverse outcomes in elderly multimorbid patients hospitalized. Further research is required to elucidate better the therapeutic potential of IGF-1 in pathological aging processes.



THE CHALLENGE OF THE ACTIVITIES WITHIN A RESIDENTIAL CARE HOME (RSA)

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In the twenty-first century, nursing homes have become a standard form of care for the most aged and incapacitated persons. Nearly 6 percent of older adults are sheltered in residential facilities that provide a wide range of care. Yet such institutions have not always existed; rather, their history and development reflect relatively recent demographic and political realities that shape the experience of growing old. Before the nineteenth century, no age-restricted institutions existed for long-term care.
The major expansion in the charitable provision of housing for the elderly began in northern Europe in the mid fourteenth century and even at that early date has no real parallel further south. There are examples in Italy and Spain where powerful individuals used their money to found or enhance monasteries - , Lodovico Sforza's Certosa at Pavia.
The main feature of a RSA, which distinguished itself from other types of structures, is the fact of being an out-patient facility reserved for people who are not self-sufficient. Precisely for this reason, given the delicate conditions of the people hosted, the legislation provides for a series of constraints to be respected, related to the staff who must be present in the facility, the quality standards and the optimal size of the facility .There are also constraints relative to the location and the absence of architectural barriers.
For at least four decades RSA facilities have been profoundly changing compared to the role they had when they were first created: this has happened as a response to the demographic and clinical evolution of the elderly, more numerous and increasingly suffering from multiple comorbidity and complex chronicity.
Doctors, nurses, physiotherapists, educators, occupational therapists, have their own peculiarity and therefore need specific training paths.
Let's start from a simple and incontrovertible concept: severely disabled elderly people, both from a cognitive and behavioral point of view and from a motor and functional point of view, do not always live better at home. This concept is undeniable, for several reasons: there are no "miraculous" drugs that solve problems (for example behavioral disorders in dementia patients) and it is therefore necessary to have specific knowledge and skills to care for these patients; in most cases today's families are not able to offer good continuous assistance, 24 hours a day; the network for home care services is absolutely inadequate to give concrete answers to this type of patients and their families; home care services makes use of a network of caregivers, with little knowledge of the services and often "elusive", whose training is questionable. We know from epidemiological data that in the future we will have a very remarkable growth of the elderly with less and less family support and more and more complex clinical problems. Therefore, the organization of well-structured training courses can no longer be postponed, learning how to take care of both fragile and lonely elderly people on the territory as well as elderly with serious diseases needing assistance in Residential Care Homes.
.We can't procrastinate anymore, we need to create a network of services suitable for the care of the elderly, with a graduality of approaches and services proportionate to the needs, carried out by operators who have followed specific training paths
The RSA in Italy manage host/patients with increasingly critical conditions where clinical complexity is one of the components of the fragility of the elderly. In 2005 the average stay of guests in RSA was 2.7 years and the high annual turnover of beds, about 40% mainly caused by mortality, indicates that people arrive in these Facilities from homes and hospitals in conditions of increasing severity and clinical instability. This situation requires to allocate more and more health resources in terms of medical and nursing presence and competence.
The SOSIA system (Observation Card of Intermediate Assistance), used in Lombardy to account for the costs of care for each guest in the RSA facility, uses as a criterion for the detection of the commitment of human and technological resources the one of clinical care complexity of each guest, measured as disability in ADL cognitive deficit and degree of comorbidity. On the other hand, the clinical instability present in many guests is not providing margins of predictability and programmino.This should be a challenge for the physicians, nurses , physiotherapists that are managing these peculiar patients and a need of updated organization and medical knowdledge is often required.

UNMASKING HYPEREOSINOPHIA: WHEN THE TRUTH IS HIDDEN (BEYOND STEROIDS)

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Case description and methods: We report the case of a male 83-year-old Caucasian patient with a complex medical history characterized by longstanding eosinophilia, chronic rhinosinusitis with nasal polyposis, and bronchial asthma, who recently developed diffuse pruritic eczema. In the months preceding hospital evaluation, the patient experienced widespread pruritic skin eruptions in the form of erythematous macules and patches, prompting his admission to the Immunology and Allergology outpatient clinic. His clinical history was remarkable for hypertension, autoimmune thyroiditis, hypercholesterolemia, previous ocular vascular events, benign prostatic hyperplasia, and glaucoma. Approximately 10 years prior to immunological evaluation, the patient was diagnosed with chronic rhinosinusitis with nasal polyposis - requiring functional endoscopic sinus surgery with rapid recurrence - and bronchial asthma. Serial complete blood tests over the past 10 years documented persistent elevations in both absolute and relative eosinophil counts, with values fluctuating between 200 cells/μL and 1110 cells/μL under steroid therapy (monthly intramuscular triamcinolone and/or oral methylprednisolone). In the absence of steroid therapy, eosinophil counts markedly increased (exceeding 1500 cells/μL on at least three separate occasions, at least 4 weeks apart), raising clinical suspicion for an underlying hypereosinophilic process.
The patient was subsequently admitted to the Immunology and Allergology Day Hospital, where an extensive diagnostic workup was conducted, including:
Clinical Evaluation:
Laboratory Workup:
Imaging Workup:
The workup excluded the aforementioned causes, while a skin biopsy from an affected lesion on the left thigh revealed a superficial dermal lymphomonocytic inflammatory infiltrate with a discrete eosinophilic component predominantly in a perivascular distribution, and intercellular edema in the basal epidermal layer with minimal intraepidermal exocytosis. These morphological findings excluded a cutaneous lymphoma and supported the diagnosis of an eosinophilic dermatitis with features of associated vasculitis.
Conclusion: The constellation of persistent eosinophilia, a history of asthma and sinusitis with polyposis, and cutaneous manifestations with histologic evidence of eosinophil-rich inflammation and vasculitis favored a diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA). Based on these findings, targeted therapy with subcutaneous mepolizumab 300 mg every 4 weeks was initiated alongside a structured corticosteroid tapering regimen. This case underscores the diagnostic challenges inherent in EGPA, particularly when steroid therapy modulates clinical manifestations, thereby obscuring the underlying systemic eosinophilic process. Notably, prolonged steroid use delayed the definitive diagnosis by over 10 years and adversely affected the patient's overall health.

PROGNOSIS OF NONVARICEAL UPPER GASTROINTESTINAL BLEEDING DURING ANTIPLATELET AND ANTICOAGULANT THERAPY

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Background: Upper gastrointestinal bleeding (UGIB) is the most common gastrointestinal pathology necessitating hospitalization. It affects more and more the elderly and frail. Anticoagulant and antiplatelet therapies are recognized risk factors for UGIB. [1] However, evidence regarding prognostic factors in UGIB occurring during these therapies is scarce. [2] We aim to assess short-term mortality and prognostic factors in patients with nonvariceal UGIB on anticoagulant and antiplatelet therapy.
Methods: We conducted a retrospective monocentric cohort study. All patients admitted to Santa Croce e Carle Hospital in Cuneo for nonvariceal upper gastrointestinal bleeding (NVUGIB), from 2021 to 2024, were enrolled. Cases were divided into 4 gropus: 1. patients under antiplatelet therapy, 2. patients under anticoagulant therapy, 3. patients under both ("DUAL" therapy), 4. controls. We collected demographic, anamnestic, clinical, laboratoristic and instrumental variables, and assessed comorbidity status via the Charlson Comorbidity Index (CCI). The outcome was 30-days mortality. We performed univariate and multivariable analyses to identify prognostic factors.
Results:

	Totale n = 321	Antiaggregati n = 80 25%	Anticoagulati n = 61 19%	DUAL n = 16 5%	Controlli n = 164 51%
M	216 (67%)	56 (70%)	42 (68%)	9 (56%)	109 (66%)
Età	71 ± 14	75 ± 9	78 ± 9	79 ± 10	66 ± 16
CCI	4,3 ± 2	4,8 ± 1	5,4 ± 2	5,9 ± 2	3,4 ± 2
Neoplasia	48 (14%)	8 (10%)	12 (19%)	3 (18%)	25 (15%)
FANS	46 (33%)	5 (12%)	5 (26%)	2 (20%)	34 (49%)
PPI	92 (28%)	32 (40%)	13 (21%)	9 (56%)	38 (55%)
ICU	105 (32%)	25 (31%)	26 (43%)	4 (25%)	50 (30%)
LOS	12 ± 15	11 ± 15	14 ± 12	9 ± 6	12 ± 17
Ulcera peptica	225 (70%)	55 (68%)	37 (60%)	6 (37%)	127 (77%)
Sangue vivo	85 (26%)	23 (28%)	18 (29%)	4 (25%)	40 (24%)
Emostasi endoscopica	164 (51%)	41 (51%)	33 (54%)	7 (43%)	83 (50%)
≥ 2 U.E.C.	175 (54%)	44 (55%)	38 (62%)	8 (50%)	85 (52%)
Decesso 30 gg	30 (9%)	4 (5%)	12 (19%)	1 (6%)	13 (8%)

321 patients were included (mean age 71 years ± 14, M:F ratio = 2,1:1) (Tab.1). 25% of them were under antiplatelet therapy when the bleeding occurred, 19% took anticoagulants and 51% neither. Antiaggregated and anticoagulated patients were older and more comorbid than controls (mean age respectively 75 ± 9 and 78 ± 9 versus 66 ± 16; mean CCI score 4,8 ± 2 and 5,4 ± 2 versus 3,4 ± 2). The rate of NSAIDS-related bleeding was higher in controls (49%) then in antiaggregated (12%) and anticoagulated patients (26%). Besides, 10% of the antiplatelet group, 19% of the anticoagulated group and 15% of controls were neoplastic patients. During hospital stay, intensive care was needed for 31% of antiaggregated patients, 43% of anticoagulated patients and 30% of controls. Two-thirds of the patients were diagnosed with peptic ulcers. We did not observe differences in rates of an effective endoscopic hemostasis, which were about 50% for each group. Likewise, indicators of clinical severity, such as number of red blood cells units transfused, cardiac frequency at admission and visualization of bright red blood at endoscopy, were equally represented in each group. 30-days mortality was higher in anticoagulated patients (19%) than in patients on antiplatelet therapy (5%) and controls (8%, p<0.01).

Variabile	OR	95% CI
Età	1.05	1.00 - 1.11
GFR	0.97	0.96 - 0.99
Tumore attivo	5.24	1.83 - 14.98
FC	1.03	1.01 - 1.06
Sangue	2.38	0.96 - 5.95

In logistic regression analyses, after correction for confounding factors, neither antithrombotic therapy nor endoscopic hemostasis were associated with the outcome, however age and comorbidities often were. Two prognostic models were explored, the first analysed individually the impact of outcome-related comorbidities, while the second used CCI as comorbidity indicator (Tab.2,3). In the first model, age (OR:1.05; 95% CI:1.00-1.11), glomerular filtration rate (OR:0.97; 95%CI:0.96-0.99), active cancer (OR:5.24; 95%CI:1.83-14.98), cardiac frequency (OR:1.03; 95%CI:1.01-1.06) and blood (OR:2.38; 95%CI: 0.95-5.96) were found to be 30-day mortality predictors for patients who were affected by NVUGIB under antithrombotic therapy (LR=37). In the second model, CCI (OR:1.47, 95% CI:1.22-1.77), cardiac frequency (OR 1.02 95% CI:1.00-1.05) and blood (OR 2.35, 95% CI:0.95-5.83) were negative prognostic factor, while gastrolesive medications (antiplatelet and NSAIDS) were protective prognostic factors with OR: 0.35 (95% CI:0.12-1.01) (LR=34).

Variabile	OR	95% CI
CCI	1.47	1.22 – 1.77
FC	1.02	1.00 – 1.05
Sangue	2.35	0.95 – 5.83
Antiaggregante e/o FANS	0.35	0.12 – 1.01

Conclusion: Anticoagulant and antiplatelet therapy are not associated with higher odds of death in patients experiencing NVUGIB. However, anticoagulated patients have an elevated 30-days death rate of 19% when NVUGIB occurrs. Comorbidity and active cancer are negative prognostic factors. Therefore, prescriptions of antithrombotic therapies should be carefully evaluated in multimorbid, neoplastic and elderly patients, who may benefit from lower doses of antithrombotic therapies and choice of medications associated with a lower risk of bleeding from the gastrointestinal tract [3].

EARLY CARDIAC ABNORMALITIES DETECTED BY ADVANCE ECHOCARDIOGRAPHY PARAMETERS IN ADOLESCENTS WITH ANOREXIA NERVOSA

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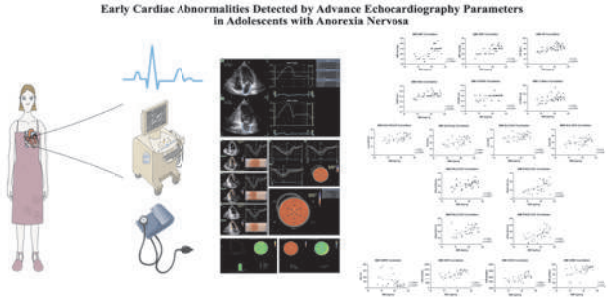
Patients diagnosed with anorexia nervosa (AN) have an increased risk of cardiac anomalies, including pericardial effusion and myocardial dysfunction. Standard ultrasound methods reveal relatively preserved systolic and diastolic functions. However, novel echocardiography parameters, utilizing speckle tracking echocardiography (STE), which can detect subtle and early alterations in left ventricular (LV) and left atrial (LA) function, are underutilized in AN patients. We assessed the cardiac function evaluating LV and LA strains, as well as myocardial work (MW), and hypothesized possible alterations. Sixteen patients (mean age 20.1±5.6y; all women) with AN diagnosed with DSM-5 diagnostic criteria and sixteen control patients (mean age 22.8±5.9y; all women) were enrolled and underwent a transthoracic Doppler echocardiography. Diastolic and systolic function was investigated using standard (PW and TDI Doppler and cardiac chamber quantification) and advanced parameters (LV and LA strain and LV MW). We evaluated Constructive MW (CMW), MW index (MWI), MW efficiency (MWE), and wasted MW (WMW). Echocardiography revealed a structurally normal heart in all patients. Pericardial effusion was observed in 6 (37.5%) of AN patients. Interestingly, AN patients had a statistically significant difference in both atrial and ventricular strain as well as MW parameters except for MWE, which wasn't statistically significant for a small margine. This observed trend in patients with anorexia nervosa (AN), not present in the control group, strongly supports early detection of myocardial dysfunction in this population. These parameters can assist in identifying patients at a high risk of cardiac dysfunction, warranting closer follow-up.



UNRAVELING THE RISK FACTORS FOR TYPE II DIABETES IN SEVERE OBESE PATIENTS WITH INDICATION FOR BARIATRIC SURGERY: RETROSPECTIVE ANALYSIS

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Questo studio indaga i fattori di rischio per il diabete mellito di tipo II (T2DM) in pazienti gravemente obesi sottoposti a valutazione per chirurgia bariatrica. Abbiamo condotto un'analisi retrospettiva di 734 individui, valutando le associazioni tra T2DM e variabili clinico-demografiche tra cui età, sesso, ipertensione, dislipidemia, abitudine al fumo e indice di massa corporea (BMI). La regressione logistica e il test esatto di Fisher sono stati utilizzati per identificare i predittori significativi.
La coorte aveva un'età media di 39 anni (DS = 11,5) e un BMI medio di 41,92 kg/m² (DS = 5,16). La prevalenza di T2DM era del 9,5%, con tassi più elevati

tra i pazienti con ipertensione, dislipidemia e anamnesi di fumo. Il sesso non ha mostrato alcuna associazione significativa con il T2DM (p = 0,4818). Al contrario, ipertensione (p = 0,0098; OR = 2,344), dislipidemia (p = 0,0009; OR = 2,467) e fumo (p = 0,00097; OR = 2,367) erano significativamente più frequenti nei pazienti diabetici.
La regressione logistica multivariata, raffinata secondo il criterio informativo di Akaike (AIC), ha identificato età (OR = 1,0245), ipertensione (OR = 1,9083), dislipidemia (OR = 2,0851) e fumo (OR = 2,259) come fattori predittivi indipendenti del diabete di tipo 2. Il modello ha dimostrato un'eccellente sensibilità (0,98) ma una bassa specificità (0,116), con un elevato valore predittivo negativo (0,987), a supporto del suo utilizzo nell'esclusione del diabete di tipo 2 tra i soggetti a basso rischio.
I nostri risultati sottolineano la natura multifattoriale del diabete di tipo 2 nell'obesità grave. Fattori modificabili come fumo, ipertensione e dislipidemia offrono obiettivi concreti per un intervento precoce. Una stratificazione completa del rischio può migliorare la valutazione preoperatoria e orientare le strategie preventive nelle popolazioni obese ad alto rischio.

Punteggio di Rischio Clinico per la valutazione del rischio di DM di tipo II nei pazienti Obesi

Il modello di regressione logistica può consentire di assegnare la probabilità di presenza di DM di tipo 2 in funzione del valore di predittori statisticamente significativi (Fumo, Età, Dislipidemia, Ipertensione) utilizzando la seguente equazione per calcolare un punteggio clinico:

$$y = a_0 + a_1F + a_2E + a_3D + a_4I$$

e la funzione logistica standard per valutare la probabilità di accadimento del diabete melito di tipo 2:

$$P(T2DM|F,E,D,I) = p = \frac{1}{1+e^{-y}}$$

dove:

- F: Fumatori, fattore binario. codificato come Vero=1 e Falso=0
- E: Età in anni, codificata come valore intero
- D: Dislipidemia, fattore binario, codificato come Vero=1 e Falso=0
- I: Ipertensione, fattore binario, codificato come Vero=1 e Falso=0

e

Parametro	Valore	Errore standard	p-value
a_0	-4.37	0.56	$< 10^{-6}$
a_1	0.815	0.26	0.0023
a_2	0.0242	0.012	0.0484
a_3	0.735	0.285	0.0099
a_4	0.646	0.27	0.0185

Considerando l'intervallo della variabile "Età", da 16 a 70 anni, il punteggio clinico y è stato normalizzato nell'intervallo 0-10 e i pazienti sono stati raggruppati in quattro classi, in base al loro punteggio clinico e alla sensibilità (0,986) e specificità (0,116) scelte:

- Rischio basso, da 0 a 2,5
- Rischio moderato, da 2,5 a 5
- Rischio elevato da 5 a 10

Abbiamo eseguito un test χ^2 test per verificare l'esistenza di un'associazione tra la presenza di DM di tipo 2 e la classe di rischio. Il valore di probabilità dei risultati ($\chi^2 = 28.2, df = 2, pvalue < 10^{-6}$) mostra una relazione statisticamente significativa tra la classe di rischio e l'insorgenza didiabete di tipo 2.

NON-ONCOLOGIC MORBIDITY IN INTERNAL MEDICINE

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Introduction: Patients admitted to Internal Medicine departments are generally of advanced age and present with a wide variety of clinical conditions, including oncological and non-oncological conditions. However, the perception of frailty and the need for palliative care tends to be differentiated between these two groups. Active oncology (OAt) patients receive special attention in terms of palliative support, while non-oncology (NO) patients, while often presenting with a significant burden of chronic conditions, are less frequently considered candidates for palliative care. This study aims to analyze and compare clinical characteristics, perceived frailty, and access to palliative care between OAt and NO patients admitted to our wards.
Methods: This observational study is based on the analysis of clinical data collected through a multifunctional collector for the collection of multiple prospective data. It included 823 patients divided into various groups, with a main focus on comparing OAt and NO patients. Data analyzed included demographic characteristics, comorbidities, functional status assessed through several scales, including the Barthel, Physician Global Assesment and EQ5D. The expected treatment goals at admission and the propensity to refer study patients to palliative care were also recorded. Statistical analysis was contucted using: the Mann-Whintey test for the analysis of continuous variables that do not follow a normal distribution between two independent groups; the chi-square test to test the association between two categorial variables and sign test to assess possible statistical differences in a variable measured multiple times. Data were expressed using percentages for categorical variables and medians with interquartile range for continuous variables.
Results: NO patients have more chronic conditions than OAt patients, with a significant prevalence of heart failure (19% vs 11%, p=0.004), COPD (16% vs 11%, p=0.042), dementia (12% vs 5%, p=0.001), diabetes (7% vs 3%, p=0.027) and hemiplegia (3% vs 1%, p=0.029). In addition, NO patients are found to be more affected by dysphagia (14% vs 7%, p=0.002), more dependent on others (18% vs 9%, p=0.002) and require more home care (16% vs 6%, p<0.001). Despite this high multimorbidity and vulnerability, patients in the NO group are empirically perceived as less frail than patients in the OAt group (61% vs 77%, p=0.002). However, the goal of palliative care placement is predominantly offered to OAt patients (5% vs 22%, p<0.001), while NO patients, although presenting with severe clinical conditions and an often poor prognosis, less frequently receive this type of care, presenting mainly stabilization or returned ad integrum as the goal of hospitalization.
Discussion: The results of our study highlight a discrepancy in access to palliative care between oncology and nononcology patients. The traditional association between palliative care and neoplastic diseases seem to influence clinical decisions, leading to an underestimation of the need for palliative support in patients with chronic nononcologic diseases. This phenomenon could be explained by several factors, including the perceived more predictable course of oncologic diseases compared with chronic degenerative conditions, which often have a less defined clinical course. In addition, frailty is often assessed based on the primary diagnosis rather than the patient's actual functional status. This approach could lead to a disparity in care management and treatment planning. NO patients, while having a high disease burden and impaired quality of life, could benefit significantly from early integration of palliative care into their care pathway.
Conclusions: This study underscores the importance of reevaluating access to palliative care by extending it more equitably to patients with severe chronic conditions. Internal medicine, because of its multidisciplinary nature, has the potential to promote a more balanced approach to the management of frailty, ensuring that even nononcology patients receive appropriate palliative care. Second, it is important to ensure a comprehensive assessment of the clinical case, without identifying a frail oncology patient only by the neoplastic condition.

CLINICAL AND ATOPIC FEATURES OF PATIENTS WITH WHEAT ALLERGY DEPENDENT ON AUGMENTATION FACTORS (WALDA) PRESENTING WITH URTICARIA: A MONOCENTRIC STUDY

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Background: IgE-mediated wheat allergy imposes a significant burden on patients due to possibly severe manifestations, including anaphylaxis, which is often characterised by cardiovascular involvement, and management-related issues, such as wheat avoidance with its associated nutritional impact [1)- 3)]. Omega-5 gliadin (O5G) is the most common allergen involved in wheat anaphylaxis dependent on augmentation factors (WANDA), [1)-4)]. In this form of IgE-mediated food allergy, allergic reactions usually occur when wheat is ingested concomitantly with a cofactor, such as physical exercise, nonsteroidal anti-inflammatory drugs, or alcohol, and are usually severe, with frequent cardiovascular involvement, including cases of refractory anaphylaxis. Clinical and laboratory features of wheat allergy dependent on augmentation factor (WALDA) are scarcely characterised as compared to wheat anaphylaxis dependent on augmentation factor (WANDA).
Aims: The clinical background and sensitisation profile of patients with WALDA presenting with urticaria, to look for demographic, comorbid clinical presentation patterns and laboratory related factors, which may help identify salient clinical features and biomarkers of this subset of wheat allergic patients.
Methods: This was a monocentric, observational, retrospective study conducted in a tertiary referral centre specialized in the diagnosis and management of wheat-related disorders, including coeliac disease and wheat allergy, with a combined gastroenterology and allergy outpatient clinic (Fondazione IRCCS San Matteo, Pavia).We herein retrospectively enrolled all consecutive adult (≥18 years) patients who were diagnosed with O5G allergy over the last five years (2021-2025), since the start of the allergy outpatient clinic.The diagnosis of WALDA related to O5G was made through adaptation of the criteria proposed by Jiang et al [5] for wheat-dependent, exercise-induced anaphylaxis. WALDA diagnosis was based upon recognised clinical/serological criteria, including positivity for omega-5 gliadin (O5G). Clinical, atopic features, allergy tests (skin prick tests, specific IgE) and gastrointestinal comorbidities were evaluated in patients with WALDA and compared to a cohort of O5G negative

patients sensitised/allergic to wheat and one of patients sensitised/allergic to shrimp.
Results: Overall, we recruited 11 patients with WALDA presenting with intermittent urticaria (median age 44 years, IQR 29-58, F:M ratio 1.7:1). Atopy was a frequent finding among patients (8/11, 72.7%), with food allergy (6/11, 54.5%) followed by respiratory allergies (5/11, 45.5%). With regards to gastrointestinal comorbidities, irritable bowel syndrome (IBS) was a frequent finding in these patients (4/11, 36.3%).Shrimp sensitisation was present in 8/11 patients (72.7%); half of them were also clinically reactive to shrimp. The prevalence of shrimp sensitization was four times lower and estimated at 15.3% (p=0.01), in a group (n=13) of O5G negative patients with wheat sensitisation/allergy (median age 31 years, IQR 27.7-52.0, F:M ratio 0.4:1). On the contrary, in a group of patients with shrimp allergy (n=13) with or without allergic rhinitis, the prevalence of O5G positivity was 0% and that of IBS 7.7%.
Conclusions: The results of the present study suggest that patients with WALDA and urticaria may constitute a specific subset of wheat allergic patients and possibly a different phenotype, characterised by specific demographic features (female sex) and a high prevalence of atopic comorbidities, as opposed to patients with WANDA. Moreover, IBS is one of most frequent clinical nonatopic comorbidities of patients with WALDA-urticaria, implying that gastroenterological evaluation/referral in these patients is required. Finally, shrimp and house dust mite sensitisation/reactivity appears to be one relevant aspect, among others, in the management of allergic comorbidities in these patients.
Refererences: *Chin Med J (Engl)*

PROGNOSTIC IMPACT OF VITAMIN D DEFICIENCY AND SECONDARY HYPERPARATHYROIDISM ON 12-MONTH OUTCOMES IN PATIENTS HOSPITALIZED FOR HIP FRACTURE

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Background: Hip fractures (HF) are among the most serious consequences of osteoporosis, with a substantial impact on morbidity, functional decline, and mortality. Vitamin D deficiency (VDD) and secondary hyperparathyroidism (SHPT) are common in this population and may contribute to skeletal fragility. While their role in bone health is well recognized, their independent prognostic significance for post-fracture mortality remains controversial. This study aimed to assess the prevalence of VDD and SHPT in patients hospitalized for HF and their association with 12-month outcomes, including mortality.
Methods: We enrolled patients aged ≥50 years who were admitted with fragility HF at the Azienda Ospedale-Università Padova between March 2023 and September 2024, as part of our Fracture Liaison Service. Serum 25-hydroxyvitamin D [25(OH)D] and parathyroid hormone (PTH) levels were measured upon admission. VDD was defined as 25(OH)D <50 nmol/L; SHPT was defined as elevated PTH (>36.8 ng/L) in the context of normal or low calcium levels. Clinical and laboratory data were collected at admission. A nested case-control study, following propensity score matching for age, sex, and Charlson Comorbidity Index (CCI), was conducted to reduce bias from baseline differences between patients with and without VDD. Cox regression models were used to assess the association of VDD and SHPT with mortality.
Results: Among 711 patients (mean age 83.9 ± 8.6 years; 70.4% women), VDD was present in 58.5% and SHPT in 42.9% of evaluable cases. Patients with VDD had a higher comorbidity burden (CCI 5.5 vs. 5.1, $p < 0.001$), were slightly older, although not significantly (84.3 vs. 83.4 years, $p = 0.170$), and had a higher proportion of males (39.9% vs. 17.5%, $p < 0.001$). To account for these baseline differences, we conducted a nested case-control study as previously described, including 149 patients with and 149 without VDD. From a laboratory perspective, patients with VDD—matched for age, sex, and comorbidity burden—had markedly lower 25(OH)D levels (24 vs. 73 nmol/L, $p < 0.001$), lower serum calcium (8.5 vs. 8.7 mg/dL) and phosphate levels (2.8 vs. 3.0 mg/dL), and higher levels of bone turnover markers, including bone-specific alkaline phosphatase (15 vs. 13 µg/L) and C-terminal telopeptide of type I collagen (CTX) (455 vs. 332 pg/mL), suggesting an unfavourable bone turnover and mineralization status. Regarding 12-month outcomes, we observed a non-significant trend toward a lower incidence of refractures in patients without VDD compared to those with VDD (2.7% vs. 5.4%, $p = 0.377$). Similarly, patients without VDD showed a non-significant tendency toward a higher survival rate (HR 0.77, 95% CI 0.48–1.25, $p = 0.289$). Within the nested case-control study, we identified patients with and without SHPT. Those with SHPT were significantly older (87.0 ± 7.1 vs. 83.5 ± 8.1 years, $p < 0.001$) and had a higher comorbidity burden (CCI 5.5 vs. 5.1, $p = 0.035$). They had a lower estimated glomerular filtration rate (61 vs. 79 mL/min/1.73 m^2, $p < 0.001$) and a higher prevalence of VDD (61.9% vs. 37.1%, $p < 0.001$). They also had significantly higher serum CTX levels (475 vs. 307 pg/mL, $p = 0.001$), indicating increased bone turnover. In terms of prognosis, they experienced a higher incidence of acute heart failure episodes (16.9% vs. 3.4%, $p = 0.002$) and acute myocardial injury (10.1% vs. 2.5%, $p = 0.043$), and had a longer median hospital stay (14 vs. 12 days, $p = 0.037$), suggesting more severe illness or complications during hospitalization. Patients with SHPT also had a significantly higher 12-month mortality rate (29.5% vs. 16.4%, $p = 0.022$), with an increased risk of death in univariate analysis (HR 1.93, 95% CI 1.13–3.31, $p = 0.017$). However, after adjustment for age and CCI, the association was no longer statistically significant (HR 1.54, 95% CI 0.89–2.69, $p = 0.124$).
Conclusions: VDD is highly prevalent among patients hospitalized for HF and is associated with impaired bone turnover and a greater burden of comorbidities. However, VDD was not independently associated with 12-month mortality or refracture risk, suggesting that its prognostic impact may be largely mediated by underlying health conditions rather than by the deficiency itself.SHPT, frequently observed in patients with VDD, identifies a subgroup of older, frailer individuals with more severe comorbidities, reduced renal function, and higher bone turnover markers. Similarly to VDD, SHPT did not appear to be independently associated with 12-month mortality after adjustment for age and comorbidity burden. Altogether, these findings underscore the importance of integrated clinical approaches that address both bone health and multimorbidity to improve outcomes in this vulnerable population.

ECTOPIC CUSHING SYNDROME CAUSED BY ACTH-PRODUCING LUNG NEUROENDOCRINE CARCINOMA

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Introduction and Aim: The aim of our work is to illustrate a rare case of ectopic Cushing syndrome caused by ACTH-producing lung neuroendocrine carcinoma.
Methods: A 66 years old woman, suffering from arterial hypertension and diabetes mellitus type 2, was admitted to the emergency room for aphasia after losing weight and progressive worsening of her general conditions. In the emergency room, severe hypokalemia (1.9 mEq/l) and uncontrolled blood pressure values (178/110 mmHg) were found, therefore admission to medicine. Negative head CT. Electroencephalogram suggestive for epilepsy. Levetiracetam, potassium chloride 2400 mg/day and amlodipine 10 mg/day were started. For persistence of hypokalemia (2 mEq/l) he performed an abdominal CT which excluded adrenal lesions but showed a 3.5 cm lung lesion which was probably neoplastic and liver lesions which were probably secondary, as well as hormonal tests which excluded primary aldosteronism (basal aldosterone <20 pg/ml, basal renin <0.1 ng/dl), but showed high urinary cortisol (13128.5 mcg/24 h). After liver biopsy, the histology revealed metastasis of ACTH-producing neuroendocrine carcinoma of probable origin in the lungs.
Results: Nugent test was positive for hypercortisolism due to probable neoplastic ectopic ACTH syndrome (basal ACTH 255 pg/ml, basal cortisolemia 249.3 mcg/dl; post-dexa ACTH 160 pg/ml, post-dexa cortisolemia 231.6 mcg/dl). Severe hypokalemia persisting (2.2 mEq/l) also resistant to canrenone (started up to 200 mg/day) and potassium chloride increased up to 7200 mg/day and physical changes occurred with facies lunaris, hirsutism, oedema and skin hyperpigmentation, metyrapone 250 mg three times a day was started, with good clinical response (normalized potassium levels 4.2 mEq/l and decrease in oedema). However, worsening of glycemic control, for which metyrapone was replaced with osilodrostat 2 mg twice daily. The situation was complicated by the onset of nosocomial right-sided pneumonia with acute respiratory failure requiring non-invasive ventilation. The bronchoalveolar lavage showed Pneumocystis carinii infection which was treated with trimethoprim/sulfamethoxazole, with gradual normalization of respiratory exchanges. PET-DOTA was scheduled, chemotherapy was then started and the osilodrostat dosage was increased. However, the situation worsened again and acutely after the onset of a further infectious process starting from the urinary tract, leading to the patient's death.
Conclusions: In conclusion, our case reflects the difficult management of these patients.

1DETERMINAZIONE DEGLI ANTICOAGULANTI ORALI DIRETTI SU CAMPIONI DI URINA A CONFRONTO CON LE CONCENTRAZIONI PLASMATICHE IN PAZIENTI AMBULATORIALI AFFETTI DA FIBRILLAZIONE ATRIALE E OBESITÀ

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Background: Obese patients with atrial fibrillation (AF) and high thromboembolic risk need anticoagulant therapy. Few data are available on direct anticoagulants (DOACs) in this population and a point-of-care method has been validated to support rapid clinical decisions and to identify on-off threshold plasma concentrations. The aim of the present study was to evaluate the sensitivity, specificity, positive and negative predictive values (PPV and NPV) of testing for DOACs from urine samples of obese patients taking DOACs for AF.
Methods: Cross-sectional study on obese AF outpatients referring to Policlinico Umberto I of Rome. Inclusion criteria were patients of both sexes, aged ≥18 years, Body Mass Index (BMI) ≥30 Kg/m² and receiving a DOAC for AF over at least 7 days. Exclusion criteria were denial of written informed consent, inability to provide a spontaneous urine sample, any contraindication to the administration of DOACs and conditions with known haematuria and blood components such as urobilinogen, which alter the colour of urine and may compromise the interpretation of pad colours of DOAC dipstick. patients were consecutevly enrolled from 2022 to 2024. Trough and peak plasma concentrations and urinary Dipstick were assessed, which determines separate pads for factor Xa (FXA-i) and thrombin inhibitor (THR-i) DOACs. Study endpoints were the sensitivity, specificity, positive and negative predictive values (PPV and NPV) of DOAC Dipstick compared to plasma concentrations. Sub-analysis according to obesity severity and type of DOAC was performed.
The study was approved by the local ethic committee of Sapienza University (No. 0234/2022) and was conducted according to the 1975 Declaration of Helsinki.
Results: 320 paired plasma and urine samples were available from 160 enrolled patients (mean age 73.2±9.1 years) see Table 1. Comparing to trough plasma concentrations, DOAC Dipstick showed a sensitivity (mean, 95% confidence interval, CI) of 99.24% (95.82-99.98), specificity of 6.89% (0.85-22.76), PPV 82.80% (81.32-84.18), NPV 66.67% (15.79-95.52) see Table 2. On the other hand, comparing to peak plasma concentrations, DOAC Dipstick showed a sensitivity of 97.8% (93.7-99.5), specificity of 0% (0.0-15.4), PPV of 85.9% (85.6-86.2)
Urinary Dipstick showed a sensitivity of 99.10% (95.4-100.0), specificity of 4.70% (0.60-16.20) and a PPV and NPV of 74.50% (73.2-75.8) and 66.70 (15.7-95.6), compared to plasma thresholds >30 ng/mL of FXA-I and THR-I.
Sub analyses showed similar results between FXA-I and THR-i.
Conclusions: The urine point-of-care has high sensitivity, acceptable PPV, but low specificity and NPV in AF obese patients.

Table 1. Characteristics of patients according to anti-Xa inhibitors and anti-thrombin inhibitor anticoagulant

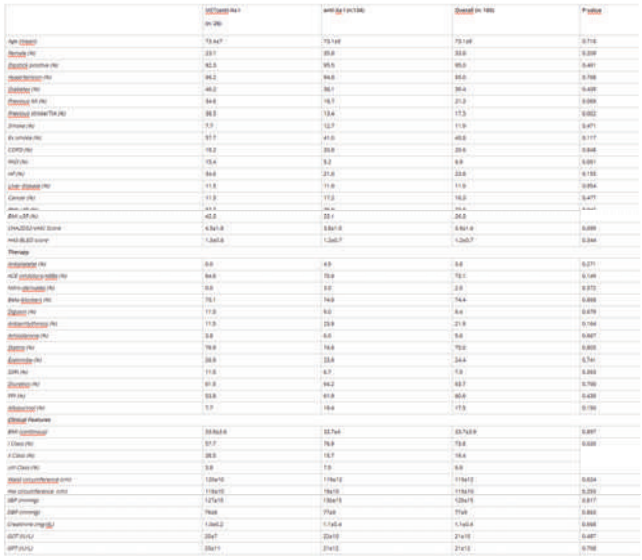
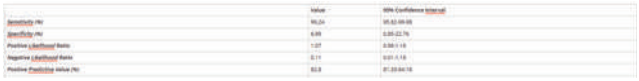


Table 2. Sensitivity, specificity and predictive values of urniary dipstick



ASSOCIATION BETWEEN PRIMARY HYPERPARATHYROIDISM AND VENOUS THROMBOEMBOLISM IN PATIENTS WITH FRAGILITY HIP FRACTURES

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Background: Primary hyperparathyroidism (PHPT), a condition characterized by elevated parathyroid hormone (PTH) levels and hypercalcemia, may be implicated in promoting a prothrombotic state through several mechanisms, including activation of the coagulation cascade, platelet dysfunction, and endothelial inflammation. While the musculoskeletal and renal complications of PHPT are well established, its potential association with venous thromboembolism (VTE) remains poorly understood. This study aims to investigate the relationship between PHPT and VTE in patients hospitalized for fragility hip fractures.
Methods: We enrolled patients aged 50 years or older who were admitted for fragility hip fractures—excluding those resulting from trauma or pathological conditions—at the "Azienda Ospedale-Università di Padova" between March 2023 and March 2024, within the framework of a Fracture Liaison Service program. Clinical and laboratory data were collected, including comorbidities assessed using the Charlson Comorbidity Index (CCI). PHPT was defined as PTH levels >36.8 ng/L in the presence of corrected serum calcium >10 mg/dL. Written informed consent was obtained from all participants.
Results: A total of 508 patients were enrolled (mean age 84 ± 9 years; 71% female), of whom 32 (6.3%) had a history of VTE. Patients with and without VTE showed no significant differences in age, sex, BMI, comorbidity burden, prior osteoporotic fractures, or fracture risk scores. However, PTH levels were higher in patients with VTE (46.3 ng/L, IQR 31.4–62.0 vs. 35.7 ng/L, IQR 25.6–49.7; p=0.02), despite similar serum 25-OH vitamin D levels and estimated glomerular filtration rates. PHPT prevalence was also higher in the VTE group (18.5% vs. 6.3%; p=0.02), while no differences were observed for secondary hyperparathyroidism.
Conclusion: Our data suggests an association between PHPT and VTE in fragility hip fracture patients, supporting the hypothesis that PHPT may contribute to a prothrombotic state. Further research is needed to clarify pathophysiology and specific management strategies in this population.

METABOLIC IMPACT OF GLUTEN FREE-DIET: THE MODEL OF PATIENT WITH THE ASSOCIATION OF CELIAC DISEASE AND TYPE-1 DIABETES MELLITUS

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Background: Gluten-free diet (GFD) is to this date the only available treatment for Celiac Disease (CD), however previous publications raised concern on the possible detrimental effect of GFD on glycol-lipid metabolism. We aimed to analyse the changes in the metabolic parameters after the start of GFD using as model a population of Type-1 Diabetes Mellitus (T1DM) patients diagnosed with CD.
Methods: wo large databases of patients with CD and patients with T1DM (1296 and 1197 patients respectively) were searched to identify 86 patients with both CD and T1DM. Metabolic parameters were evaluated at the start of GFD and then 12 and 24 months after the start of GFD, to evaluate their variation over time.
Results: Significant trends were identified for BMI (p=0.002), total cholesterol values (Tot-C) (p=0.003), and HDL cholesterol values (HDL-C) (p=0.025). BMI increased significantly after the first 12 months of GFD, remaining stable between 12 and 24 months of GFD, thus BMI after 24 months of GFD confirmed higher than baseline. A similar trend was observed for Tot-C, while HDL-C, after a similar increse after 12 months, remained persistently higher after 24 months of GFD when compared to baseline. These date are summarized in table 1 and 2.All patients received constant nutrition counselling during the follow-up period, and no modification of anti-dyslipidaemia therapy were needed in our patients.
Conclusion: Our study demonstrated a limited impact of GFD on the development of metabolic syndrome, with an initial detriment of metabolic parameter that can be efficiently managed with non-pharmacologic interventions, as nutritional counselling.

	Start of GFD	12 months of GFD	24 months of GFD	p
BMI (Kg/m2)	22.6 (13.7-37.4)	23.6 (15.4-39.0)	23.54 (14.7-38.93)	0.002
HbA1c (mmol/mol)	59 (35-158)	60 (33-104)	58 (36-95)	0.914
Insulin requirement (UI/kg)	0.6 (0.1-1.1)	09.7 (0.1-1.1)	0.6 (0.1-1.1)	0.380
Total Cholesterol (mg/dL)	172.5 (124.0-258.0)	187.5 (129.0-278.0)	177.0 (111.0-283.0)	0.003
Triglycerides (mg/dL)	71 (31-541)	73 (36-244)	72 (39-195)	0.714
HDL Cholesterol (mg/dL)	58 (26-91)	60 (32-96)	59 (38-90)	0.025

	Timespan	Increase – n (%)	Descrease – n (%)	Stability – n (%)	p
BMI	Start of GFD – 12 months of GFD	61 (70.1%)	24 (27.6%)	2 (2.3%)	0.002
	12 months of GFD – 24 months of GFD	45 (51.7%)	34 (34.4%)	8 (13.9%)	0.105
	Start of GFD – 24 months of GFD	63 (72.5%)	19 (21.8%)	5 (5.7)%	<0.001
Total Cholesterol	Start of GFD – 12 months of GFD	56 (64.3%)	27 (31.0%)	4 (4.7%)	0.014
	12 months of GFD – 24 months of GFD	26 (29.9%)	59 (67.8%)	2 (2.3%)	0.065
	Start of GFD – 24 months of GFD	50 (57.5%)	35 (40.2%)	2 (2.3%)	0.629
HDL Cholesterol	Start of GFD – 12 months of GFD	54 (62.1%)	28 (32.2%)	5 (5.7%)	0.015
	12 months of GFD – 24 months of GFD	25 (28.7%)	44 (50.6%)	18 (20.7%)	0.842
	Start of GFD – 24 months of GFD	53 (60.9%)	32 (36.8%)	2 (2.3%)	0.004

CLINICAL PRESENTATION OF CELIAC DISEASE IN PATIENTS WITH TYPE-1 DIABETES MELLITUS: INSIGHT FROM A NOT-ROUTINELY-SCREENED POPULATION

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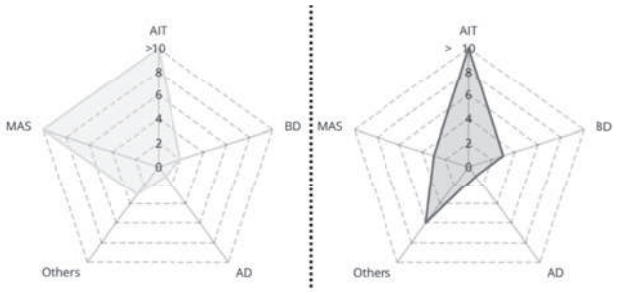
Background and Aims: Celiac disease (CD) and Type-1 Diabetes Mellitus (T1DM) share the autoimmune pathogenesis, and their association has been widely reported in literature, thus current guidelines for both diseases suggest reciprocal screening. The aim of our study is to analyse the presentation of CD in a population of paediatric and adults T1DM not undergone a routine and standardized screening, to identify the potential clinical relevance of CD in this scenario.
Materials and methods: We analysed the clinical features and epidemics of CD in a population of patients previously diagnosed with T1DM, comparing them with a control group of non-T1DM patients matched 3:1 according to age at diagnosis of CD and sex.
Results: Patients with associated T1DM were more often affected by classical CD when compared with non-T1DM patients, with also a higher occurrence of miscarriage and development of further autoimmune diseases. This data are summarised in table 1. Figure 1 reports the absolute prevalence of autoimmune comorbidities in the two groups.
Discussion and conclusion: Our data showed that CD, if not recognized early, trends towards the development of malabsorptive syndromes in T1DM patients, in both adults and paediatric patients. The higher occurrence of miscarriage represents a further motivation to screen T1DM patients for CD, due to reduction of miscarriage in CD patients after the start of GFD, as well as the higher occurrence of polyautoimmunity should rise the level of clinical attention.



	Matched population (236)	T1DM (59)	Control (177)	p
Sex, female	240 (59.3%)	35 (59.3%)	105 (59.3%)	1
Age at diagnosis, years median (range) –all patients	22.37 (1.91-67.56)	21.23 (4.26-63.5)	22.42 (1.91-67.6)	0.906
Family history of autoimmunity	13 (5.5%)	8 (13.6%)	5 (2.8%)	0.004
Symptoms at diagnosis, any	196(83.1%)	46 (78.0%)	150 (84.7%)	0.234
Classical presentation	107 (45.3%)	41 (69.4%)	65 (36.7%)	<0.001
Diarrhoea	79 (33.5%)	26 (44.1%)	53 (29.9%)	0.056
Weight loss	49 (20.9%)	15 (25.4%)	34 (19,4%)	0.357
Iron deficiency anaemia	95 (40.4%)	22 (36,6%)	73 (41.2%)	0.357
High liver enzymes	18 (7.8%)	3 (5.6%)	15 (8.4%)	0.442
History of miscarriage (counting only female patients)	16 (11.4%)	10 (29.4%)	6 (5.7%)	0.001

TEST AND SCOPE TO IDENTIFY GASTRIC PRECANCEROUS LESIONS IN 2171 DYSPEPTIC PATIENTS.

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Introduction: Helicobacter pylori (H. pylori) infection is a recognized primary

cause of sporadic gastric cancer. Chronic infection induces long-term gastric inflammation, potentially progressing to glandular atrophy, impaired gastric function, and a microenvironment conducive to malignancy. The extent of mucosal atrophy correlates with cancer risk. While primary prevention via vaccination is unavailable, identification and eradication of H. pylori remain the most effective strategy. In areas with a high prevalence of infection, the "Test and Treat" approach—non-invasive testing followed by eradication therapy—has been advocated. A more refined "Test and Scope" strategy integrates endoscopic evaluation for histological risk stratification and detection of antibiotic resistance. This prospective cohort study aimed to assess whether initial non-invasive H. pylori testing can effectively identify patients requiring esophagogastroduodenoscopy (EGD) for gastric cancer risk stratification in a medium-to-high prevalence setting.

Materials and methods: This prospective cross-sectional study was conducted between January 2022 and August 2024 in the Emilia-Romagna region of Northern Italy. From 2,213 individuals referred for dyspepsia without alarm symptoms, 42 were excluded based on pre-defined criteria, resulting in a final sample of 2,171 patients. Regardless of H. pylori status, patients underwent EGD with six gastric biopsies for histopathological assessment and OLGA (Operative Link on Gastritis Assessment) staging. H. pylori detection was confirmed using histology, culture, rapid urease test (RUT), and breath test, with at least three concordant tests required in case of discrepancy. Biopsy evaluations were performed jointly by two pathologists.

Results: Among the 2,171 patients, 640 (29.5%) tested positive for H. pylori. Gastric atrophy was significantly more common in H. pylori-positive patients (22.2%) compared to H. pylori-negative ones (1.3%) ($p<0.001$). High-risk OLGA stages (III–IV) were exclusively found in H. pylori-positive individuals (9/640; 1.4%), with none observed in the H. pylori-negative cohort. OLGA stage II was present in 35 patients (1.6%), with 34 of them being H. pylori-positive. Logistic regression showed that age and H. pylori positivity were independently associated with increased risk of OLGA stage II. Smoking also showed a significant association with high-risk gastritis (OLGA stages III–IV), with an adjusted OR of 1.71 (95% CI=1.12–2.57).

Conclusion: This study confirms the strong association between H. pylori infection and histologically confirmed gastric atrophy, particularly in higher-risk OLGA stages. The integration of non-invasive H. pylori testing with targeted EGD and biopsy-based OLGA staging offers a valuable approach for stratifying patients' cancer risk. In settings with intermediate-to-high H. pylori prevalence, the "Test and Scope" strategy is a biologically and clinically sound method for secondary prevention of gastric cancer. Early identification of high-risk patients enables timely surveillance and potential eradication therapy, ultimately improving outcomes and optimizing healthcare resources.

RETROPERITONEAL FIBROSIS MIMICKING INFLAMMATORY ANEURYSM: THE DIAGNOSTIC VALUE OF HISTOLOGY IN A MULTIDISCIPLINARY WORKUP

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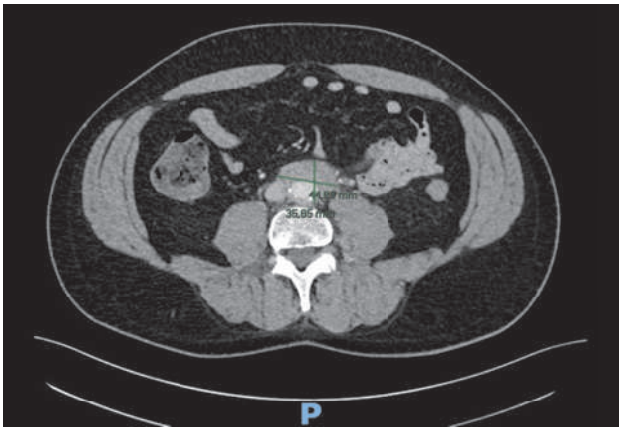
We report the case of a 55-year-old man who presented to the emergency department with irradiated hypogastric pain in the left iliac fossa for three days. Abdominal CT angiography revealed aneurysmal dilatation (~35 mm) of the subrenal abdominal aorta with increased enhancement in basal and post-contrast phases, and parietal thickening of the common and left internal iliac arteries, suggestive of an inflammatory aneurysm. The patient was an active smoker with a history of percutaneous transluminal coronary angioplasty of the anterior interventricular artery (2020). Blood tests showed no abnormalities in blood count, coagulation profile or electrolytes, with only a slight increase in CRP (8.8 mg/L vs. normal 3.5).

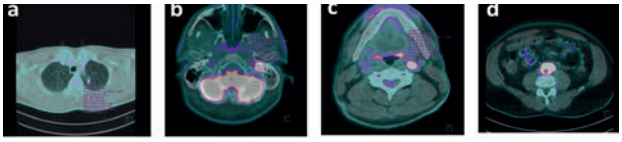
Admitted to our Cardiovascular Internal Medicine Department, a repeat contrast-enhanced abdominal CT scan 72 hours later confirmed retroperitoneal solid tissue encasing the subrenal aorta and the common, left internal, and obturator arteries. Retroperitoneal fibrosis or IgG4-related periaortitis was suspected. Extensive laboratory tests were inconclusive (normal protein electrophoresis, autoantibodies, IgG subclasses, rheumatoid factor, complement; weakly positive ANA). An FDG PET-CT scan showed intense uptake at the periaortic tissue and at multiple other sites: a pulmonary nodule (8 mm), left petrous bone, left carotid bifurcation, and distal colon.

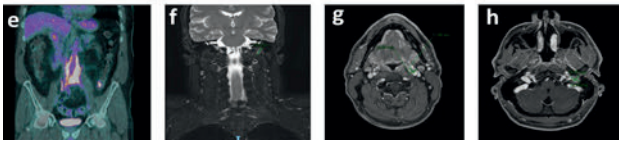
Due to the presence of cephalic hypercaptant lesions, further history revealed a paternal family history of paraganglioma. Brain MRI showed pathological uptake in PET-CT-correlated sites, but without signal characteristics typical of paraganglioma, schwannoma, or lymphoproliferative disease. Tumor markers were negative. Bronchoscopic biopsy was not feasible. Rheumatology consultation suggested periaortic tissue biopsy; however, the Vascular Team ruled out percutaneous approaches due to high procedural risk and low diagnostic yield. Empirical immunosuppressive therapy was also excluded due to the possibility of underlying malignancy.

After cardiovascular risk stratification, the patient was scheduled for laparoscopic biopsy of the retroperitoneal lesion and atypical thoracoscopic resection of the pulmonary nodule. A follow-up CT scan three weeks later confirmed stability of the periaortic findings, and the patient was discharged to await elective surgery. During home stay, he remained clinically stable. He later underwent surgery: histological analysis of the periaortic tissue showed mixed B and T cell infiltrate with numerous polytypic plasma cells (IgG4/IgG ratio <15%), while the pulmonary nodule was benign. A diagnosis of probable IgG4-related retroperitoneal fibrosis was made. The patient was referred to the rheumatology clinic, where he began treatment with deltacortene, a proton pump inhibitor, mycophenolate mofetil, and cholecalciferol, with follow-up PET-CT planned at 3 months.

Discussion: Retroperitoneal fibrosis (RPF) is a rare condition characterized by inflammatory-fibrotic tissue in the retroperitoneum, typically encasing the infrarenal aorta and iliac arteries, and potentially involving ureters or other structures. It can be idiopathic (often IgG4-related) or secondary to various causes. Clinical presentation often includes dull abdominal or back pain and potential renal impairment. Diagnosis is primarily radiological, with contrast-enhanced CT or MRI, but biopsy is often necessary. In this case, the diagnostic challenge was heightened by non-contributory labs and PET-CT findings suggestive of malignancy, reinforcing the importance of histological confirmation.







FROM THE MEDICAL EXAMINATION TO THE LYMPHOMA DIAGNOSIS: THE ROLE OF POCUS IN URGENT CARE CENTERS (CAUS)

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Introduction: Urgent Care Centers (CAU – Centro di Assistenza e Urgenza) in Reggio Emilia are territorial healthcare facilities designed to manage low-complexity emergencies. A key feature of these centers is the availability of using first-level diagnostic tools such as ultrasound (US), point-of-care tests (POCT), and electrocardiography (ECG), which are generally not available in local general practitioners' offices. This enhanced diagnostic capability allows the physician to manage more complex cases and facilitates early diagnosis of pathology when possible.
Clinical Case: A 48-year-old patient presented to the Urgent Care Center (CAU) of Reggio Emilia reporting persistent abdominal tension and a progressive worsening of discomfort with pain over the previous days. The patient denied the presence of further associated clinical manifestations and reported no chronical diseases. After the arrival at the CAU, a physical examination of the abdomen was conducted, revealing mild abdominal tension in the right iliac fossa.
To study this clinical finding and the reported symptoms, an abdominal ultrasound was performed. The ultrasound examination revealed the presence of significant peri-aortic lymphadenomegaly, associated with an increased volume of the spleen (splenomegaly). Based on these diagnostic findings, the patient was promptly referred to a specialist hematologist for further investigations and diagnostic definition. Advanced imaging with CT and PET confirmed a diagnosis advanced-stage (stage IV) Hodgkin lymphoma. The patient was subsequently started on chemotherapy.
Discussion: Hodgkin's Lymphoma is a hematological neoplasm with high remission rates, especially if diagnosed early. Its clinical presentation, often characterized by lymphadenopathy, systemic symptoms (such as fever, night sweats, generalized itching), can overlap with benign conditions, delaying the definitive diagnosis. A diagnostic delay can lead to disease progression, worsening the outcome. Early identification through careful clinical evaluation, imaging tests, and subsequently, lymphonode biopsy with histological examination, is essential for accurate risk stratification and the identification of an appropriate treatment.
Conclusions: This case significantly highlights the clinical value of integrating first-level diagnostic tests, particularly ultrasound, even in local clinics (like the CAU). The availability of such a tool, together with the possibility of performing blood chemistry tests (although not performed in this case study), proved crucial for the early identification of radiological signs suggestive of a systemic condition that would have been difficult to suspect based on the initial clinical presentation. This diagnostic capability within a primary care center allows for rapid specialist referral, accelerates the initiation of appropriate diagnostic and therapeutic pathway and potentially improving the prognosis in complex diseases such as Hodgkin lymphoma.

PROSIT: IMPACT OF REMOTE MONITORING ON ENHANCING WELL-BEING AND REDUCING MEDICATION AND ORGAN DAMAGE IN HYPERTENSIVE PATIENTS

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Background: Hypertension is a major risk factor for cardiovascular diseases. The negative impact of hypertension and its complications on patients' Quality of Life (QoL) is significant, influenced by age, education, gender, disease duration, and medication burden. Furthermore, QoL reduction correlates with hypertension-mediated organ damage (HMOD).
Educational interventions are essential to enhance patient involvement in hypertension management. Telemedicine and e-Health can bridge the gap between healthcare providers and patients. This study aimed to assess the effectiveness of telemonitoring in improving QoL, clinical outcomes, and patient compliance, while identifying barriers to widespread adoption.
Methods: We conducted a single-center, prospective, randomized controlled trial with 100 hypertensive patients, randomized into three groups ensuring baseline homogeneity in age, gender, left ventricular ejection fraction, atrial fibrillation, and pulmonary embolism:
The app for Groups A and B suggested patient-physician interactions based on data input. The telemonitoring system included a cloud-based mobile application allowing manual reporting of vital signs, feedback provision, and real-time clinical alerts for healthcare providers. The wearable ECG device used in Group A continuously recorded cardiac function, transmitting data wirelessly to a clinical platform for analysis.
Baseline characteristics, including comorbidities and medication regimens, were similar across groups. At study initiation, no significant differences were observed in clinical, laboratory, or echocardiographic parameters.
Results: Patients valued multiple app features, with 50% citing functionality as the most appreciated aspect, followed by the speed of interactions (19%). No significant differences in acceptance of technology were observed at baseline. However, a strong correlation was found between digital literacy and engagement with telemonitoring, particularly among those with higher education levels.
Telemonitoring increased patients' sense of security. Although no significant changes were found in QoL domains at different time points, Groups A and B showed significant improvements in Emotional Well-being ($p<0.05$) compared to Group C.
In terms of blood pressure control, no significant differences were observed between groups at any time point, except for a slight reduction in diastolic blood pressure at T3 in Group B ($p=0.04$). Heart rate showed minor but statistically significant increases at certain time points in Groups A and B, although within normal values.
QoL, assessed via SF-36, improved significantly in Groups A and B, particularly in perceived safety. Patients in Group A reported a shift from "a lot of the time" to "always" feeling calm and peaceful, while Group B shifted to "almost always." Group C showed no changes.
Therapeutic adherence, evaluated using the MARS-5 scale, increased significantly across all groups at T1 and remained stable throughout the study. Groups A and B demonstrated higher adherence compared to Group C. Notably, early therapeutic adjustments were more frequent in Groups A (17.14% at T1) and B (12.5% at T1), whereas late modifications predominated in Group C (17.14% at T4).
A significant reduction in the number of prescribed medications was observed in Groups A and B, with a median decrease from 2 [2-3] at baseline to 1 [0-3] at T4 and T5. Conversely, Group C required more frequent dosage escalations without reducing total medication burden. This correlates with better diastolic blood pressure control at four months in Group B compared to baseline ($p<0.05$).
At the six-month follow-up after washout, echocardiography in Group A revealed significant reverse cardiac remodeling, including reduced interventricular septum thickness, left ventricular mass, and left ventricular mass indexed for body surface area (BSA) and height^{2,7} ($p<0.05$). Additionally, kidney function, assessed via creatinine and estimated glomerular filtration rate (eGFR), improved in Groups A and B, while fasting glucose levels worsened in Group C at T5. These findings suggest potential long-term structural benefits of telemonitoring.
Conclusion: This study demonstrates the feasibility and effectiveness of telemonitoring in managing hypertension. Telemonitoring enhances engagement, improves QoL, and boosts adherence to treatment. It also increases care

accessibility for vulnerable groups. Telemonitoring allows for personalized hypertension care, enabling early treatment adjustments and reducing medication burden, which helps control organ damage. These findings support the integration of telemonitoring into routine practice for individualized care. Future research should validate these results in larger populations and explore AI's potential to enhance risk prediction and interventions, improving outcomes and reducing healthcare costs.

PANDORA'S BOX: A CASE REPORT OF MARFAN DISEASE RIVEALED TWO MORE CASES OF THE SYNDROME

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Background: Marfan syndrome (MFS) is one of the most common inherited disorders of the connective tissue. It is an autosomal dominant condition with a reported incidence of 1 in 3000 to 5000 individuals. There is a wide range of clinical severity associated with MFS with classic ocular, cardiovascular and musculoskeletal abnormalities, while some patients demonstrate significant involvement of the lung, skin and central nervous system. The diagnosis of MFS relies essentially on the fulfillment of clinical diagnostic criteria as outlined by the revised Ghent score.
Case report: A 22 year old male, with no previous medical history, presented accompanied by his mother to our Department with abdominal pain e diarrhoea from 1 month. The pain was not related to food intake. The patient did not have a family history of a similar problem. On general examination he was comfortable at rest, extremely tall (1.97 meters) and thin with typical musculoskeletal features of MFS. These included arachnodactyly with positive wrist and thumb signs, pectus carinatum deformity, hind foot valgus, dolichostenomelia (< 0.78), increased arm span/height, scoliosis, dolichochepaly, enophthalmos, downslanting palpebral fissures, malar hypoplasia, and retrognathia. His total systemic revised Ghert score was 10. He was normotensive with a sinus bradycardia of 60 beats per minute. The first heart sound was soft with a murmur of mitral regurgitation graded as 2/5 Levine. There were no clinical features of infective endocarditis or cardiac failure. Respiratory examination demonstrated pectus carinatum and was otherwise normal. Ophthalmology examination revealed a left dense cataract with lens subluxation but no dislocation, iridodonesis, an old retinal detachment and minimal light perception. The right eye had a clear lens with no subluxation or dislocation, but showed iridodonesis with myopia. Laboratory tests were within normal limits (full blood count, urea and electrolytes, calcium, magnesium and phosphate, liver function tests, growth hormone, prolactin, troponin T, creatine kinase). Chest X-ray showed an increased cardiothoracic ratio of greater the 50%. Echocardiography demonstrated prolapse of the anterior mitral valve leaflet with moderately severe mitral regurgitation and aortic root dilatation measuring 5 cm. The ejection fraction was 65% and no evidence of aortic dissection was noted. Computerised tomography (CT) showed dilatation of the aortic sinuses of Valsava extending to the ascending aorta. The aortic root was dilated measuring 6.3 X 6.4cm, while the ascending aorta measured 3.1cm. There was no dissection or calcification of the aorta. The arch of the aorta and its main branches were within normal limits. The root of the main pulmonary artery was dilated measuring 4.1 cm, while the rest of the pulmonary arterial system was within normal limits. All renal arteries were patent and there was appropriate and symmetrical enhancement of the kidneys. The coeliac axis and the superior mesenteric arteries arose from the abdominal aortic aneurysm. The inferior mesenteric artery arose from the normal abdominal aorta. The lung fields were clear and the cranio-cervical junction was normal with no subluxation. He was instructed to restrict strenuous activity and was commenced on losartan. Because of his sinus bradycardia, the patient was not started on beta blocker therapy, The patient was counseled on his medical condition and offered surgery for his mitral valve and aortic root dilation. On further enquiry, the patient confessed that also his brother and his sister were very tall and slender and they had problems with their back, and an evident arachnodactyly was releved in the photos of both, brother and sister, showed by our young patient. All three of the lady's young sons wore glasses and all three had a decidedly Marfanoid appearance, but despite the presence of clear signs of the disease they had been ever underestimated! After consultation with his family he declined surgical intervention, although he required elective replacement of the aortic root and mitral valve replacement. So, he was discharged on losartan and periodic follow-up. His brothers were convocated to start the diagnostic steps of Marfan syndrome.
Discussion: Marfan syndrome is almost exclusively inherited in an autosomal dominant manner with most patients harboring mutations involving the gene (FBN1) encoding the connective tissue protein fibrillin-1. In less than 10% with typical Marfan phenotype, no mutations in FBN1 is identified and mutations in a gene encoding for transforming growth factor- beta receptors (TGFBR) maybe responsible While most individuals with MFS have an affected parent, about 25 % have MFS as a result of a de novo mutation. Mortality is related to cardiac complications, which is frequently associated with aortic dissection. Our patient had no family history of MFS and genetic testing was not performed, but we know that even in the presence of a FBN1 mutation, the diagnosis of MFS relies on fulfillment of clinical diagnostic criteria according to the revised Ghent nosology.

IPERTENSIONE ARTERIOSA ED IPOKALIEMIA

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Introduzione: L'ipertensione arteriosa è la prima causa di mortalità cardiovascolare. Dati epidemiologici dimostrano che circa il 10% dei pazienti con ipertensione ha una forma di ipertensione secondaria e, tra questi, quelli con ipertensione secondaria ad endocrinopatie sono il 15%.
Caso clinico: A.V., paziente maschio caucasico di 38 anni viene inviato dal proprio medico curante presso l'ambulatorio di ipertensione e prevenzione cardiovascolare edificio 1 dell' AOU 'Federico II' di Napoli per ipertensione arteriosa sisto-diastolica non adeguatamente controllata dalla terapia ed ipokaliemia (2.6 mEq/l). Durante la prima visita ambulatoriale si registrano i seguenti valori di pressione arteriosa: braccio sinistro in clinostatismo 160/110 mmHg; braccio destro in clinostatismo 165/110 mmHg; bilateralmente in ortostatismo 155/100 mmHg. Vengono eseguiti un tracciato elettrocardiografico ed un ecocolordoppler cardiaco che non evidenziano segni di cardiopatia ipertensiva o anomalie specifiche. La terapia in atto (Lercanidipina 20 mg 1 cp/die; Doxazosina 2 mg 1cp al mattino; Doxazosina 4 mg 1 cp ore 18:00 e KCL retard 3 cp/die) veniva implementata con canrenone 100 mg 1cp x 2/die e si programmava un ricovero in regime di Day Hospital per esecuzione di Risonanza Magnetica (RM) addome con mezzo di contrasto e test da carico salino. La RM rilevava la presenza un adenoma di 25x19 mm localizzato al surrene sx. Il test da carico salino eseguito secondo modalità standard (infusione di 2 litri di soluzione salina allo 0,9% per 4 ore e valutazione dei livelli di aldosterone e renina prima e dopo il test), rilevava livelli circolanti di aldosterone (768,3 pg/ml) e renina (<1,1 pg/ml), compatibili con una diagnosi di iperaldosteronismo. Si programmava quindi un ricovero in regime ordinario per esecuzione di Angio TC per reni e surreni e di sampling delle vene surrenaliche attraverso accesso in vena femorale. .A.V. veniva ricoverato presso il reparto di Medicina Interna, V piano edificio 1 dell'AOU Federico II ed il 25/10/2024 viene sottoposto alla procedura del sampling. Vengono raccolti campioni ematici della vena cava inferiore, vena surrenale dx e vena surrenale sx ai tempi 0 e 15 minuti per valutare i livelli di aldosterone, renina, 17 idrossiprogesterone e cortisolo. I valori di aldosterone risultano sensibilmente più alti nei campioni raccolti in vena surrenale sx. Tuttavia, essendo risultato non soppresso il test di ACTH da 1mg eseguito la sera prima dell' intervento,non è stata esclusa la possibilità che la neoformazione potesse essere anche cortisolo secernente (o comunque secernente altri steroidi). Inoltre, gli indici di lateralizzazione (calcolati mediante il rapporto tra la concentrazione di aldosterone/cortisolo in una vena surrenalica e la concentrazione di aldosterone/cortisolo nella vena surrenalica contro-laterale) non erano completamente a favore di una localizzazione sinistra della condizione di iperaldosteronismo. Considerati l'età di insorgenza dell'ipertensione arteriosa (<35 anni), l'unilateralità della lesione surrenalica evidenziata alle indagini strumentali, i livelli di aldosterone e renina prima e dopo test da carico idrosalino e l'ipokaliemia viene proposto ad A.V. un intervento di surrenalectomia sx che viene eseguito in data 13/12/2024 (figura 1). Il referto istologico conferma la natura secretoria mista dell' adenoma.Un mese dopo l'intervento, in assenza di terapia antiipertensiva, A.V. presentava i normali valori di pressione arteriosa e normali livelli di kaliemia (4,98 mEq/L). Si programma un test al Synacten per la valutazione della riserva surrenalica.
Conclusioni: L' iperaldosteronismo primitivo è una condizione rara. Tuttavia, è causa di un gran numero di casi di ipertensione secondaria. Le procedure di cardiologia interventista di sampling surrenalico e la successiva operazione chirurgica di surrenalectomia sx hanno permesso di migliorare decisamente il quadro pressorio ed elettrolitico del paziente. L'intervento chirurgico tuttavia potrebbe predisporre A.V. ad un quadro di ipocorticosurrenalismo e rende necessaria una valutazione periodica della riserva surrenalica tramite test da stimolo.

Figura 1. Surrene sx.

R.B.: MULTIPLE MYELOMA WITH HYPERCALCEMIA

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Introduzione: Il mieloma multiplo è un tumore delle plasmacellule, la cui presentazione clinica è definita dall'acronimo CRAB (ipercalcemia, insufficienza renale, anemia e lesioni ossee).
Presentazione del caso: Si presenta il caso clinico di una donna R.B., caucasica, di Casoria (NA), di 60 anni, giunta all'osservazione dell'equipe medica dell'UOSD "Emergenze mediche in oncologia ed ematologia" dell'edificio 1 dell'AOU "Federico II" di Napoli, il 29 Marzo 2024, per ipercalcemia (calcio corretto per albumina sierica pari a 12 mg/dl) in condizioni di normofosforemia (fosforo pari a 3.5 mg/dl) post intervento chirurgico di artroprotesi dell' anca destra per frattura patologica della testa del femore e dell'osso iliaco destro.
Nel 2018 la paziente è stata sottoposta, in un altro nosocomio, ad asportazione di meningioma cerebrale.
Nel mese di settembre 2023, in seguito ad una crisi epilettica di nuova insorgenza, è stata sottoposta, in un altro nosocomio, a TC encefalica che ha evidenziato la presenza di una massa che attraverso la teca cranica aveva infiltrato parte dell'encefalo, alterando le connessioni sinaptiche neuronali fisiologiche, con insorgenza ex novo di crisi epilettiche.
La massa è stata bioptizzata e l'esame istologico ha evidenziato infiltrazione cerebrale da mieloma multiplo. Alla fine del 2023, le è stata confermata la diagnosi di una forma aggressiva di mieloma multiplo, cioè con infiltrazioni midollari, costali, vertebrali e craniche, propriamente definita leucemia plasmacellulare.
All'inizio di marzo 2024, a causa di una frattura patologica del femore e dell'osso iliaco destro, è stata sottoposta, in un altro nosocomio, ad artroprotesi di anca destra.
All'ingresso nel nostro reparto, sono stati eseguiti esami ematochimici che hanno confermato un incremento dei livelli sierici di calcio, l'elettrocardiogramma di ingresso evidenziava un QTc nei limiti dell'intervallo di riferimento, pari a 400 millisecondi.
E' stata idratata e sottoposta a iniezione intra-muscolo di 100000 U.I. di colecalciferolo e successivamente all'infusione endovenosa di aminobifosfonati, quale l'acido zoledronico, alla dose di 4mg/5ml ml con azione antiriassorbitiva sull'osso, con conseguente normalizzazione della calcemia.
Durante il ricovero nel nostro reparto, considerando l'elevata proteinuria, nel sospetto di una coesistente amiloidosi è stato effettuato un ecocolordoppler cardiaco a riposo, una ecografia dell'addome e la biopsia del grasso periombelicale che ha escluso la presenza di amiloidosi, mentre l'esecuzione di una PET total body e di una biopsia osteo-midollare hanno confermato la diagnosi di mieloma multiplo.
Durante l'ospedalizzazione nel nostro reparto, dalla ferita chirurgica dell'intervento di artroprotesi fuoriusciva una secrezione siero-purulenta e maleodorante.
E' stato eseguito un tampone cutaneo sulla ferita chirurgica, il cui esame colturale è risultato positivo ad Acinetobacter Baumanii, batterio gram negativo, resistente a vari antibiotici.
Successivamente, la paziente è stata sottoposta ad artrocentesi d'anca; il colturale del liquido prelevato ha confermato la contaminazione batterica da parte di A.Baumanii, quindi l'infezione della protesi. I parametri vitali della paziente, nonostante l'infezione, si mantenevano stabili, presentando un SOFA score pari a 1.
In attesa della revisione chirurgica della protesi, le è stata somministrata una terapia antibiotica mirata con Merrem e Daptomicina.
Il 15 maggio 2024, è stata sottoposta a intervento chirurgico di revisione delle protesi dell'anca, con debridement e sostituzione della parte protesica infetta con un distanziatore rivestito da antibiotico.
L'infezione della protesi ha rallentato l'inizio del trattamento per il mieloma, che la paziente ha iniziato il 24 maggio 2024 con somministrazione sottocutanea, una volta alla settimana, di due anticorpi monoclonali: Bortezomib e Daratumumab, con la supplementazione di eritropoietina e filgrastim per sostenere l'anemia e la neutropenia importante, conseguente alla chemioterapia.
Dopo una settimana dalla prima chemioterapia, la paziente ha sviluppato faringodinia, febbre e sintomi influenzali, inizialmente supportata con antipiretici, idratazione e cortisone, sospendendo la somministrazione della seconda chemioterapia.
Entro 24 ore, i parametri vitali sono peggiorati drasticamente; la paziente è andata in shock settico con un Sofa score pari a 18 e nonostante l'ossigenoterapia e la somministrazione di Noradrenalina, dopo poche ore è morta.
Conclusione: La leucemia plasmacellulare è una forma rara e aggressiva di gammopatia monoclonale che per la presenza di plasmacellule disseminate nel sangue periferico si può considerare una malattia sistemica, con ripercussioni sul metabolismo minerale pericolose per la vita, quali l'ipercalcemia e le fratture patologiche. Una frattura patologica in un paziente immunocompromesso è molto rischiosa per la possibile evoluzione in sepsi. Sarebbe opportuno, come tale, valutare quotidianamente il SOFA score anche se il paziente si presenta apiretico e senza altri segni e sintomi clinici di infezione.

1PHENOAGE IS ASSOCIATED WITH IN-HOSPITAL MORTALITY IN NON-CRITICAL PATIENTS

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Backgroundand Aim: Biological ageing—the progressive functional and structural decline of an organism—has emerged as a key risk factor for age-related diseases and mortality. A recently developed biological clock model, PhenoAge, based on routine laboratory parameters, offers an estimate of biological age. This study aims to investigate the association between PhenoAge and clinical outcomes in multimorbid elderly patients hospitalized in the Internal Medicine Department and enrolled in the Clinical Outcomes in HOspitalized patients Receiving Treatment at San Andrea Hospital (COHORTS) study.
Methods: A total of 198 patients (100 men, 98 women), aged ≥65 years, were enrolled and stratified into tertiles according to PhenoAge. PhenoAge was computed using chronological age and nine biomarkers: albumin, creatinine, fasting glucose, log-transformed C-reactive protein (CRP), lymphocyte percentage, mean cell volume, red cell distribution width (RDW), alkaline phosphatase, and white blood cell (WBC) count. The Charlson Comorbidity Index was used to quantify multimorbidity. Associations between PhenoAge and clinical parameters were analyzed using univariate analysis, and logistic regression was employed to assess the relationship between PhenoAge and in-hospital mortality.
Results: The entire cohort had a mean chronological age of 80 ± 7 years and a mean PhenoAge of 92 ± 14 years. Patients in the highest PhenoAge tertile were more likely to be female and older. They had significantly higher levels of WBC, RDW, CRP, creatinine, uric acid, and fasting glucose, along with lower levels of red blood cells, hemoglobin, and albumin compared to those in lower tertiles. Elevated PhenoAge was also associated with a higher prevalence of diabetes ($p < 0.03$) and chronic kidney disease ($p < 0.001$). Importantly, individuals in the highest PhenoAge tertile exhibited a 4.6-fold increased risk of in-hospital mortality (OR 4.6, 95% CI 1.66–13.2), independent of sex and Charlson Comorbidity Index.
Conclusion: PhenoAge appears to be a promising predictor of adverse clinical outcomes in hospitalized, multimorbid elderly patients. These findings support the potential utility of biological age assessments in routine clinical practice. Further research is needed to explore its prognostic value across different healthcare settings.

IMPACT OF EMPAGLIFLOZIN AS ADD-ON TO METFORMIN VS METFORMIN CONTINUATION ON MASLD PROGRESSION IN TYPE 2 DIABETES: FINDINGS FROM THE PROSPECTIVE OBSERVATIONAL IMAGIN STUDY

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Background: MASLD is the leading cause of chronic liver disease, significantly contributing to morbidity and mortality. This study evaluated the effects of empagliflozin + metformin (combination therapy) versus metformin monotherapy (control) on MASLD progression in type 2 diabetes (T2DM) patients.
Methods: This single-center, prospective observational study included SGLT2i-naïve adults with metformin-treated T2DM, eGFR ≥45 mL/min/1.73 m², and MASLD. FibroScan®/CAP, biochemical, and anthropometric assessments were conducted at baseline, 6 months, and 12 months. An exploratory baseline analysis of miR-122 and miR-21 was performed.
Results: Eighty-eight patients were enrolled (47 controls, 41 combination therapy). At 12 months, combination therapy led to significantly greater improvements in BMI, ALT, HbA1c, CAP, and liver stiffness ($p < 0.05$). It was associated with higher odds of steatosis (OR 9.79, $p < 0.001$) and fibrosis improvement (OR 5.31, $p = 0.001$). Changes in BMI and HbA1c did not correlate with liver stiffness or CAP improvement. Exploratory miRNA analysis ($n = 17$) suggested potential associations between baseline miR-122 and steatosis improvement and miR-21 and fibrosis improvement.
Conclusions: Empagliflozin + metformin improved liver parameters more effectively than metformin alone in T2DM patients with MASLD. Baseline miR-122 and miR-21 may serve as potential biomarkers for steatosis and fibrosis improvement, respectively.

Table 1. Baseline clinical characteristics of the study sample

	BASELINE			
Variable	**Overall (n=88)**	**Control group (n=47)**	**Combination group (n=41)**	**p-value**
Age, mean (SD)	62 ± 11	63 ± 11	61 ± 11	0.423
Sex, n (%)				0.878
Male	48 (54.5)	26 (55.3)	22 (53.6)	
Female	40 (45.5)	21 (44.7)	19 (46.4)	
Hypertension, n (%)	58 (65.9)	28 (59.6)	30 (73.2)	0.323
Diabetes duration yrs, median [IQR]	5.0 [2.0-12.0]	3.0 [1.0-5.0]	10.0 [3.5-14.5]	**0.033**
Diabetes familiarity, n (%)	16 (18.2)	7 (14.9)	9 (21.9)	0.873
CAD familiarity, n (%)	5 (5.7)	1 (2.1)	4 (9.8)	0.225
IA familiarity, n (%)	15 (17.1)	5 (10.6)	4 (24.4)	0.208
Smoking habit, n (%)	30 (34.1)	15 (31.9)	15 (36.6)	0.664
ACEI, n (%)	19 (21.6)	13 (27.7)	6 (14.6)	0.141
ARB, n (%)	20 (22.7)	14 (29.8)	6 (14.6)	0.093
Diuretics, n (%)	13 (14.8)	8 (17.0)	5 (12.2)	0.527
Beta-blockers, n (%)	20 (22.7)	10 (21.3)	10 (24.3)	0.750
Alfa-blockers, n (%)	3 (3.4)	1 (2.1)	2 (4.9)	0.481
Ca antagonists, n (%)	6 (6.8)	3 (6.4)	3 (7.3)	0.863
Statins, n (%)	45 (51.1)	21 (44.7)	24 (58.5)	0.197
Antiaggregants, n (%)	14 (15.9)	6 (12.8)	8 (19.5)	0.492

SD standard deviation; IQR interquartile range; yrs years; CAD coronary artery disease; IA hypertension; ACEi angiotensin converting enzyme inhibitor; ARB angiotensin receptor blocker; Ca calcium

Table 2. Comparison of baseline and follow-up anthropometrical and laboratory data of the study sample

	PROGRESSION TIME								
	Time 0 (Baseline)			Time 1 (=6 months)			Time 2 (=12 months)		
Variable	**Control group (n=47)**	**Combination group (n=41)**	**p-value**	**Control group (n=47)**	**Combination group (n=41)**	**p-value**	**Control group (n=47)**	**Combination group (n=41)**	**p-value**
BMI, mean (SD)	30.8 (4.9)	29.8 (4.3)	0.180	31.4 (4.7)	28.4 (3.4)	**0.020**	30.7 (4.9)	28.5 (3.7)	**0.040**
SBP, mean (SD)	127.9 (8.7)	128.8 (18.4)	0.447	122.5 (15.2)	130.0 (17.4)	0.432	123.0 (8.6)	122.2 (9.4)	0.589
DBP, mean (SD)	75.8 (9.6)	70.0 (12.0)	0.532	75.0 (4.3)	80.0 (10.4)	0.505	77.3 (4.4)	75.0 (5.3)	0.397
HbA1c, median [IQR] (% and mmol/mol)	7.0 [6.3-7.5] 53 [45-58]	6.0 [7.2-8.8] 64 [55-73]	**0.001**	7.2 [6.3-7.5] 55 [45-58]	7.2 [6.8-7.9] 55 [51-63]	0.483	7.0 [6.5-7.5] 53 [45-58]	7.0 [6.5-7.5] 53 [48-58]	0.960
Ast, median [IQR]	34.0 [20.3-42.0]	42.0 [23.0-47.0]	0.420	18.0 [24.5-44.5]	41.5 [24.0-46.5]	0.602	34.0 [24.0-43.0]	30.0 [20.0-44.3]	0.595
Alt, median [IQR]	44.0 [24.3-84.3]	68.5 [41.50, 88.00]	0.215	44.5 [33.5-48.3]	45.00 [38.00, 48.00]	**0.020**	31.0 [32.0-70.0]	40.0 [22.3-45.0]	**0.001**
Platelet (x10^3/uL), median [IQR]	210.0 [143.5-258.3]	239.5 [203.0-290.0]	**0.015**	220.5 [147.0-242.5]	237.0 [199.5-290.0]	0.103	231.0 [147.0-261.0]	230.0 [201.3-255.0]	0.597
Albumin, median [IQR]	4.3 [3.8-4.4]	4.0 [3.8-4.3]	0.310	4.2 [3.9-4.3]	4.1 [3.9-4.4]	0.920	4.2 [3.9-4.3]	4.0 [3.9-4.2]	0.252
Uric acid, median [IQR]	5.3 [3.9-6.1]	4.7 [4.2-6.2]	0.853	5.3 [4.2-6.5]	4.4 [3.4-5.3]	0.584	4.5 [4.4-6.5]	4.6 [3.8-7.7]	0.795
eGFR, median [IQR]	91.4 [78.5-95.8]	83.0 [67.0-84.7]	0.268	90.7 [77.0-107.0]	81.0 [63.0-87.6]	0.297	86.0 [76.0-94.0]	91.0 [78.8-98.9]	0.731
Stiffness kPa, median [IQR]	7.2 [5.5-9.5]	7.1 [4.6-9.9]	0.927	7.3 [5.5-9.9]	6.8 [5.1-8.2]	0.557	7.4 [6.0-8.6]	6.2 [4.7-7.4]	**0.017**
CAP, median [IQR]	280.0 [246.0-319.5]	287.0 [267.8-305.8]	0.330	284.0 [246.0-313.0]	287.0 [259.0-282.0]	0.131	281.0 [233.3-328.8]	250.0 [236.3-288.8]	**0.008**
FIB-4, median [IQR]	1.3 [1.0-2.2]	1.5 [1.2-2.7]	0.687	1.5 [1.1-1.8]	1.4 [1.3-1.6]	0.895	1.4 [1.1-1.7]	1.5 [1.3-1.4]	0.328

BMI body mass index; SD standard deviation; SBP systolic blood pressure; DBP diastolic blood pressure; HbA1, glycated haemoglobin; IQR interquartile range; AST aspartate aminotransferase; ALT alanine aminotransferase; CAP controlled attenuated parameter; FIB-4 fibrosis-4; eGFR estimated glomerular filtration rate

THE ROLE AND MOLECULAR MECHANISM OF ANABOLIC ANDROGENIC STEROIDS IN HEPATOCARCINOGENESIS

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Anabolic androgenic steroids (AAS) are a class of hormones employed in hormone replacement therapy for male hypogonadism and, to a lesser extent, for other medical conditions such as certain forms of anemia and in the female-to-male gender transition process. However, AAS are frequently misused for their anabolic properties, particularly for enhancing muscle mass and physical strength. Among their adverse effects, androgens can exert hepatotoxic actions and promote hepatocyte proliferation, potentially leading to malignant transformation. Hepatocellular adenoma (HCA) and hepatocellular carcinoma (HCC) are two primary liver neoplasms that have been linked to AAS exposure. Our review presents an up-to-date analysis of the molecular mechanisms by which androgens may drive liver carcinogenesis, among them the Wnt/β-catenin pathway seems to have the highest amount of evidence.
Both androgens and estrogens play intricate roles in hepatocarcinogenesis, significantly influencing the pathogenesis and progression of HCA and HCC. Their reciprocal interaction exerts profound effects on the development of these liver neoplasms, indicating the involvement of endocrine regulatory mechanisms that remain only partially elucidated. Due to this complexity, a deeper understanding of the role of sex hormones within the hepatocellular microenvironment is essential. Enhanced insight into androgen-mediated regulation of hepatocyte proliferation may contribute to a better understanding of HCC pathogenesis and potentially facilitate the identification of novel and highly specific therapeutic targets, thereby expanding current treatment strategies.
In light of the increasing prevalence of non-medical use of AAS, it is imperative for healthcare professionals to recognize the elevated risk of liver tumors in a patient population that is typically young and does not present with traditional risk factors for chronic liver disease.
The available literature on this topic is relatively outdated, which limits the reliability of prognostic assessments, especially considering the considerable advancements in diagnostic techniques and therapeutic approaches for HCA and HCC in recent years.

SEPTIC SOURCE MATTERS: HOW INFECTION SITE AND MICROBIAL ETIOLOGY AFFECT SEPSIS PROGNOSIS

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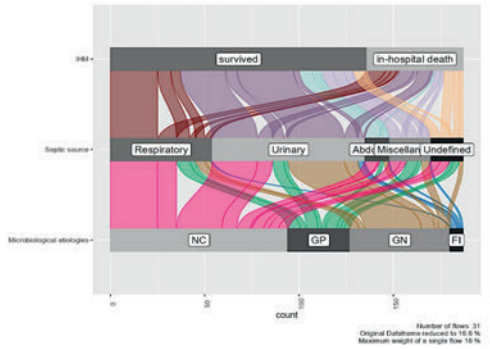
Background: Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. Despite advances in critical care, mortality remains high. This study assesses the relationship between septic source, microbial etiology, and in-hospital mortality.
Methods: This prospective observational study was conducted at the St. Anna University Hospital of Ferrara, Italy, from October 2021 to February 2022. Adult patients with suspected sepsis and a qSOFA score ≥ 2 were included. Data collected included vital signs, laboratory values, septic source classification, microbial etiology, and in-hospital mortality. Statistical analyses were performed using SPSS and jamovi, with an alluvial diagram to visualize relationships.
Results: Of 200 screened patients, 187 were included (mean age 85.0±9.6

years). In-hospital mortality was 27.3%. The most common septic sources were urinary (43.3%) and respiratory (28.9%), followed by miscellaneous (11.8%), abdominal (7.0%), and undefined (9.1%). Undefined sources had the highest mortality (58.8%), followed by respiratory (31.5%) and urinary sepsis (22.2%) (p=0.002). Microbial etiology varied by source, with negative cultures (50.3%) being the most common result. No direct association between microbial etiology and mortality was found (p=0.470), but mortality differed when analyzed in conjunction with septic source. The alluvial diagram highlighted complex interactions between infection site, microbial etiology, and survival demonstrating that the septic source significantly impacts in-hospital mortality (p=0.012).
Conclusion: Septic source significantly impacts in-hospital mortality, with undefined infections carrying the highest risk. The interplay between microbial etiology and infection site influences outcomes. Early infection source identification and tailored antimicrobial strategies are crucial for improving sepsis management.

Figure 1. Alluvial diagram illustrating the relationship between microbial etiology, septic source, and in-hospital mortality. The septic source significantly impacts in-hospital mortality (p= 0.012).



Note: FI: Fungal infection; GN: Gram negative; GP: Gram positive; NC: Negative culture.

ACUTE ONSET OF BILATERAL MYDRIASIS, HEADACHE AND VOMITING: NOT A TYPICAL INTRACRANIAL HYPERTENSION CASE

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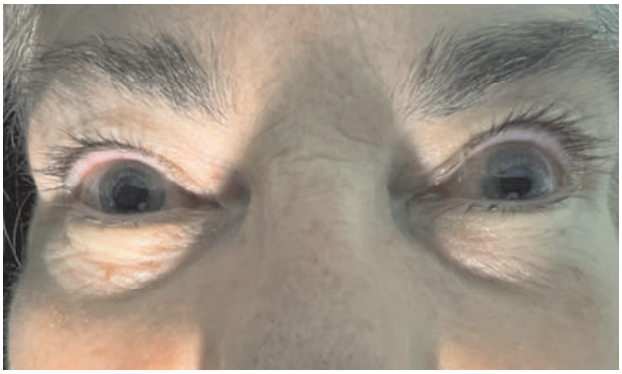
We report the unusual case of a 65-year-old woman who presented to the Emergency Department (ED) with acute bilateral mydriasis, severe headache, blurred vision, photophobia, and vomiting, following a recent episode of fever with respiratory symptoms. At initial evaluation, she was alert and afebrile, with normal vital signs except for transient hypertension. Clinical examination revealed bilateral mydriasis with poor light reactivity, but no focal neurological deficits or meningeal signs. Given the concerning constellation of symptoms, an urgent diagnostic work-up was undertaken to investigate potential neurological, infectious, or toxicological causes, including brainstem pathology, intracranial hypertension, serotonin syndrome, and meningoencephalitis.
Cranial CT with contrast was unremarkable. Laboratory tests showed mild leukocytosis and elevated C-reactive protein. Lumbar puncture revealed clear cerebrospinal fluid with mild neutrophilic pleocytosis and no microbiological evidence of infection. Empiric therapy with ceftriaxone, ampicillin, and acyclovir was initiated and later de-escalated based on negative findings. A neurologist suggested the possibility of dextromethorphan-related toxicity, as the patient had recently taken an over-the-counter cough suppressant.
Approximately 19 hours after presentation, the patient developed ocular pain, conjunctival hyperemia, and worsening visual acuity. An ophthalmologic consultation revealed markedly elevated intraocular pressure (57 mmHg), corneal edema, and narrowing of the anterior chamber in both eyes, leading to the diagnosis of bilateral acute angle-closure glaucoma. Immediate treatment with intravenous mannitol, oral acetazolamide, topical beta-blockers, and miotic agents was initiated, followed by YAG laser peripheral iridotomy after corneal clarity improved. The patient's condition rapidly improved, and she was discharged in good clinical status after four days.
This case underscores the diagnostic challenges posed by atypical presentations of ophthalmological emergencies. Bilateral acute angle-closure glaucoma is rare, as the condition typically presents unilaterally with eye pain and visual disturbances. The absence of ocular pain and conjunctival injection at first contact misled the diagnostic process toward neurological and infectious etiologies. The case illustrates the importance of re-evaluating clinical findings over time and maintaining a broad differential diagnosis, especially when initial investigations are inconclusive.
Furthermore, it highlights the value of a multidisciplinary approach involving emergency physicians, neurologists, infectious disease specialists, and ophthalmologists in reaching an accurate diagnosis and initiating timely treatment in rare and deceptive clinical scenarios.



THE LONG-TERM EFFECTS OF SIRNA VS PSCK9I AND STATINS THERAPY ON SUBCLINICAL CARDIOVASCULAR DAMAGE

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Background: The reduction of LDL-c circulating levels is the primary target of hypolipidemic therapies to improve clinical prognosis in patient with cardiovascular diseases.. New therapeutic strategies have been developed proprotein convertase subtilisn/kexin type 9 (PCSK9) inhibitors (Evolocumab and Alirocumab), and recently small interfering RNA (siRNA) therapy (Inclisiran).
Purpose: Our purpose was to evaluate the effects of si-RNA vs PCSK9i and statins therapy, in patients with established coronary artery disease or at high cardiovascular risk who were statin-intolerant and/or not reaching the target of LDL-C<55 mg/dl; study enpoints was a 15% improvement in GLS and a reduction of 1 m/sec of PWV.
Methods: We enrolled 158 patients with mean age 67.12+9.09 years, 79.1% was man. Among the PCSK9i's population (83 patients), 87.9% showed Ischemic Heart Disease (IHD), 38.8% Chronic Kidney Disease (CKD), 44.5% Type 2 Diabetes Mellitus (T2DM), 43.4% Chronic Heart Failure (CHF), 30.1%. Concerning the Inclisiran's population (36 patients), 75% showed IHD 69.4% CKD, 36.1% T2DM, 52.7% CHF NYHA. Regarding the Statin+Ezetimibe population (39 patients), 66.6% showed IHD (79.4% CKD, 28.2% T2DM, 53.8% CHF. Initially all patients were treated with high-intensity statins and Ezetimibe. Statin intolerance was defined as documented side effects of at least three statins including low dose statins.
Results: After 18 months follow-up we observed a significant reduction of LDL-c (ΔPCKS9i = -66.6%; ΔInclisiran 63.5%; ΔStatin+Ezetimibe 44.4%, p<0.0001); and reduction of high-sensitivity C-reactive protein , from 2 (1.0-4.5) to 1.8 (0.9-3.2) mg/l, p<0.0001. The improvement of 15% of GLS was observed in 61 patients (38.6% of all population), the endpoint was obtained in the siRNA group (69.4%), followed by PCSK9i (31.1%) and Statin+Ezetimibe (25.6%) (p=0.0007). Regarding 1 m/sec reduction of PWV, the achievement of the endpoint was obtained in 71 patients (44.9% of all population); respectively siRNA group 72.2%, PCSK9i 42.1% and Statin+Ezetimibe 25.6% (p=0.0002). Stepwise multivariate logistic regression model show that, siRNA was associated with a 5.42-fold improvement in 15% GLS (OR 5.429; 95% CI: 2.418-12.191, p<0.001)and a 5.57-fold reduction in PWV of 1 m/sec (OR 5.574; 95% CI: 2.321-13.384, p<0.001); finally, the presence of ischemic heart disease showed a statically significant association with a 65% reduced probability of 1 m/s reduction in PWV (OR 0.355; 95% CI: 0.156-0.808; p=0.014).
Conclusion: Our study demonstrated that siRNA therapy was able to improve global cardiac performance, to reduce arterial stiffness and inflammation indices . Our results could be partially explained by an improvement of lipid profile associated to a reduction of CV events, and by reduction of inflammation state, which is responsible of atherosclerosis and CV diseases.

EARLY EFFECT OF ESSENTIAL AMINO ACID SUPPLEMENTATION ON CARDIAC PERFORMANCE IN ELDERLY PATIENTS WITH HEART FAILURE AND SARCOPENIA

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Background: Sarcopenia is syndrome characterised by the progressive loss of muscle mass and strength, which affects approximately 20% of patients with chronic heart failure (CHF) compromising quality of life and prognosis. Today, no specific metabolic therapy exists, but these interventions may improve cardiac function and muscle performance.
PORPOUSE: The aim of this study was to evaluate the early effects of supplementation with free-form essential amino-acids on cardiac and muscular performance in elderly patients with CHF and sarcopenia.
Methods: We enrolled 60 caucasian patients affected by heart failure with reduced ejection fraction (HFrEF) NYHA class II (35%) and class III (65%), and sarcopenia; mean age was 80.1±1.1 years; 78% was male. Patients were on optimal medical therapy and received nutritional supplementation with essential amino acid preparations (L-Leucine 2500mg, L-Isoleucine 1250mg, L-Valine 1250mg) twice daily. A simple linear regression model was performed, with the changes in Global Longitudinal Strain (GLS) between baseline and follow-up as the dependent variable. Variables that correlated significantly were entered into a stepwise multivariate regression model to assess the degree of correlation with the dependent variable.
RISULTS: Following 6 months of therapy we observed, a significant improvement in clinical symptoms (KCCQ-CS 60.9±1.4 vs 64.6±1.6pt, p=0.001) and enhancement in muscle and physical performance parameters (Hand grip strength increased from 18.9±5.3kg to 21.5±5.2kg, p<0.0001; Short Physical Performance Battery score increased from 5.2 ± 1.7 to 6.8±1.7 p<0.0001). The echocardiographic parameters exhibited improvement in VTDVS/BSA (from 90.1±9.0 to 82.5±9.9 ml/m2, p<0.0001); Left Ventricular Ejection Fraction (from 34.3±1.5 to 35.8±1.7. %, p<0.0001); GLS (from -8.5±1.1 to -11.9±1.2%, p<0.0001). Significant improvements were observed in HbA1c, LDL-cholesterol and triglycerides, with reduced levels of the oxidative stress biomarkers Nox-2 (from 0.7±0.1 to 0.5±0.1 nmol/L, p<0.0001) and 8-isoprostane (from 73.2±10.7 to 54.9±9.9 pg/mL, p<0.0001) and reduced circulating levels of hs-CRP (from 7.6±0.5 to 6.8±0.5 mg/l, p<0.0001). The multivariate stepwise regression model, with ΔGLS as the dependent variable, demonstrated that changes in hs-CRP, HOMA, and Nox-2 exhibited a significant correlation with the dependent variable. The entire model exhibited a correlation of 43.7% with changes in GLS.
Conclusion: This study support the early use of essential aminoacids in patients with HFrEF and sarcopenia, confirming its clinical, biochemical and metabolic benefits and how its use can improve muscular and cardiac performance.

RECOVERY OF ADAMTS13 ACTIVITY IN IMMUNE THROMBOTIC THROMBOCYTOPENIC PURPURA: A RETROSPECTIVE STUDY

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Background: Caplacizumab has revolutionized and improved the treatment of immune thrombotic thrombocytopenic purpura (iTTP). However, recent studies suggested that caplacizumab may lead to delayed normalization of ADAMTS13 activity.
Aims: To assess the recovery of ADAMTS13 activity in patients with acute iTTP treated with or without caplacizumab.
Methods: In a retrospective analysis we compared data of acute iTTP cases treated with or without caplacizumab between 2017 and 2024 at the University Hospital of Verona (Italy).
Results: Data of 14 acute iTTP cases in 9 patients (2 males and 7 females) were available. The main clinical and therapeutic characteristics of iTTP cases treated with (n=8) or without (n=6) caplacizumab are summarized in Table 1A. Caplacizumab-treated iTTP cases showed a statistically non-significant trend to both a lower median number of plasma exchange (PEX) and a longer time to achieve ADAMTS13 activity of either 10% or 20% (Table 1A). High initial levels of anti-ADAMTS13 IgG antibody, defined as above the median value (≥52 U/mL) and more frequent in males and younger subjects, were associated with significantly higher PEX number and longer time to recovery of ADAMTS13 activity (Table 1B). A significant interaction was found between anti-ADAMTS13 IgG levels and therapy with caplacizumab in predicting the number of PEX which was the largest in cases with high levels of anti-ADAMTS13 IgG and not treated with caplacizumab (Figure 1A). On the other hand, an additive effect was observed for time to recovery of ADAMTS13 activity which increased from the cases with low levels of anti-ADAMTS13 IgG and not treated with caplacizumab to those with high levels of anti-ADAMTS13 IgG and treated with caplacizumab (Figure 1B).
Conclusions: In acute iTTP cases there could be an interaction between treatment with caplacizumab and initial levels of anti-ADAMTS13 antibodies in modulating PEX requirement and time to recovery of ADAMTS13 activity.

1A)

	iTTP cases treated with caplacizumab (n=8)	iTTP cases treated without caplacizumab (n=6)
First episode/Recurrence (n/n)	5/3	2/4
Males/Females (n/n)	1/7	3/3
Age (years)	55 (19-75)	64 (38-73)
Corticosteroids (n)	8	6
Rituximab (n)	4	4
Caplacizumab (n)	8	0
Number of PEX (n)	7 (4-12)	11 (5-25)
Anti-ADAMTS13 IgG antibody initial level (U/mL)	55 (6-100)	42 (19-95)
Time from first PEX to ADAMTS13 activity of >10% (days)	31 (5-72)	18 (6-48)
Time from first PEX to ADAMTS13 activity of >20% (days)	34 (5-76)	18 (6-48)

1B)

	iTTP cases with anti-ADAMTS13 IgG antibody <52 U/mL^ (n=7)	iTTP cases with anti-ADAMTS13 IgG antibody ≥52 U/mL (n=7)
First episode/Recurrence (n/n)	2/5	5/2
Males/Females (n/n)	0/7	4/3*
Age (years)	72 (53-75)	40 (19-58)*
Corticosteroids (n)	7	7
Rituximab (n)	3	5
Caplacizumab (n)	4	4
Number of PEX (n)	6 (4-10)	12 (6-25)*
Anti-ADAMTS13 IgG antibody initial level (U/mL)	21 (6-46)	71 (57-100)*
Time from first PEX to ADAMTS13 activity of >10% (days)	8 (5-72)	37 (22-69)
Time from first PEX to ADAMTS13 activity of >20% (days)	8 (5-72)	43 (24-76)*

*; p <0.05 by Mann-Whitney test or by Fisher's exact-test

Table 1. 1A 1B

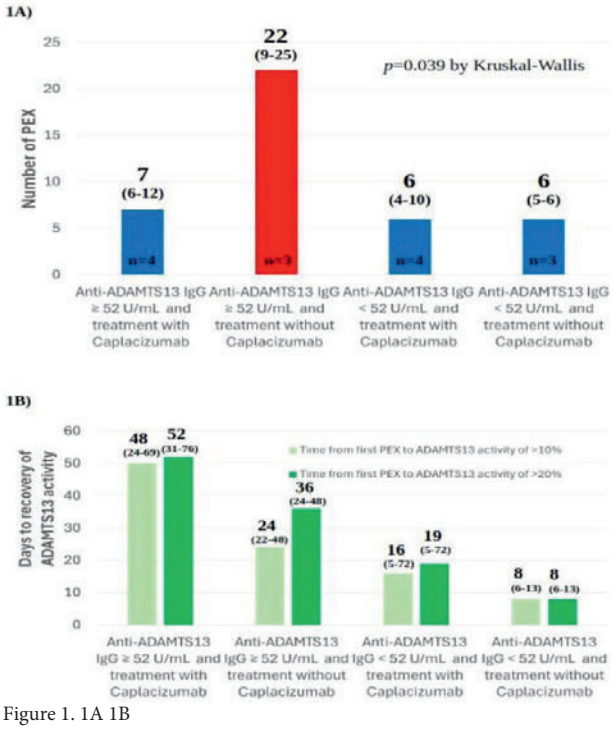

Figure 1. 1A 1B

PROGNOSTIC ROLE OF SERUM ALBUMIN IN ELDERLY PATIENTS WITH NON-VALVULAR AF

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Background: Atrial fibrillation (AF) is the most common arrhythmia in the elderly, and is associated with an increased risk of cardiovascular events (CVE). Hypoalbuminemia is an independent predictor of all-cause and cardiovascular mortality in general population.Therefore, the purpose of this work is to evaluate the possible predictive value of serum albumin (SA) on MACE occurrence, in a cohort of elderly patients with Non-valvular AF and several comorbidities for long-term follow-up.
Methods: 1057 elderly with non-valvular AF were enrolled (75.92 ±6.1years; 295 on VKAs and 762 on DOACs) and stratified according to median value of SA, 532 patients with SA ≤3.6 g/dl and 525 patients with SA >3.6 g/dl. MACE (non-fatal ischemic stroke, non-fatal myocardial infarction, and cardiovascular death), and non-cardiovascular mortality occurrence were evaluated during a median follow-up of 5.5 years (IQR 2.1-7.2).
Results: In the whole observational study, patients with SA ≤ 3.6 g/dL enhanced the risk of MACEs by 66%. In addition, 10 years of age, a 2MACE score > 4 pt and female gender are associated with an increased risk of MACE; in contrast, therapy with SGLT2i, DOACs and statins are associated with a reduced risk of MACE.
Conclusion: Elderly patients with Non-Valvular AF with SA ≤ 3.6 g/dL show a higher risk of MACE and non-cardiovascular mortality.

SLCO1B1 AND FEMALE GENDER ARE RISK FACTOR FOR STATIN INTOLERANCE IN PATIENTS WITH HYPERCHOLESTEROLEMIA INDEPENDENTLY FROM FH MUTATION

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Background: and Objectives: The aim of this study is to analyze lipid target achievement in patients attending our dyslipidemia center using real-life data. The presence of the SCLO1B1 mutation were evaluated to identify potential differences in achieving lipid targets and statin intolerance, in patients with hypercholesterolemia with and without FH.
Methods: The study involved 185 patients (96 females, 89 males), stratified based on the presence or absence of familial hypercholesterolemia (FH+ and FH-). All patients underwent genetic analysis as part of the LIPIGEN project, screening for mutations in LDLR, APOB, PCSK9, LDRAP1, LIPA, SLCO1B1, and ABCB1. Data were collected and analyzed to assess lipid target achievement and statin intollerance, comparing results by gender and SCLO1B1 mutation status.
Results: Females showed greater difficulty compared to males, associated with a higher rate of statin intolerance. Patients with a positive SCLO1B1 mutation demonstrated slightly more difficulty in achieving lipid targets. Mutations in LDRAP1, LIPA, and ABCB1 genes were found in several patients, distributed evenly regardless of gender or the presence of the SCLO1B1 mutation.
We further subdivided our patients as follows:
Men with FH+
Women with FH+
Men with FH-
Women with FH-
Conclusions: Likely, female gender and the presence of the SCLO1B1 mutation are two independent risk factors both for achieving lipid targets and for the degree of statin intolerance. Although limited to a single-center study, these results suggest that older individuals, women, obese patients, and carriers of the SCLO1B1 mutation face greater challenges in reaching lipid goals. Further multicenter studies are needed to confirm these trends and improve dyslipidemia management in more vulnerable patient subgroups.

CLINICAL IMPACT OF SYNDROMIC MOLECULAR PANELS IN THE EARLY IDENTIFICATION OF PNEUMONIA ETIOLOGY IN THE EMERGENCY DEPARTMENT: RESULTS FROM THE HCAPPED-II CASE-CONTROL STUDY.

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Background: Pneumonia remains the leading cause of infectious mortality worldwide and is among the most common reasons for emergency department (ED) visits and hospital admissions. In recent years, partly due to the over-prescription of antibiotics, the incidence of pneumonia caused by antibiotic-resistant bacteria (ARBs) originating from the community has increased. Since the initial treatment of pneumonia is generally empirical, it is crucial to identify patients who may require antibiotic coverage against ARBs. To overcome the limitations of conventional diagnostic methods novel molecular techniques, such as syndromic molecular panels (SMPs), have been introduced. These panels can be performed on respiratory samples such as BAL (bronchoalveolar lavage), BAS (bronchoaspirate), and ETA (endotracheal aspirate).
Materials and methods: This was a monocentric, retrospective-prospective observational study. Two non-contemporaneous populations of patients with healthcare-associated pneumonia (HCAP), defined according to the 2005 IDSA/ATS criteria, were enrolled: a) A prospective cohort of patients with HCAP who underwent respiratory sample collection (BAL, BAS, ETA), processed using a syndromic molecular panel (BioFire FilmArray Pneumonia panel), and were subsequently treated with targeted antibiotic therapy (results available within approximately 1 hour);b) A retrospective cohort of patients treated with standard empirical antibiotic therapy.
The BioFire FilmArray Pneumonia panel detects 15 bacterial pathogens, 9 viral pathogens, 3 atypical pathogens, and 7 resistance genes.
The primary objective of the study was to assess whether the use of SMPs had a clinical impact in terms of 30-day mortality reduction, decreased length of hospital stay, and reduced 30-day readmission rates.
Results: Between January 1st, 2023, and December 30th, 2024, a total of 472 patients with HCAP who presented to the ED of Careggi University Hospital and met the study's inclusion criteria were enrolled. Of these, 93 patients underwent respiratory sample collection, testing with SMPs, and were treated with targeted therapy between January 1st and December 31st, 2024.The control group consisted of 379 patients treated with standard antibiotic therapy, retrospectively selected among those who accessed the ED between January 1st and December 31st, 2023.
The length of hospital stay was significantly lower in the group treated with targeted antibiotic therapy guided by SMP results (p=0.047), with an average duration of hospitalization 25% shorter, as demonstrated by Cox regression analysis (HR 0.75, 95% CI 0.57–0.99).The 30-day readmission rate was also significantly lower in the targeted therapy group, at 7.3% vs. 16.9% (p=0.045). Regarding 30-day mortality, logistic regression analysis showed a lower mortality rate in the group treated with SMP-guided therapy. Early SMP testing on BAL/BAS/ETA samples in the ED was identified as a potential protective factor, with an OR of 0.55 (95% CI 0.43–0.68) in multivariate analysis.Additionally, Cox regression analysis showed that treatment guided by BAL sampling was associated with an HR of 0.65 (p=0.01).
Conclusions: This case-control study support the clinical utility of integrating SMPs on BAL/BAS/ETA samples into routine practice for the management of patients with HCAP and risk factors for MDR pathogens, to improve clinical outcomes and reduce rehospitalization rates.However, these preliminary results need confirmation through studies involving larger populations and randomized sampling. Careful evaluation and selection of patients who may benefit from this diagnostic and therapeutic approach—based on severity criteria and co-morbidities—remain essential.

FBS-ASAP: FIBROBRONCHOSCOPY IN ASPIRATION PNEUMONIA IN THE EMERGENCY DEPARTMENT. A PROSPECTIVE OBSERVATIONAL STUDY

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Background: Aspiration pneumonia (AP) is a frequent diagnosis among patients with pneumonia evaluated in the Emergency Department (ED). These patients are often burdened with multiple comorbidities, and AP represents a

significant cause of morbidity and mortality; in other cases, AP may complicate pre-existing conditions such as polytrauma, epilepsy, stroke, or coma. Therapeutic management typically includes antibiotic therapy, oxygen supplementation, and supportive care. Additionally, airway secretion clearance is frequently performed using one of two main techniques: laryngotracheal aspiration (LTA) or fibrobronchoscopic aspiration (FBA). Despite the widespread use of both methods, there is currently a lack of studies directly comparing their clinical outcomes.

Materials and methods: This prospective, single-center, observational pilot study was conducted in the Emergency Department of Careggi University Hospital, Florence, Italy. Adult patients with radiological evidence of pneumonia, a clinical diagnosis of aspiration pneumonia (AP), and requiring high-flow oxygen therapy were included between December 12, 2023, and December 31, 2024. Fibrobronchoscopic aspiration (FBA) was performed by trained emergency physicians with specific expertise in the procedure. Patients were divided into two groups based on the airway clearance technique received—FBA or laryngotracheal aspiration (LTA)—and were prospectively enrolled following the procedure.

The primary endpoints were 30-day mortality and length of hospital stay. Secondary endpoints included level of care upon admission, changes in the Horowitz index and oxygen delivery device, and procedure-related complications. Statistical analysis was conducted on the entire sample and subsequently on a 1:1 propensity score–matched (PSM) population to reduce potential selection bias.

Results: 257 patients with a mean age of 78,0±15,2 years were included in the study. 65.2% were males. Most frequent underlying conditions were cardiovascular disease (66.7%) and COPD (40.6%). The mean time from symptom onset to hospital admission was 2.9 days. Fever (67.9%) and dyspnea (60.9%) were the most common symptoms. CURB-65 was ≥2 in 52.9% and PSI class IV-V in 39.1%.

There were no significant differences between LTA and FAB groups regarding 30-day mortality (37.7% FBA group vs 32% LTA group; p=0.28) and length of hospital stay (11.8±11.0 days FBA vs 9.5±9.1 days LTA group; p=0.45). No significant differences were observed for all secondary outcomes among the two groups. Also considering selected population based on PSM, no significant differences were observed, confiming the previous results.

Conclusion: In this study, we evaluated the efficacy of bronchial toilet performed via FBA versus LTA suction in patients diagnosed with aspiration pneumonia. No statistically significant differences were identified between the two approaches regarding mortality or hospital length of stay. Both interventions demonstrated favorable safety profiles, with only minor complications reported and no procedure-related fatalities.Despite technological progress in both diagnosis and treatment, the consistently high mortality rate associated with aspiration pneumonia highlights the necessity for larger-scale studies employing more robust experimental methodologies. Such investigations are essential to better define the indications, risk-benefit ratio, and cost-effectiveness of these two airway clearance strategies in this clinical context.

CLINICAL IMPACT OF DIFFERENT EMPIRICAL ANTIBIOTIC THERAPY REGIMENS IN PATIENTS WITH COMMUNITY-ACQUIRED PNEUMONIA IN DIFFERENT CURB65 RISK CLASSES: A COHORT STUDY OF PATIENTS ADMITTED TO THE EMERGENCY DEPARTMENT OF A TERTIARY CARE HOSPITA.

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Introduction: Community-acquired pneumonia (CAP), with or without risk factors for multidrug-resistant (MDR) pathogens, is one of the leading causes of hospitalization in emergency departments and requires prompt and effective empiric antibiotic therapy, which is often guided by disease severity and the presence of specific risk factors. The appropriate selection of antibiotics is crucial to reduce both morbidity and mortality. However, antibiotics are frequently marketed without randomized studies directly comparing the efficacy of different antibiotic regimens. This study aims to compare the effectiveness of first-line versus second-line antibiotic regimens in the treatment of CAP, stratified by CURB-65 risk classes.

Methods: This retrospective cohort study analyzed data extracted from the electronic health records of the Emergency Department at AOU Careggi. All patients admitted between January 1, 2022, and December 31, 2022, with a diagnosis of pneumonia and treated with antibiotics were included. Patients were stratified according to their CURB-65 score. The primary objective was to assess differences in mortality and hospital length of stay between patients receiving different antibiotic regimens and different risk classes. Antibiotic treatments were categorized as first-line (Amoxicillin, Amoxicillin/Clavulanic Acid, Ceftriaxone and other parenteral or oral cephalosporins, Azithromycin and other macrolides, Levofloxacin) and second-line therapy (Piperacillin/Tazobactam, Meropenem and other carbapenems, Linezolid, Vancomycin).

Results: During the study period, 99,620 patients were evaluated in the Emergency Department, of whom 1,782 (1.8%) were diagnosed with pneumonia. Among these, 1,347 patients (75.6%) received antibiotic therapy directly in the ED: 986 (73.2%) were treated with first-line empiric antibiotic therapy, while 361 (26.8%) received second-line therapy.

The study population had a mean age of 75.1 ± 16.8 years, with females accounting for 46.5%. The mean CURB-65 score was 2.41 ± 0.93. ROC analysis showed an AUC of 0.724 (95% CI: 0.691–0.753; p<0.001).

The overall 30-day mortality rate was 20.8%. Mortality was significantly lower in patients treated with first-line antibiotics (15.7%) compared to those receiving second-line therapy (38.9%, p<0.001) (Figure 1).

Mortality across the CURB-65 risk classes was as follows:

Low risk (CURB-65 <2): 8/213 (3.7%)

Intermediate risk (CURB-65 = 2): 75/550 (13.6%)

High risk (CURB-65 >2): 197/554 (35.5%) (p<0.001)

When stratified by CURB-65 class and antibiotic regimen, 30-day mortality was consistently higher in patients treated with second-line therapy:

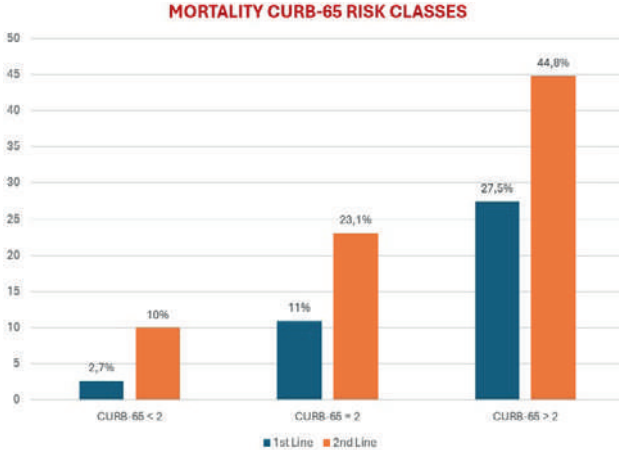
CURB-65 <2: 5/183 (2.7%) in first-line vs. 3/30 (10%) in second-line (p=0.087)

CURB-65 = 2: 47/429 (11%) in first-line vs. 28/121 (23.1%) in second-line (p<0.001)

CURB-65 >2: 103/374 (27.5%) in first-line vs. 94/210 (44.8%) in second-line (p<0.001)

In multivariate analysis, treatment with second-line antibiotics was independently associated with increased 30-day mortality (OR 2.5, 95% CI: 1.8–3.1; p=0.024).

Conclusions: This study revealed significant differences in clinical outcomes among pneumonia patients treated with first- and second-line antibiotics across different CURB-65 risk classes. Patients treated with second-class antibiotics had a higher mortality which can be largely explained by the greater severity of the disease, however these findings suggest that the use of second-line antibiotics should be carefully considered, particularly in higher-risk patients, balancing the potential therapeutic benefit against the increased mortality risk observed in multivariate analysis. Further studies—ideally randomized controlled trials—are warranted to confirm these results, keeping in mind the principle that sometimes "less is more."



GENDER DIFFERENCES IN THE PERFORMANCE OF THE CHEST PAIN SCORE AND MODIFIED HEART SCORE IN RISK STRATIFICATION FOR CARDIAC EVENTS IN PATIENTS PRESENTING TO THE EMERGENCY DEPARTMENT WITH CHEST PAIN

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Background: Early risk stratification of patients with chest pain (CP) is crucial. Gender differences in CP presentation may affect the accuracy of clinical scores. Women often present with atypical symptoms, potentially leading to misclassification and missed diagnoses.

Purpose: To assess the performance of the Chest Pain Score (CPS) (Table 1)

and modified HEART score (mHS) in predicting major adverse cardiac events (MACE) in male and female patients.

Chest Pain Score		Score
Location	Substernal, precordial	+3
	Left hemitorax, neck, jaw, epigastrum	+2
	Apical	−1
Character	Crushing, pressing, squeezing	+3
	Heaviness, tightness	+2
	Sticking, stabbing, pinprick, catching	−1
Radiation	Either arm, shoulder, back, neck, jaw	+1
Associated symptoms	Dyspnoea, nausea, diaphoresis	+2
Score < 4: Low probability of angina pectoris **Score ≥ 4:** Medium-high probability of angina pectoris		

Methods: This single-center, prospective observational study is a secondary analysis of a database containing prospectively collected data from patients presenting to the emergency department (ED) with CP as their primary symptom (1st Jan 2022 and 31st Dec 2022).
The primary objective is to evaluate the performance of CPS and mHS in predicting Major Adverse Cardiac Events (MACE), defined as acute myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, or death, in male and female patients. Performance will be assessed using the area under the curve (AUC) in receiver operating characteristic (ROC) analysis. AUC comparisons between genders performed using the DeLong test. Statistical analysis will be conducted using SPSS 29.0.
Results: We included 1,484 CP patients from Careggi University Hospital, 594 (40.0%) were female. The mean age was 60.2±15.6 years, with no significant gender difference (males: 59.2±15.5; females: 61.7±15.7; p=0.59). MACE occurred in 212 patients (14.3%), more frequently in males (18% vs. 8.6%, p<0.001).
Regarding cardiovascular risk factors, diabetes (23.9%), hypertension (27.1%), dyslipidemia (35.2%), smoking (15.8%), family history of cardiovascular disease (CVD) (7.6%), and obesity (8.1%). Diabetes (30.7% vs. 19.4%, p<0.001) and family history of CVD (10.3% vs. 5.7%, p=0.02) were more frequent in females, while dyslipidemia was more common in males (38.0% vs. 31.0%, p=0.04). No significant gender differences were found for hypertension, obesity, or smoking.
For the CPS, the mean value in the overall population was 5.9±1.9, with an AUC of 0.71 (95% CI: 0.67–0.75). The AUC in males was 0.74 (95% CI: 0.70–0.79), while in females it was 0.64 (95% CI: 0.56–0.71) (Figure 1), with a statistically significant difference (p=0.02).
The mean mHS in the overall population was 3.5±2.1, with an AUC of 0.83 (95% CI: 0.80–0.85). The AUC in males was 0.83 (95% CI: 0.81–0.87), while in females it was 0.82 (95% CI: 0.76–0.87) (Figure 1), with no significant differences between the AUCs (p=0.52). Regarding the individual components of the mHS, a significant difference was observed between male and female patients in the classification of typical versus atypical CP in relation to cardiovascular events (p<0.001).

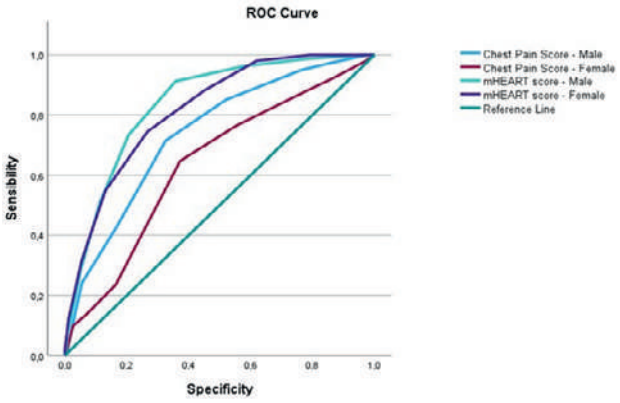

Figure 1. ROC curves of the scoring systems (modified HEART score and Chest Pain score) in male and female gender

Conclusion: CPS shows significantly lower performance in females. Furthermore, the slightly worse performance of the mHS in females, though not statistically significant, appears to be due to its rough classification of pain. This study represents a secondary analysis; therefore, further dedicated prospective studies are needed to develop prognostic scores that account for the differing characteristics of CP between genders.

WAIST-TO-HEIGHT RATIO SUPERIORITY OVER BMI IN PREDICTING METABOLIC DYSFUNCTION: EVIDENCE FROM A SPECIALIZED OBESITY CARE CENTER

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Introduction: Obesity is a chronic and relapsing disease that represents one of the major health challenges globally, strongly associated with increased cardiovascular and metabolic morbidity and mortality. Growing evidence highlights that not just excess body weight but specifically fat distribution, particularly visceral adiposity, is a key determinant of cardiometabolic risk. Although widely adopted, body mass index (BMI) fails to capture fat distribution and may underestimate risk in normal-weight individuals with central obesity, limiting the accuracy of metabolic risk assessment across different clinical phenotypes. Waist-to-height ratio (WHtR) is a simple, low-cost and physiologically relevant marker of visceral fat. Despite robust evidence supporting its superior predictive value for metabolic dysfunction compared to BMI, it remains underutilised in clinical practice.The aim of the study was to compare the predictive ability of WHtR and BMI in detecting metabolic alterations in a real-world outpatient setting and to assess whether WHtR can stratify cardiometabolic risk independently of BMI classification.
Methods: We conducted a retrospective cross-sectional study on patients referred to the Metabolic Health Clinic at IRCCS Ospedale San Raffaele, Milan, between November 2024 and March 2025. Standardised anthropometric measurements were performed by trained personnel and included weight, height, waist and hip circumference. Waist-to-height ratio (WHtR) was calculated as waist circumference divided by height, with WHtR >0.6 indicating visceral adiposity. BMI was classified according to WHO criteria.Capillary blood samples were collected to measure glycated haemoglobin (HbA1c), HDL and LDL cholesterol, triglycerides and high-sensitivity C-reactive protein (hs-CRP). Associations between anthropometric indices and metabolic parameters were assessed using Spearman's correlation. Group comparisons based on WHtR (≤0.6 vs >0.6) were analysed using Mann–Whitney U tests. Subgroup analyses investigated sex-specific patterns and body weight change at follow-up.
Results: A total of 465 patients were included, with a mean age of 52.3 ± 13.6 years and a predominance of females (72%). WHtR exceeded 0.6 in 91% of the cohort, indicating a high prevalence of visceral adiposity. Compared to individuals with WHtR ≤0.6, those with WHtR >0.6 had significantly higher HbA1c levels (39 [36–44] vs 36 [33–38] mmol/mol, p = 0.01), lower HDL cholesterol (47.5 [42–54] vs 55.8 [48–63] mg/dL, p < 0.001), and a smaller BMI reduction at follow-up (−1.1 vs −2.3 kg/m^2, p = 0.03). WHtR was positively correlated with HbA1c (ρ = 0.32, p < 0.001) and hs-CRP (ρ = 0.22, p = 0.005), and negatively correlated with HDL cholesterol (ρ = −0.19, p = 0.003) and weight variation (ρ = −0.25, p = 0.002). In contrast, BMI showed only a weak correlation with HbA1c (ρ = 0.14, p = 0.045) and no significant association with HDL, LDL cholesterol or inflammatory markers. WHtR >0.6 was associated with a higher waist-to-hip ratio and lower HDL levels in males, suggesting a sex-specific visceral risk profile. Stratification by BMI categories showed a lower discriminative ability in detecting metabolic abnormalities compared to WHtR.
Conclusion: In a real-world outpatient setting, WHtR proved superior to BMI in identifying visceral adiposity and associated metabolic abnormalities. As a simple, non-invasive and cost-free tool, WHtR offers enhanced clinical utility for early risk detection and personalised metabolic care. Its systematic integration into obesity management pathways should be prioritised, and further research is warranted to consolidate its role across diverse populations and clinical settings.

BLOOD PRESSURE AND INTRACRANIAL HEMORRHAGE PROGRESSION IN ELDERLY MTBI PATIENTS: IS EARLY INTERVENTION ALWAYS NECESSARY?

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Background: Mild traumatic brain injury (MTBI) is the most common form of traumatic brain injury, with substantial public health implications. It is typically defined by a loss of consciousness lasting less than 30 minutes, post-traumatic amnesia under 24 hours, and a Glasgow Coma Scale score between 13 and 15. Common causes include falls, motor vehicle accidents, and sports-related injuries. Although most patients experience full recovery, a significant subset develops persistent symptoms—known as post-concussion syndrome—such as headaches, dizziness, cognitive impairment, and emotional disturbances. Diagnosis is primarily clinical, with neuroimaging used selectively to rule out intracranial complications. Management involves relative rest, patient education, and a gradual return to activities. Early recognition and treatment of persistent symptoms are essential to support optimal functional recovery.
Study Design: This retrospective observational study included patients aged over 75 years who presented to the Emergency Department of Chieti Hospital between March 24-January 25, with a triage diagnosis of "Trauma/Head Trauma" and radiological evidence of post-traumatic intracranial hemorrhage documented at discharge or hospital admission (t0).
Exclusion criteria included absence of radiological follow-up, incomplete clinical records, and early neurological deterioration within the first hours of ED observation (including cases progressing to coma).
Patients were stratified by age, sex, systolic/diastolic/mean arterial pressure (SBP, DBP, MAP) on admission, and timing of radiological monitoring, with assessment of stability, improvement, or worsening of the hemorrhage.
Endpoints included:
• Timing of radiological worsening
• Correlation between blood pressure values and hemorrhagic progression
Materials and methods: A total of 57 patients were included in the study (27 women and 30 men). The mean age was 85 years, ranging from 76 to 97 years. All patients met the inclusion criteria of mild traumatic brain injury (MTBI) with radiological evidence of post-traumatic intracranial hemorrhage at initial imaging (T0) and were observed in the Emergency Department of Chieti Hospital during the study period.
Data were collected retrospectively from medical records, including demographic variables, initial blood pressure values (systolic, diastolic, and mean arterial pressure), and results of radiological follow-up (stability, improvement, or worsening of the hemorrhage).
For statistical analysis, the following tests were used:
Spearman's rank correlation coefficient
Chi-square test
ANOVA test
Statistical significance was set at $p < 0.05$.
Results: The Spearman correlation test showed no statistically significant association between MAP ($\rho = -0.25$, $p = 0.168$), SBP ($\rho = -0.13$, $p = 0.352$), or DBP ($\rho = -0.06$, $p = 0.687$) and CT progression. Although MAP displayed the strongest (negative) correlation, it remained statistically non-significant.
Similarly, the chi-square test revealed no significant relationship between CT worsening and categorical stratification of blood pressure values (MAP $p = 0.391$; SBP $p = 0.495$; DBP $p = 0.337$).
Analysis of variance (ANOVA) further confirmed the absence of statistically significant differences among patients with and without radiological progression when stratified by blood pressure parameters (MAP $p = 0.155$; SBP $p = 0.442$; DBP $p = 0.738$).
Scatter plots of blood pressure values versus CT outcomes showed no clear pattern or trend suggestive of correlation.
Overall, none of the blood pressure parameters demonstrated a statistically significant association with radiological worsening in patients with mild traumatic brain injury.
Discussion: These findings align with existing literature suggesting that, in cases of MTBI, elevated blood pressure within the normal-high range does not necessarily exacerbate intracranial bleeding.
Clinically, these results suggest that aggressive management of normal-high blood pressure in elderly MTBI patients may not be necessary solely to prevent hemorrhagic progression. Overtreatment could potentially lead to hypotension, which is known to be detrimental in traumatic brain injury cases. Therefore, a more conservative approach to blood pressure management may be appropriate in this patient population.
Additionally, our study found no instances of radiological worsening within the first 24 hours post-injury. This observation supports the notion that immediate repeat CT scans may not be required in the absence of clinical deterioration, aligning with guidelines that recommend imaging based on neurological status rather than routine scheduling.
In summary, our findings contribute to the growing body of evidence that supports individualized patient management strategies in MTBI, emphasizing the importance of clinical assessment over routine interventions.

RECURRENT PERICARDITIS WITH NORMAL C-REACTIVE PROTEIN: CLINICAL AND LABORATORY FEATURES, BIOMARKERS AND OUTCOME IN A NON-INFLAMMATORY PHENOTYPE

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Background: Differences in recurrent pericarditis with normal vs. elevated C-reactive protein (CRP) are unknown.
Materials and methods: We studied 448 patients with recurrent or incessant pericarditis. CRP levels <10 mg/L were considered normal. Forty-one patients with normal CRP were tested for interleukin 6 (IL-6), serum amyloid A (SAA) and soluble urokinase plasminogen activator receptor (suPAR).
Results: Among the cohort (median age 43 years, 48.4% females), 336 patients (75%) had elevated CRP, while 112 (25%) had normal levels. CRP-negative patients were younger (38.6 vs. 43.5 years, p=0.007) and predominantly female (67.9% vs. 42.0%, p<0.001). They presented less often with fever (23.2% vs. 74.1%, p<0.001), pleural involvement (7.1% vs. 61.6% p<0.001), and neutrophilic leucocytosis (WBC 6760 vs. 12315/μL, p<0.001). Pericardiocentesis was performed rarely in CRP-negative patients (2.7% vs. 13.4%, p=0.001). Recurrence rates were similar (5.4 vs. 5.5/100 months-patient, p=0.918). Among CRP-negative patients, 53 (47.3%) had an incessant course characterized by persistent symptoms (pain and tachycardia); abnormal instrumental findings included ECG changes (28.6%), mild pericardial effusion (86.6%), and cardiac magnetic resonance evidence of effusion/oedema/late gadolinium enhancement (43.7%). Anakinra was administered to 48 CRP-positive (14.3%) and 10 CRP-negative patients (8.9%), leading to good responses with discontinuation of NSAIDs and corticosteroids in 39/48 (81.2%) and 5/10 (50.0%), respectively.
Among the 41 CRP-negative patients tested, IL-6 and suPAR levels were always normal, while SAA was elevated in 17.1%.
Conclusions: Pericarditis with normal CRP exhibits distinct clinical and laboratory features, often presenting with an incessant course. Although rarely elevated, SAA may help to identify inflammation beyond CRP.

QUALITÀ DELLA TERAPIA ANTICOAGULANTE COME PREDITTORE DELLA RISOLUZIONE DELLA TROMBOSI ENDOVENTRICOLARE SINISTRA: UNO STUDIO MULTICENTRICO RETROSPETTIVO

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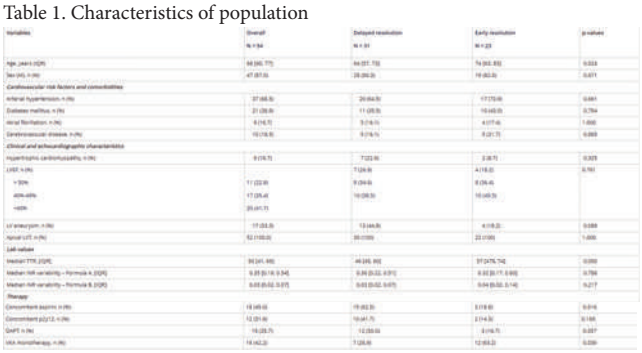
Introduction: International guidelines on the therapeutic management of left ventricular thrombosis (LVT) recommend oral anticoagulant therapy with vitamin K antagonists (VKAs) for at least 3 to 6 months. VKAs seemed to afford for a high rate of thrombus resolution (up to 80% of patients), for a relatively low rate of stroke (10%), and for an acceptably low rate of bleeding events (2%). Maintaining a good quality of VKAs therapy is, therefore, mandatory to achieve these outcomes. The most used tool in clinical practice is

the time in therapeutic range (TTR). High TTR values have been associated with favourable outcomes and prognosis in other clinical setting (e.g., atrial fibrillation, mechanical valves). Other strategies are available to evaluate the quality of VKAs therapy, such as the International Normalized Ratio (INR) variability, but these are rarely used and their ability to predict patients' outcomes is poorly defined. Therefore, the objective of this study was to evaluate the association between the quality of anticoagulant therapy with VKAs and early LVT resolution.
Methods: Patients with LVT referred to three Italian Anticoagulation Clinics between 2011 and 2023 were retrospectively enrolled if they received VKAs. Outcome was the effect of Time in Therapeutic Range and of INR variability defined according to validated formulas on early thrombus resolution (within 6 months).
Results: Fifty-four patients were included, 23 of whom (42.6%) had early thrombus resolution. Median age was 68 years and 87.0% were male (Table 1). Overall, 41.7% and 35.4% of patients had a reduced or moderately reduced left-ventricle ejection-fraction and aneurysm, respectively. For the prediction of early LVT resolution, the best value of TTR was 56% (sensitivity, 57%; specificity, 71%; AUC, 0.657), that of INR variability, formula A was 1.65 (sensitivity, 0%; specificity, 96%; AUC, 0.478) and that of formula B 0.40 (sensitivity, 4%; specificity, 100%; AUC, 0.599). The cumulative incidence of early LVT resolution was higher in patients with TTR values ≥56% (57.1%; 95% confidence interval -CI-, 32.8.4%-75.5%) than <56% (30.3%; 95%CI, 15.6%-46.4%).
Discussion: This results suggest that the quality of VKAs may be associated with early LVT resolution. TTR have a slightly greater accuracy for this outcome compared to INR variability. Even if proved in other clinical conditions needing VKAs therapy, scanty information on the quality of anticoagulation in the setting of LVT has been available. There is only one study including 84 patients and reporting a slightly higher incidence of LVT resolution and lower incidence of systemic embolism in patients with TTR values more than 50% compared to patients with less than 50%. Our study confirms these results and allows a better understanding of the relevance of the quality of anticoagulation on early LVT resolution. The major limitation of our study is the low number of patients not being representative of LVT population.
Conclusions: The quality of anticoagulation may be a relevant driver for early LVT resolution. TTR evaluation appears to have a slightly greater accuracy for this outcome compared to INR variability formulas.

Table 1. Characteristics of population



CEFIDEROCOL-INDUCED DELIRIUM

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Introduction: Cefiderocol is a novel siderophore cephalosporin developed for the treatment of infections caused by multidrug-resistant (MDR) Gram-negative bacteria [1]. Although neurological side effects of cephalosporins have been extensively described in the literature [2], data on cefiderocol are limited. Furthermore, to our knowledge, no studies on the neurotoxicity of cefiderocol have been published yet.
Case presentation: An 84-years old man, with a past medical history of hypertension, chronic heart failure, atrial fibrillation, chronic obstructive pulmonary disease and chronic kidney disease, was admitted to our Internal Medicine ward after one month history of hospitalization in Intensive Care Unit for severe respiratory failure needing for invasive ventilation.
At presentation, he was alert and oriented to all spheres and his vital signs were stable. Significant laboratory examination findings included white blood cells count (WBC) of 7650/mm^3 (Reference Range (RR): 4000-10000/mm^3), creatinine of 1.75 mg/dL (RR: 0.67-1.2 mg/dL) and blood urea nitrogen of 20 mg/dL (RR: 10-23 mg/dL).
After 10 days from admission, the patient developed a sudden deterioration in general conditions, with the onset of shivers without fever and oliguria. Initial workup revealed a total WBC count of 6540/mm^3, with 56% of neutrophils. Creatinine was 1.62 mg/dL, while electrolytes were unremarkable. Lactic acid was 0.7 mmol/L (RR: 0.5-1.6 mmol/L) and inflammatory markers showed a C-reactive protein of 33.5 mg/l (RR: <5 mg/L), and a procalcitonin of 10.05 ng/ml (RR: < 0.5). Furthermore, urinalysis was normal. In order to exclude a new infection, three sets of blood cultures were performed and resulted positive for MDR Acinetobacter baumannii. Therefore, according to the infectious disease specialists, therapy with cefiderocol and fosfomycin was started, after a dose adjustment based on renal function.
After 24 hours, inflammatory markers were downtrending and diuresis improved. However, on the third day of therapy, the patient developed an acute confusional state, with altered consciousness, reduced ability to concentrate and maintain attention, and visual hallucinations. His vital signs were normal, while the speech was dysarthric and a peripheral paralisis of the facial nerve was observed. No recent medications had been administered that could impact neurological status. Repeted laboratory workup revealed normal levels of electrolytes, WBC, blood glucose, thyroid-stimulating hormone, ammonia, lactic acide and arterial blood gas. Besides, creatinine had mildly improved. To exclude a stroke we performed a computed tomography and a magnetic resonance imaging of the brain, which showed no acute intracranic events.
Given these results, cefiderocol neurotoxicity was suspected. The Naranjo advese drug reaction probability scale was 7 points, making it probable and the drug was discontinued.
After 48 hours of wash out, we observed a complete resolution of neurological symptoms and there was no recurrence of delirium or others acute neurologic symptoms.
Discussion: Neurologic complications of antibiotics are overall well documented and, beta-lactams (particularly penicillins, fourth-generation cephalosporins and imipenem) are recognized to be the most common to cause neurotoxic effects. The clinical manifestations of this phenomenon may range from mild delirium, to seizures and coma. The main risk factors are renal failure with delayed antibiotics excretion, and the presence of preexisting neurologic disease [2]. The most important clinical interventions are antibiotic discontinuation or hemodialysis.
Up to date, cefiderocol has been approved for use in adults with complicated urinary tract infections and hospital-acquired or ventilator-associated pneumonia due to otherwise highly resistant gram-negative bacteria when there are no alternative treatment regimens, including MDR A. Baumannii [1,3].
Among the recognized side effects of cefiderocol, neurologic complications were described rarely (less than 2%), and there were no reports of them in the post-marketing experience of the drug.
In our case, cefiderocol-induced delirium was suspected given the absence of acute intracranial events, metabolic disorders, signs of sepsis or uremia, nor the patients was taking concomitant medications that could have caused an acute alteration of mental status.
Even if there is no proven evidence of cefiderocol's neurotoxic effects, the known neurological side effects of beta-lactams, the temporal relationship between initiation of therapy and symptoms onset, the evidence of resolution of delirium upon discontinuation of the drug support the suspected causality.
Conclusions: This case illustrates the potential of cefiderocol to induce acute mental status changes and the associated risk factors. Physicians should consider the possibility of neurotoxicity during treatment with cefiderocol and, if possible, discontinue administration.
References
1. Zhanel GG et al. Drugs. 2019 Feb;79(3):271-289.
2. Sutter R et al. Neurology 2015; 85:1332.
3. Stevens RW et al. Pharmacotherapy 2019; 39:1113.

A CURIOUS CASE OF PERICARDITIS: WHEN THE CULPRIT WEARS A WOOL COAT

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Keywords: *Coxiella burnetii*, Q fever, pericarditis, zoonosis, veterinarian
Introduction:Q fever is a zoonotic disease caused by Coxiella burnetii, an intracellular Gram-negative bacterium that primarily affects the respiratory system but can also involve multiple organs. Transmission occurs through inhalation of contaminated aerosols originating from infected animals. While acute Q fever most commonly presents as a febrile illness or atypical pneumonia,

pericarditis is a rare and often underrecognized manifestation, particularly during the acute phase. Our report describes a rare case of acute pericarditis in an immunocompetent adult woman, attributed to C. burnetii infection, thus highliting the importance of considering atypical pathogens in the differential diagnosis of pericarditis.
Case presentation: We present the case of a 58-year-old previously healthy female who presented to the Emergency Department with a 5-day history of low-grade fever, fatigue, and pleuritic chest pain, worsened by lying supine and relieved when leaning forward. She also reported paroxysmal atrial fibrillation. The patient was a professional veterinarian who performed animal dissections, including ovine species (sheep and goats), lemurs, and alpacas, without using protective equipment such as face masks, thus increasing the risk of aerosol-borne zoonotic infections.
On clinical evaluation, she was febrile (38.2 °C), tachycardic (102 bpm), and normotensive. A pericardial friction rub was noted. ECG demonstrated diffuse ST-segment elevation and PR-segment depression. Chest radiography revealed interstitial pneumonia, while transthoracic echocardiography showed a moderate pericardial effusion (up to 12 mm), without tamponade. Laboratory tests indicated elevated inflammatory markers (C-reactive protein 181 mg/L), normocytic anemia, leukocytosis, and mild transaminase elevation. Cardiac MRI confirmed the presence of pericardial inflammation. A CT-PET was also performed, which showed pathological iperaccumulation in the pericardium e in the aorta. As atrial fibrillation was datable, the patient underwent successful pharmacologic cardioversion with amiodarone. Diagnosis of pleuropericarditis was made, and the patients was discharged with colchicine (0.5 mg daily), ibuprofen (600 mg TID), and levofloxacin. Blood cultures and autoimmune panels were negative. Urinary antigens for Legionella and Streptococcus Pneumoniae were negative.
After the discharge, the patient continue to experiment fever (up to38.5°C) and thoracic pain at home, thus conditioning a new access to the Emergency Department. Given her occupational exposure and unresolved symptoms, infectious disease and rheumatology teams recommended an extended serological workup. Testing for Mycobacterium Tuberculosis, Rickettsia, Brucella, Mycoplasma pneumoniae, HIV, Treponema pallidum, Hepatitis viruses, and Coxiella burnetii was performed. Serology returned positive for high titers of C. burnetii phase II IgG (1:256) and IgM (1:64), consistent with acute Q fever. Antibiotic therapy with doxycycline100mg BID was started for a6-month course. At the end of the treatment, ecocardiography showed complete resolution of the pericardial effusion, while CT-PET excluded pathological accumulation previously detected. The patient remained clinically stable, afebrile, and asymptomatic. No progression to constrictive physiology or chronic Q fever was observed.
The final diagnosis was acute pleuropericarditis and artertic involvement due to C. burnetii infection, likely acquired via aerosol inhalation during animal handling.
Discussion: Although pericarditis is a rare manifestation of Q fever, it can occur during the acute phase, especially in patients with direct occupational exposure to infected animals. The diagnosis is often missed due to its non-specific presentation and the lack of routine screening for atypical pathogens in pericarditis cases. Serological testing remains the diagnostic gold standard. In contrast to the well-established link between chronic Q fever and endocarditis, pericardial involvement is typically acute and self-limited. Treatment with doxycycline is effective and can prevent complications such as constrictive pericarditis or progression. A high index of suspicion is essential, particularly in endemic regions or in patients working with livestock or exotic animals without adequate protective measures.
Conclusion: This case highlights an intriguing but underrecognized zoonotic cause of acute pericarditis. While often associated with farmers and shepherds, Coxiella burnetii infection should also be considered in individuals with professional animal exposure—particularly veterinarians— especially when personal protective equipment is not used. Awareness, timely diagnosis, and appropriate treatment are crucial to ensure complete recovery and prevent complications. Routine use of personal protective equipment may reduce the risk of aerosol transmission in high-risk settings. This case reinforces the importance of interdisciplinary collaboration and the inclusion of atypical pathogens like C. burnetii in the differential diagnosis of pericarditis.

RULING OUT CLINICALLY SIGNIFICANT PORTAL HYPERTENSION AND HIGH-RISK VARICES IN AUTOIMMUNE HEPATITIS: EVALUATION OF NON INVASIVE TESTS

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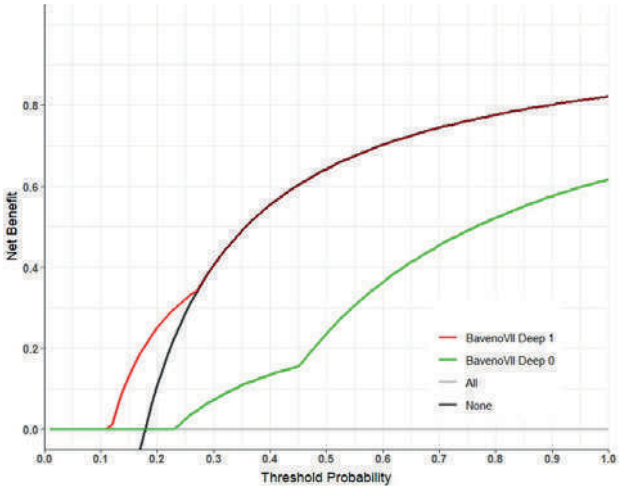
Introduction: Autoimmune hepatitis (AIH) is an inflammatory liver disease that leads to cirrhosis and its complications. Non-invasive tests (NITs) are valuable tools to rule out clinically significant portal hypertension (CSPH) and high-risk esophageal varices (HRV), reducing the need for invasive endoscopic procedures. As NITs have been mainly validated in patients with viral or metabolic liver diseases, our aim is to compare biochemical-based criteria and elasthography-based criteria in AIH-related compensated advanced chronic liver diseases (cACLD) and to assess the impact of hepatic cytolysis on NIT performance.
Materials and methods: We collected a total of 184 patients with AIH-related cACLD from two Italian referral centers. All patients underwent esophagogastroduodenoscopy (EGD) to look for signs of portal hypertension. Biochemical evaluation and liver stiffness measurement were performed within six months from EGD. Remission status, determined according to standard criteria, was recorded. Deep remission was defined as AST and/or ALT ≤ 0.5 times the upper limit of normal (ULN). RESIST, Baveno VI (BVI), and Expanded Baveno VI (ExpBVI) criteria were tested to exclude HRV. Baveno VII (BVII) criteria were used in the AIH cohort to rule out varices as a sign of CSPH. Decision curve analysis (DCA) was used to assess the net benefit of NIT.
Results: Among the 184 individuals, 118 (64.1%) had no varices, 58 (31.5%) had low-risk varices, and eight (4.4%) had HRV (F2-F3). The negative predictive value for HRV was 100% for RESIST and both BVI and ExpBVI criteria (0% false-negative rate - FNR), with spared endoscopy rates of 55.4%, 54.2%, and 65.9%, respectively. To rule out CSPH, the Baveno VII criteria showed a FNR of 19.6% for any size of EV. Remission occurred in 147 (79.9%) patients, deep remission in 36 (19.6%). In patients with biochemical remission, the FNR slightly decreased to 19.2%, while in those with deep remission, it dropped further to 11.8% compared to those with AST/ALT > 0.5 ULN (23.1%). The figure below shows the DCA analysis.
Conclusions: Biochemical-based criteria are comparable to elastography-based approaches in excluding high-risk varices. Markers of hepatic cytolysis may influence the diagnostic accuracy of these non-invasive methods. Patients in deep remission, who underwent EGD according to the Baveno VII criteria, have a lower risk of developing CSPH, suggesting that these criteria are more reliable in this patient subgroup.



EPIDEMIOLOGY, THERAPY AND OUTCOMES IN 20 YEARS TIME OF HEPATOCELLULAR CARCINOMA IN PIEDMONT, ITALY

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Introduction: Hepatocellular carcinoma (HCC) is the most prevalent primary

liver malignancy, accounting for approximately 75% of liver cancer cases. Globally, liver cancer is the fourth leading cause of cancer-related death and its incidence is expected to increase in the coming decades. The primary risk factors include chronic hepatitis B and C virus infections (HBV, HCV), alcohol-related liver disease, and, increasingly, non-alcoholic fatty liver disease (NAFLD), which is associated with rising rates of obesity, type 2 diabetes, and metabolic syndrome (1). Although universal HBV vaccination and widespread use of direct-acting antivirals (DAAs) for HCV have altered the etiologic landscape of HCC, metabolic liver diseases are becoming more prominent. Advances in imaging techniques and treatment modalities have improved diagnostic accuracy and therapeutic outcomes. However, global surveillance programs remain underutilized, and HCC outcomes vary widely. This study aims to investigate the evolution of HCC epidemiology, clinical characteristics, and treatment approaches comparing two decades (2000–2009 and 2010–2019) in a single-center population in Piedmont, Italy

Materials and methods: This retrospective cohort study analyzed data from 574 patients diagnosed with HCC at "Santa Croce e Carle" General Hospital in Cuneo between June 30, 2000, and December 31, 2019. Patients were grouped based on the decade of diagnosis (2000–2009 vs. 2010–2019). Etiologic classification was performed based on clinical history, laboratory findings, and serologic markers, including HBV, HCV, alcohol consumption, and other causes such as NAFLD, autoimmune hepatitis, and idiopathic cases. Clinical data included demographic variables, liver function (Child-Pugh score, MELD score), tumor characteristics (size, number, morphology), staging (Barcelona Clinic Liver Cancer – BCLC), and therapeutic interventions (curative vs. non-curative). Diagnostic methods (biopsy vs. imaging) and laboratory markers (including alpha-fetoprotein levels) were also collected. Treatment modalities were categorized into curative (resection, ablation, transplantation) and non-curative (TACE, SIRT, systemic therapy, palliative care). Descriptive statistics and comparative analyses between the two cohorts were conducted.

Results: Among the 574 patients, 246 were diagnosed in the first decade and 328 in the second. The mean age at diagnosis slightly decreased from 70.0 to 68.9 years, with a male predominance in both periods (73% vs. 78%). HCV was the leading etiology (45%), but its prevalence significantly declined from 58% in the first period to 41% in the second ($p < 0.05$). Alcohol-related HCC remained stable (18%), while NAFLD and idiopathic cases accounted for 21% of all diagnoses. Diagnosis was mostly achieved through imaging (79% → 86%) and AFP >100 ng/mL levels were more frequent in the second period (54% → 82%). Portal vein thrombosis increased from 11% to 16%. At diagnosis, 44% of tumors were unifocal, with a mean size increasing from 4.0 cm to 4.6 cm. BCLC staging revealed a shift from early stages (A and B) to more advanced stages (C and D), with BCLC-C rising from 10.5% to 34.5%. Curative therapies were applied in 24% of cases, mostly via percutaneous ablation (20%), and only 3.8% underwent surgical resection. Liver transplantation was rare (2 cases). Non-curative treatments were common: TACE in 37%, SIRT in 8.7%, and sorafenib in 5.4%. About 24% of patients received only palliative care or no treatment.

Discussion: The study highlights a growing number of HCC diagnosis over time, contrasting with previous expectations of decline due to reduced HCV-related cirrhosis. While the drop in HCV-related cases reflects the success of antiviral strategies, the stable prevalence of alcohol-related liver disease and underreported NAFLD likely contributed to the rising incidence. This mirrors the trend observed in Europe; although the global incidence of liver cancer has declined since 2000, steady increases have been seen in regions such as North America and Europe (2). Diagnostic advances have led to more imaging-based diagnoses and earlier detection in some cases, yet a substantial proportion of patients still presented with advanced-stage disease. The use of curative treatments remained low, possibly due to the advanced age and frailty of the patient population, as well as the real-world limitations of the BCLC staging system. TACE and SIRT were increasingly utilized in intermediate-stage cases, while systemic therapies remained stable. Despite therapeutic advancements, a considerable proportion of patients received only supportive care. Limitations of this study include its retrospective nature, single-center setting, and potential underestimation of metabolic etiologies such as NAFLD. Overall, the findings underscore the dynamic nature of HCC epidemiology and the need for ongoing surveillance and tailored public health strategies.

References:(1) Augusto Villanueva, "Hepatocellular Carcinoma", NEJM, 2019(2) Amit G. Singal et al, "Global trends in hepatocellular carcinoma epidemiology: implications for screening, prevention and therapy", Nature reviews clinical oncology, 2023

CLINICAL CHARACTERISTICS AND GENETIC PREDISPOSITION OF DYSLIPIDEMIC PATIENTS WITH STATIN INTOLERANCE

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Background: Statin therapy represents the gold standard in lipid lowering therapy, although it is associated with an increasing rate of therapeutic abandonment especially due to the onset of muscle symptoms (statin associated muscle symptoms SAMS).

In literature, a higher incidence of SAMS in the female population has already been documented, probably attributable to differences in pharmacokinetics and pharmacodynamics between genders. A relevant element in this condition would seem to reside in the SLCO1B1 gene , responsible for the tissue transport of statins, whose mutation would determine an increased plasma concentration of the same with consequent development of SAMS.

Aim: The aim of our study was to evaluate the real-life prevalence of statin intolerance in patients referred at our Center and how this determines whether or not the 2019 ESC guideline's LDL target was reached. The influence of genetic factors (specifically the SLCO1B1 mutation) and of patients' general and clinical characteristics (gender, age, BMI) on the achievement of the target was also analyzed.

Methods: We selected a population of 185 patients attending our Center and enrolled in the LIPIGEN project (96 F ; 89 M), of whom 131 FH+ (67 F ; 64 M). In 97% of the total population it was possible to evaluate the SLCO1B1 gene, which was found to be mutated in 67 out of 179 patients (37 F ; 30 M).

The mean age of our patients was 35 years (18 to 74 years; 41 f , 30 m), the mean BMI was 24.2 (23.9 f ; 24.5 m).

Discussion: In accordance with the literature, our data showed a greater statin intolerance in female (58% f vs 42% m). In particular, Atorvastatin was the worst tolerated, with predominantly SAMS development even in the absence of CPK elevation (only 2 patients). If intolerance was referred by the patient, we preferred to shift to Rosuvastatin, generally characterized by better tolerability.

Intolerance showed a continuous growth trend in relation to age in both sexes, more significant in female (5-fold increase from 35 to 75 years).

The evaluation of the BMI was affected by the different numerical representation between classes, given the prevalence of normal weight and overweight population. From our preliminary data, the BMI would seem to be directly correlated with the development of statin intolerance; less significant the correlation with the achievement of the target since the poor representation of some groups could determine confounding results.

Of the 179 patients analyzed for mutations of the SLCO1B1 gene, 37% presented its mutation. By stratifying the data based on sex, the influence of this mutation on the development of statin intolerance in female was confirmed, independently of the diagnosis of familial hypercholesterolemia, particularly in female FH+.

Conclusions: Statin intolerance still represents an obstacle to therapeutic compliance and the achievement of the LDL target. Particular importance seems to be related to age and the presence of SLCO1B1 mutations; the role of BMI/waist circumference is still uncertain.

ASTHMA REMISSION IN EGPA PATIENTS: APPLICABILITY AND CONCORDANCE OF THE MAIN INTERNATIONAL GUIDELINES

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg-Strauss syndrome, is a rare small-vessel vasculitis affecting individuals with asthma and eosinophilia. It is characterized by tissue eosinophilia, necrotizing vasculitis, and eosinophil-dominant inflammation. The condition is rare in children and progresses through three phases: allergic, eosinophilic, and vasculitic. However, these phases may overlap or not always occur. Severe asthma is a common clinical finding that is often the cause of high-dose steroid consumption and poor disease control. Recently, asthma remission has been a hot research topic, and three main guidelines have given us the definition of asthma remission. The study aims to evaluate the asthma remission in EGPA patients and the applicability and
concordance of the current guidelines.

Method: We enrolled 13 patients with severe asthma in EGPA and 13 patients with severe asthma but not EGPA, referring to our severe asthma center who had been treated with mepolizumab or benralizumab for 12 months. We collected anamnesis data regarding exacerbations, the need to use systemic corticosteroids, and asthma symptoms in the last 12 months. We also evaluated lung function at baseline and at 12 months, ACT, and ACQ at 12 months from

the start of therapy. We used the Fleiss k test to evaluate the agreement between the guidelines based on the results we obtained.
Results: The average age of the sample affected by EGPA was 56.3 years, SD 7.8, while that of the sample affected by severe asthma not in EGPA was 58.3, SD 12.6 (p=n.s. between the two groups). In each of the two groups, there were 3 males and 10 females (M 23.1%, F 76.9%). In both groups, 8 patients were being treated with Mepolizumab 100mg and 5 were being treated with Benralizumab 30mg. Each patient was naive regarding the use of monoclonal antibodies, and none of the patients were being treated with immunosuppressive drugs. At baseline, patients with EGPA had a serum eosinophil count of 726, SD 404.5 compared to a peripheral eosinophil count of 699 cells/mcl, SD 368 (p=n.s.). All patients had undergone cycles of OCS in the past. In the first group, 9 out of 13 patients (69.2%) were being treated with medium-dose ICS and 4 (30.7%) with high-dose ICS, while in the second group, 3 patients (23.1%) were being treated with medium-dose ICS and 10 (76.9%) with high-dose ICS. In the first group, 8 out of 13 patients (61.5%) were being treated with LAMA, while in the second group, 12 out of 13 patients (92.3%) were being treated with LAMA.In 7 out of 13 patients in the first group (53.8%) and 6 out of 13 patients in the second group (46.15%), the criteria for remission were met for at least one of the guidelines considered. In the first group, moreover, 1 out of 13 patients (7.7%) met the criteria for partial remission. (SANI). In the first group, 3 out of 13 patients (23.1%) met the remission criteria for all guidelines, while in the second group, this occurred in 2 out of 13 patients (15.3%). Finally, the level of agreement between guidelines based on the results obtained was almost perfect in the first group (Fleiss' kappa of 0.812, p<0.0001), while in the second group it was substantial (0.712, p<0.0001)
Conclusion: Our study has several limitations, such as a small sample size, but as we know, it is the first pilot study that explored asthma remission in EGPA; remission in severe asthma seems to be a real achievement.

CORRELATES OF POLYPHARMACY AND PRESCRIPTION CHANGES IN INTERNAL MEDICINE: A PROSPECTIVE FIVE-YEAR STUDY

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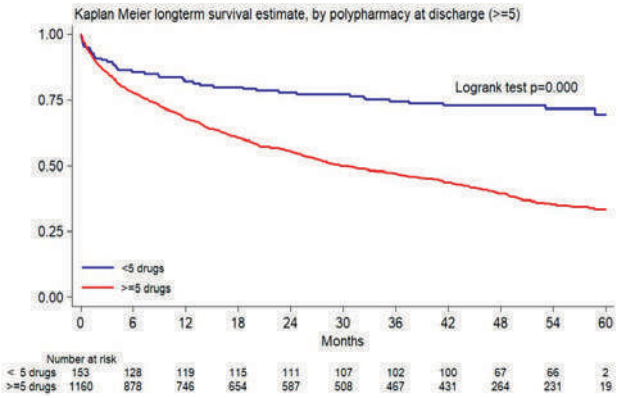
Background: and aims: Polypharmacy, as defined as the concurrent use of five or more medications, has been associated to worse health outcomes, but data in the internal medicine setting are scant. We aimed to assess the prevalence of polypharmacy, examine its associations with clinical and socioeconomic factors, and evaluate its impact on mortality in an internal medicine setting. Methods: This was part of the San MAtteo Complexity (SMAC) study (2017-2019), a prospective, observational cohort with a telephone follow-up at 4 months and annually for up to five years. Patients were consecutively and prospectively enrolled in an academic, single-centre, internal medicine ward, and were admitted from the A&D Department. Polypharmacy prevalence was assessed at admission and discharge. Sociodemographic data, Cumulative Illness Rating Scale (CIRS), Edmonton Frail Scale, comorbidity and multimorbidity, Short Blessed Test, and Barthel Index were collected. Associations with polypharmacy were analysed using logistic regression, and mortality was tracked during hospitalization, at 4 months, and up to 5 years post-discharge using Kaplan–Meier analysis. Results: Among 1419 patients (median age 80 years, IQR 69-86; F:M ratio 1.14:1), polypharmacy was observed in 71.5% at admission and 82.6% at discharge. Patients with polypharmacy were significantly older, frailer, and had lower socioeconomic status. Independent predictors included age ≥65 years (OR 4.14, 95% CI 1.60-10.69), CIRS >3 (OR 2.67, 95% CI 1.98-3.58), frailty (OR 3.85, 95% CI 0.68-1.50), comorbidity (OR 8.2, 95% CI 2.19-30.7), multimorbidity (OR 20.91, 95% CI 5.65-77.44), and cardiovascular disorders (OR 1.84, 95% CI 1.33-2.55). In-hospital and 4-month mortality were significantly higher among patients who were deprescribed (i.e., discharged with ≤5 fewer medications). Five-year mortality was significantly higher in patients with polypharmacy (HR 2.83, 95% CI 2.07-3.86; p<0.001), regardless of prescription changes (Figure). Conclusions: Our findings indicate that polypharmacy is highly prevalent in internal medicine and intertwined with several components of clinical complexity. Both deprescribing and ongoing polypharmacy at discharge are associated with increased mortality at different time points, underscoring the need for targeted medication optimization strategies.



LATENT CLASS ANALYSIS IDENTIFIES NOVEL COELIAC DISEASE SUBGROUPS WITH DISTINCTIVE CLINICAL FEATURES: A MULTICENTRIC STUDY

Lenti M.V.[1], Pala D.[2], Aronico N.[1], Dagliati A.[3], Bianchi P.I.[1], Santacroce G.[1], Quaglini S.[3], Lanzola G.[3], Corazza G.R.[1], Di Sabatino A.[1]
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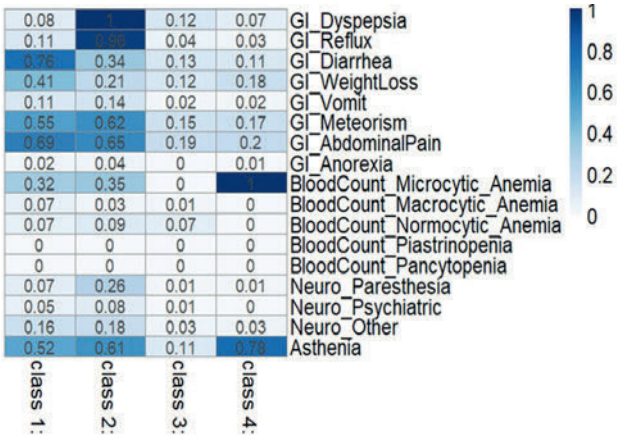
Background: Coeliac disease (CD) is a lifelong, immune-mediated disorder characterized by a wide clinical spectrum, which often challenges traditional classifications like the Oslo definitions. We aimed to identify novel CD subtypes based on clinical features using latent class analysis (LCA) and validate these phenotypes with a predictive supervised model. Methods: In this multicentric retrospective study, 2478 adult CD patients from 19 Italian centres (2011–2021) were analysed. Clinical, laboratory, endoscopic, and histological data were collected. LCA was applied to categorical symptom variables, including gastrointestinal, haematological, neuropsychiatric manifestations, and fatigue, to identify latent clusters, with the optimal number of classes determined by the Bayesian Information Criterion. The newly derived classes were compared with the traditional Oslo classification using Chi-squared tests, while multinomial logistic regression (MLR) was employed to validate the associations between latent classes and additional features. Results: LCA identified four classes, namely Class 1 (predominant lower gastrointestinal symptoms); Class 2 (upper gastrointestinal manifestations); Class 3 (mainly asymptomatic or nonspecific cases); and Class 4 (microcytic anaemia with asthenia) (Figure). Comparison with the Oslo classification revealed partial overlap, indicating potential misclassification under current criteria. MLR confirmed significant associations, with female sex strongly linked to Class 2 (OR 2.7, 95% CI 1.52-4.78). Autoimmune comorbidities (OR 1.96, 95% CI 1.18-3.25) and severe histological damage (B2 Corazza-Villanacci, OR 9.12, 95% CI 1.86-44.63) were also more frequent in Class 2. Conclusions: LCA offers a novel, data-driven approach to refine CD phenotyping, highlighting its clinical heterogeneity and paving the way for more personalized management strategies.



ISCHEAMIA OF UNKNOWN ORIGIN (I.O.K.O.): A RELEVANT CLINICAL CHALLENGE CASES SERIES FROM A TERTIARY TEACHING HOSPITAL AND LITERATURE REVIEW

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Background: Splenic infarction (SI) is a rare finding in patients presenting with abdominal pain to the Emergency Department but may be diagnosed in up to 20% of asymptomatic patients as an incidental finding on abdominal imaging (1). Up to 50% of SIs are diagnosed in association with other ischaemic lesions, such as renal and intestinal infarctions (2). The clinical significance, diagnostic work-up and treatment strategies of SI are not well studied. In patients with SI, a diagnostic work-up should be done to establish the aetiology and guide treatment. Cardio-embolic sources (i.e.: atrial fibrillation, infective endocarditis, ...) are the most common cause of SI, followed by solid tumours, haematological malignancies and arterial vascular disease (i.e.: atherosclerosis, arterial dissection or aneurysm) (1,2,3,5). Other clinical entities, such as splenic infections, have been identified as plausible causes of SI (5). However, retrospective studies showed that 25 to 45% of SIs either have no identifiable cause or have more than a plausible predisposing condition (4). Available treatment options for SI include anticoagulation (30.2%), antiplatelet therapy (6.4%), treatment of the underlying aetiology (47.2%), splenectomy (23.3%) and therapeutic abstention (18.1%) (5). A retrospective study from 2021 showed that, in 45 patients in whom malignancy, haematologic disease and infective endocarditis had been excluded, anticoagulation was associated with better survival without major bleeding risk (4). Nonetheless, up to now there is no consensus on how SI should be investigated and managed.
Case series: We have reviewed consecutive cases of SI evaluated at S.C. Medicina Generale II of hospital San Paolo, Milan. **Table 1** shows the results of the performed diagnostic work-up, the final working diagnosis for SI, and administered treatments. A final diagnosis was not reached in 2 out of 5 patients. In patient n. 3 we chose anticoagulant therapy because an occult cardioembolic origin seemed the most plausible cause. Patient n. 4 was on single antiplatelet therapy (SAPT) due to a previous ischemic stroke. Upon diagnosis of SI, which was associated with renal ischemia and subclavian artery thrombosis, anticoagulation was added on top of SAPT. After three months of dual antithrombotic therapy, a Doppler ultrasound of the subclavian artery documented complete revascularization; therefore, SAPT was stopped and oral anticoagulation was continued. The patient was referred to the Electrophysiology service for loop recorder implantation, due to the high suspicion of occult atrial fibrillation.
Conclusions: We have highlighted a gap in scientific literature affecting a considerable proportion of patients managed in Internal Medicine wards. We propose a classification of the possible aetiologies of SI based on our literature review and with relevant clinical implications for antithrombotic or aetiological treatment: (1) cardio-embolic sources; (2) atherosclerotic arterial disease; (3) acquired or congenital thrombophilia, including anti-phospholipid syndrome and myeloproliferative disorders; (4) any other systemic causes that may be suspected based on the patient's history and clinical presentation (solid tumour, autoimmune diseases such as vasculitis, infections, nephrotic syndrome, drugs, surgery). We suggest that all patients with SI undergo the following tests: transthoracic or transoesophageal echocardiography, blood cultures, 24-hour Holter monitor of the cardiac rhythm, abdomen CT with iodinated contrast and tests for acquired and/or congenital thrombophilia. In case of negative results, additional tests should be based on the patient's clinical presentation and history and may include blood smear and bone marrow biopsy to rule out myeloproliferative neoplasms, PET-CT to rule out occult malignancy, serological tests for autoimmune or infectious causes. We propose that the instances in which no cause is found or multiple putative pathomechanisms are recognized should be referred to as ischaemia of unknown origin (IOKO). In patients with a final diagnosis of IOKO, treatment selection remains challenging. Initiation of antithrombotic therapy may be considered based on the overall thrombotic risk and a careful risk-benefit assessment, considering the therapeutic regimen in place before the SI episode. In patients in whom cardio-embolic sources are ruled out, SAPT may represent a reasonable therapeutic option.

CASE NUMBER	n. 1	n. 2	n. 3	n. 4	n. 5
Sex	Male	Male	Male	Female	Female
Age (years)	54	63	56	74	91
Thrombosis and/or ischaemia site	Stroke Splenic infarction	Stroke Splenic infarction Pulmonary embolism	Splenic infarction Renal infarction	Stroke Splenic infarction Renal infarction Subclavian	Splenic infarction
Transthoracic and/or transoesophageal echocardiogram	Aortic ulcerative plaques	No relevant findings	No relevant findings	No relative findings	Vegetation on mitral prosthetic valve
Bubble test	Negative	Not performed	Negative	Not performed	Not performed
Holter ECG/ Telemetry	Negative for atrial fibrillation	Atrial fibrillation	Negative for atrial fibrillation	Negative for atrial fibrillation	Not performed
Compressive ultrasound	Negative	Negative	Not performed	Not performed	Not performed
Acquired and/or congenital thrombophilia testing	Negative	Negative (APLs only)	Negative (APLs only)	Negative (APLs only)	Not performed
Blood cultures	Negative	Not performed	Unavailable	Not performed	Negative (but drawn under antibiotic treatment)
Computed tomography or PET	Diffuse atheromasia and two ulcerative plaques of ascending and abdominal aorta	No relevant findings	No relevant findings	No relevant findings	No relevant findings
Diagnosis	Atherosclerotic plaque ulceration and embolization	Cardiac embolization secondary to atrial fibrillation	None	None	Infective endocarditis
Therapy	Dual antiplatelet therapy (+ splenectomy)	Oral anticoagulation	Oral anticoagulation	Single antiplatelet therapy + Oral anticoagulation	Antibiotic therapy

VACCINE-INDUCED IMMUNE THROMBOTIC THROMBOCYTOPENIA (VITT)-LIKE SYNDROME: A CASE REPORT

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Background: Disorders caused by platelet-activating antibodies to platelet factor 4 (PF4) are recognized as the cause of severe thrombotic events and are not limited to the classic heparin-induced thrombocytopenia.
Aims: To highlight the role of considering anti-PF4 immune disorders in differential diagnosis of thrombotic diseases.
Methods: A case of vaccine-induced immune thrombotic thrombocytopenia (VITT)-like syndrome is described.
Results: /Case Report: A 67-year-old man complained of acute abdominal pain. Two weeks before the onset of symptoms, an influenza-like infectious episode was reported. The patient had been vaccinated for COVID-19 two years before and the nasopharyngeal swab for SARS-CoV-2 was negative. Blood examination showed mild thrombocytopenia (94.000/mcL) and very high levels of D-dimer (123,062 mcg/L). The abdomen computed tomography showed a massive spleno-mesenteric-portal thrombosis causing diffuse intestinal ischemia (Figure 1). Anticoagulant therapy with intravenous unfractionated heparin (UFH) was started. The patient had neither personal nor family history of venous thromboembolism. Traditional thrombophilia testing was negative. The condition deteriorated despite UFH therapy: the patient developed also pulmonary embolism and the intestinal ischemia was complicated by sepsis with renal failure. Anti-PF4 immune thrombotic disorders were supposed and it was indicated to start argatroban in place of UFH therapy and to administer intravenous immune globulin (IVIG). The platelet count increased (Figure 2) and, although the patient underwent a ileum surgical resection due to the consequences of bowel ischemia, the clinical balance improved progressively. A standard anti-PF4/heparin assay on blood sample collected before IVIG was highly positive. On the same blood sample, subsequent platelet activation assays did not demonstrate increased activation with the addition of heparin (HIPA assays) but showed an increased activation with the addition of PF4 (PIPA assays), thus defining a VITT-like syndrome.
Conclusions: The clinical suspicion for anti-PF4 immune disorders should be raised in case of severe, otherwise unexplained, thrombotic events associated with thrombocytopenia.

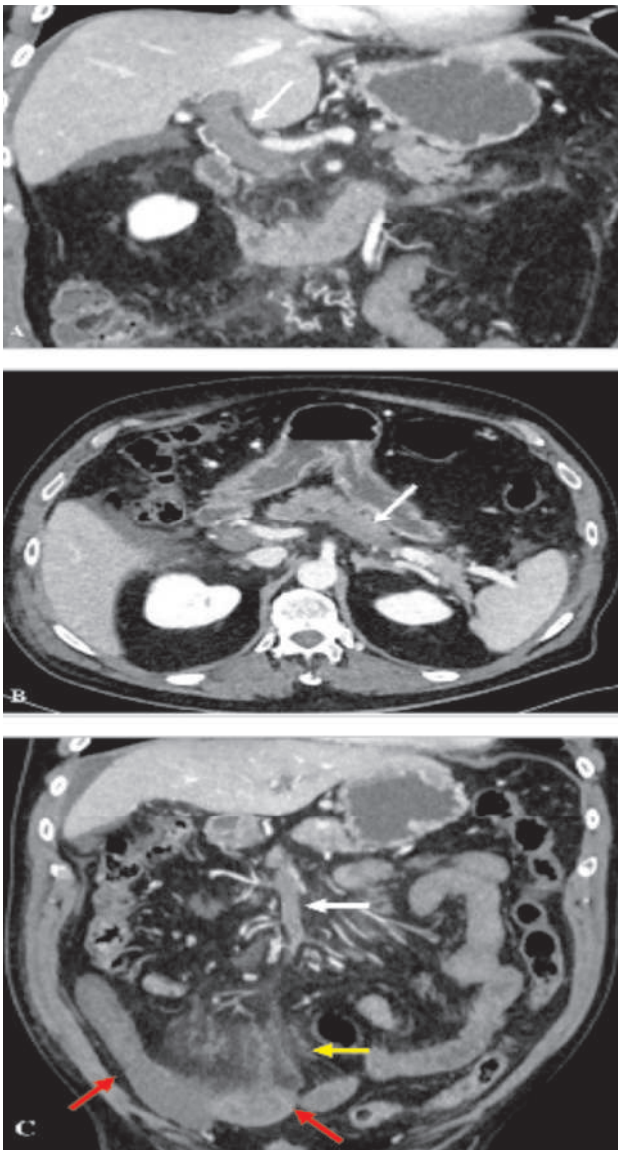

Figure 1.
A
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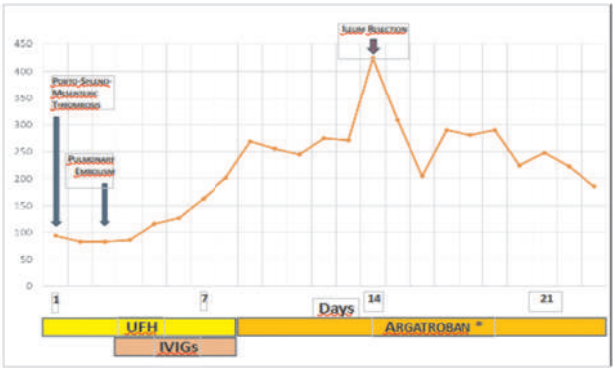

IVIG: intravenous immune globulin

UFH: unfractionated heparin

*: The change of argatroban in place of UFH therapy was performed with 5 days of delay as compared with the indication to start it together with IVIG cycle

Figure 2.

QUANDO TROMBOSI ED EMORRAGIA COESISTONO IN UN PAZIENTE ONCOLOGICO

Contaldi P., Fabozzi G., Vespoli C., Precone F.D., Biasi A., Iovino L., Di Giacomo I., Pisa E., Leo G., Confessore N., Falcone Gabriele L., Adiletta G.
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In data 05.10.2024 accedeva in Ps uomo di 55 anni per insorgenza di emilato destro insorto da qualche ora, con diagnosi iniziale di "sospetto ictus in finestra terapeutica".
In anamnesi: BPCO, Diabete Mellito tipo 2 da circa 5-6 anni, forte fumatore, dislipidemia mista. Veniva gestito in telestroke dal consulente neurologo e veniva sottoposto a trombolisi endovascolare monitorando PA.
Agli esami si evidenziava lieve insufficienza renale acuta (crea 1,29 mg/dl), iperuricemia (AU 7,5 mg/dl), trigliceridi 215, LDL 89, PCR 3,4, PCT 0,04, Hb 15.6, omocisteina 26, LAC: positivo, ACA: negativi, proteina C e s anticoagulante normali, DD post trombolisi 6492. Successivamente una Tac cranio di controllo mostrava infarcimento emorragico, riportando "verosimile ESA post-trombolisi a sede parietale destra" e come da c. neurologica non veniva iniziata né terapia antiaggregante né anticoagulante. Veniva poi trasferito in reparto di Medicina per le cure del caso.
Durante la degenza in medicina eseguiva RMN encefalo e tronco encefalico con mdc ed angio-RMN da cui risultavano multiple lesioni ischemiche in vari stadi evolutivi (di natura cardioembolica? altro?) e soltanto tracce di ESA e si introduceva Clexane 4000 sc.
Eseguiva TAC TB con mdc e si riscontrava neoformazione polmonare a sede ilare destra delle dimensioni di 54 x 21 mm dubbia per eteroplasia; inoltre era presente piccolo difetto di natura tromboembolica ai rami segmentari per il lobo inferiore di destra, enfisema polmonare, cisti complicata renale destra, multiple linfoadenopatie mediastiniche sospette per lesioni ripetitive.
Praticava FBS con biopsie multiple che concludeva per "neoformazione polmonare destra con infiltrazione e parziale lieve stenosi del ramo posteriore del lobo superiore destro".
Una TAC encefalo di controllo mostrava "lesioni ischemiche multiple sparse in fase di risoluzione come da lesioni subacute ma nessuna traccia di ESA". Veniva introdotta ASA 100 mg come da consulto neurologico, continuata terapia con clexane 4000 sc e dimesso con trasferimento al centro LARS per riabilitazione.
Dopo 2 giorni nuovo accesso in PS per malessere generale, vertigini soggettive e vomito. Eseguiva Tac cranio che mostrava "grossa area di ipodensità cerebellare sinistra come da ischemia cerebellare sinistra. Veniva posto in terapia con clexane 4000 sc, cardirene 75 mg, torvast 40 mg. Intanto giungeva il referto istologico che riportava "carcinoma polmonare non a piccole cellule".
Si trasferiva quindi in altro centro di riabilitazione con discreto recupero funzionale in attesa di referto di immunoistochimica.
Rientrava il 30.11 per Tac torace di controllo: "grossa formazione nodulare polmonare di 53 mm di tipo eteroplastico. Presenza di diverse linfoadenopatie mediastiniche, ripetitive. Diverse aree di ipodensità a carico della milza, compatibili con infarti splenici."
Intanto giungeva referto immunoistochimico che riportava "campioni bioptici di mucosa bronchiale e parenchima polmonare von pattern citocheratina 7 positiva, negativo TTF1, napsina A e p63. Il quadro descritto configura per "neoplasia epiteliale non a piccole cellule" con aspetti che favoriscono la diagnosi di adenocarcinoma scarsamente differenziato.
Giungeva inoltre il 02.12.2024 la Determinazione dello stato di PD-L1: -tumor proportion score : 1-49% -espressione stato di PD-L1: PD-L1 espresso. il paziente pertanto veniva agganciato all'ambulatorio di oncologia del PO Pagani per il prosieguo dell'iter diagnostico -terapeutico.
Dopo qualche settimana nuovo accesso in codice rosso presso PO Nocera per stato confusionale, ipostenia emisomica destra. Alla Tac cranio: "lesione ischemica subacuta con infarcimento emorragico". All'EON: "sfumata ipostenia arto inferiore destro e deficit facciale sinistro. Ipostenia emisoma destro come da esiti. Paziente non candidabile A TROMBOLISI". Veniva ricoverato in reparto di Neurologia con diagnosi di "ictus ischemico temporo-occipito mesiale di sinistra con infarcimento emorragico in regolare evoluzione. Ictus ischemico subacuto cortico-sottocorticale parietale sinistro." Purtroppo si assisteva ad un progressivo peggioramento nei giorni seguenti della sintomatologia neurologica e dello stato confusionale, con insorgenza di coma, arresto cardio-respiratorio ed exitus del paziente.

LEFT ATRIAL DYSFUNCTION AS A MARKER OF PRIMARY CARDIAC DAMAGE IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a rare systemic autoimmune disease that can lead to primary involvement of the heart. Scleroderma cardiomyopathy (SSc-CMP) is one of the main determinants of poor prognosis and quality of life. Despite that, SSc-CMP is still hard to be diagnosed and its clinical definition is not yet been universally defined. For this reason, a proper differential diagnostic work up is needed.
Left atrial strain (LAS), which reflects the global left atrial (LA) function, has been found as an early echocardiographic marker of myocardial involvement in other inflammatory diseases, including cardiac amyloidosis and cirrhotic cardiomyopathy.
Objectives: Since the nature of SSc-CMP is also linked to an inflammatory etiology, we aim to explore whether LAS analysis is able to detect early diagnosis of SSc-CMP.
Methods: The population of this retrospective observational study included SSc patients referred to the Dyspnea Lab, Cardiology Unit of Milan Policlinico Hospital for suspected cardiovascular or cardiopulmonary involvement. Patients older than 18 years with diagnosis of SSc according to the 2013 ACR/EULAR classification criteria presenting dyspnea and/or other signs or symptoms suggestive of cardiac or cardiopulmonary involvement were included in the study. Patients with overlap syndrome, patients diagnosed with any other type of cardiological involvement (e.g. pulmonary arterial hypertension and any other type of pulmonary hypertension, hemodynamic significant valvular disease, coronary artery disease and heart failure with reduced or preserved ejection fraction) and patients with interstitial lung disease or with any other type of pulmonary pathological involvement were excluded from the analysis. We also excluded patients without echocardiographic images suitable for LAS analysis in digital archive.
The characterization of the three specific functions of LAS (LAS-Reservoir or LAS-R, LAS-Conduit or LAS-CD and LAS-Contractile or LAS-CT) was performed using the echocardiographic speckle tracking technique.
Patients were evaluated through anamnesis, physical examination, blood tests including NT-proBNP and troponin T, electrocardiogram, trans-thoracic echocardiography, pulmonary function test and diffusing lung capacity for carbon monoxide and a maximal cardiopulmonary exercise testing (CPET).
Once the clinical assessment was consistent with a probable form of SSc-CMP (i.e. signs of heart dysfunction, bio-humorality activation, arrhythmias, cardiorespiratory limitation to exercise), selected patients received indication to perform Cardiac Magnetic Resonance Imaging (CMR) as reference test for detecting myocardial damage.
According to the diagnosis received, patients were divided into two groups: 1) patients with a diagnosis of SSc-CMP confirmed by any sign of myocardial damage at CMR (SSc-CMP+); 2) patients without a diagnosis of SSc-CMP nor any other type of cardiopulmonary involvement (SSc-CMP-).
Results: According to inclusion and exclusion criteria, 121 patients evaluated at the outpatient Cardiology Unit from January 2016 to December 2024 were included in the analysis. SSc-CMP was clinically suspected during clinical evaluation in 20 patients and was confirmed by CMR in 15 patients (10%). Cardiological or cardiopulmonary involvement was excluded in 20 patients that showed normal bio-humoral, morphological and functional findings (14%). No difference of autoantibodies profiles was found between the two groups. NT-proBNP was significantly higher in SSc-CMP+ compared to SSc-CMP- ($p<0.05$). TTE showed that LVEF and LAVi were similar in both groups ($p>0.05$). LAS-R% [23% (21-25) vs 32% (23-36), $p<0.05$], LAS-CD% [-11 (-15 -(-6)) vs -18% (-20-(-13)), $p<0.05$] and LA stiffness [0.4 (0.4-0.5) vs 0.2 (0.2-0.4), $p<0.05$] were significantly different between SSc-CMP+ and SSc-CMP-; differently, LAS-CT was not ($p>0.05$). See Table 1 for more details.
Conclusions: This study shows that a reduced LAS value can be considered as a marker of SSc-CMP even in early stages when LA volumetric indexes are still normal. Therefore, echocardiographic evaluation of LAS represents a noninvasive and routine screening method that can stratify SSc patients for primary myopathic involvement risk. This stratification would allow rheumatologists and immunologists to properly address patients to CMR execution. Furthermore, this study shows the potential development of SSc-CMP in all patients with SSc, irrespective of their autoantibody profile. Early and non-invasive recognition of SSc-CMP would allow to initiate a treatment targeting pro-fibrotic pathogenetic mechanisms, limiting the myocardial progression of SSc.

Table 1: Clinical, laboratoristic and echocardiographic features

	SSc-CMP+ N = 15	SSc-CMP- N = 20	SSc-CMP+ vs SSc-CMP-
Female (n, %)	14 (93%)	19 (95%)	p > 0.05
Age at first visit (median, years)	67 (61-71)	61 (52-67)	p > 0.05
Raynaud's Phenomenon (n, %)	12 (80%)	16 (80%)	p > 0.05
Disease Duration (median, years)	18 (3-20)	10 (5-12)	p > 0.05
Muscle-skeletal Involvement (n, %)	5 (33%)	3 (15%)	p > 0.05
Interstitial Lung Disease (n, %)	2 (13%)	1 (5%)	p > 0.05
Dyspnea NYHA II (n, %)	7 (47%)	11 (55%)	p > 0.05
Dyspnea NYHA III (n, %)	4 (27%)	0 (0%)	p <0.05
Palpitations (n, %)	2 (13%)	7 (36%)	p > 0.05
NT-proBNP (median, pg/mL)	**308 (170-624)**	**126 (60-153)**	**p <0.05**
Troponin T (median, ng/L)	**17 (16-26)**	**9 (6-14)**	**p <0.05**
CRP (median, mg/L)	0.3 (0.1-1.7)	0.6 (0.2-1.3)	p >0.05
ESR (median, mm/h)	22 (7-39)	14 (11-29)	p >0.05
ACA (n, %)	5 (33%)	9 (45%)	p >0.05
Anti-Scl70 (n, %)	7 (47%)	6 (30%)	p >0.05
FVC% (median, %)	**96 (82-111)**	**114 (88-123)**	**p <0.05**
LAS-Reservoir %	**23 (21-25)**	**32 (23-36)**	**p <0.05**
LAS-Conduit %	**-11 (-15 - -6)**	**-18 (-20 - -13)**	**p <0.05**
LAS-Contractile %	-13 (-17 - -9)	-12 (-18 - -9)	p > 0.05
LA stiffness (median)	**0.4 (0.4-0.5)**	**0.2 (0.2-0.4)**	**p <0.05**

WHEN MEDICAL HISTORY MAKES THE DIFFERENCE: A CASE OF A RARE FORM OF ENTEROPATHY

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L'enteropatia da Olmesartan è una rara reazione avversa al farmaco antipertensivo sartanico che agisce bloccando il recettore dell'angiotensina II. Un'associazione tra l'uso di Olmesartan e una grave enteropatia simil-sprue è stata descritta in alcuni case report ed è caratterizzata da diarrea cronica severa, perdita di peso e malassorbimento che si manifestano anche dopo mesi o anni dall'inizio del trattamento. All'esame istologico si evidenziano atrofia dei villi, linfocitosi intraepiteliale ed infiammazione della mucosa, caratteristiche che possono mimare il morbo celiaco ma in assenza di anticorpi tipici di tale malattia. La diagnosi è clinica e si basa sull'esclusione di altre cause di enteropatia e sul miglioramento dei sintomi fino alla completa risoluzione del quadro clinico dopo sospensione del farmaco. La patogenesi non è completamente nota, ma si ipotizza un meccanismo immuno-mediato.
Paziente uomo di 75 anni, giungeva alla nostra attenzione lamentando una sintomatologia caratterizzata da diarrea da oltre un anno fino a 7 scariche di feci liquide al giorno, anche notturne, senza presenza di sangue o muco. Negli ultimi due mesi aveva inoltre sviluppato edemi declivi e un aumento della circonferenza addominale con associata iporessia, dispnea e progressivo calo ponderale, arrivando a perdere circa 20 kg, ma senza manifestare nausea, vomito o dolore addominale.
Interrogando il paziente si è scoperto che per tendenza all'ipotensione circa un mese prima del ricovero era stata sospesa l'unica terapia in cronico assunta da tempo, Olmesartan 40 mg, per storia di ipertensione arteriosa.
L'esame obiettivo ha rivelato un grave stato anasarcatico con ascite, versamento pleurico bilaterale e edemi degli arti inferiori e del tronco. Gli esami ematochimici hanno evidenziato un quadro di malassorbimento severo con ipoonchia grave (albumina a 16 g/dl), anemia normocitica e carenze di acido folico, vitamina B12, ferritina, colesterolo e trigliceridi. Anticorpi anti-transglutaminasi IgA, TSH nella norma come anche gli indici di flogosi; Sierologia per HIV negativa, invece riscontro di positività per CMV DNA su sangue. Le colture delle feci e l'esame parassitologico sono risultati negativi. E' stata eseguita una paracentesi diagnostica che ha confermato la natura trasudatizia del versamento addominale.
Nel sospetto di una neoplasia occulta, è stata eseguita una TAC addome con mdc e EnteroTAC che hanno mostrato un aspecifico edema diffuso e segni di enterite diffusa con ispessimento e edema delle pareti intestinali, ma non segni di neoplasia.
Gli esami endoscopici macroscopicamente non hanno dimostrato lesioni compatibili con IBD; le biopsie eseguite durante gli esami endoscopici hanno evidenziato microlembi superficiali di mucosa enterica con flogosi attiva inoltre vi era una duodenite cronica attiva con presenza di inclusi da CMV.
Con il sospetto che la grave malnutrizione, malassorbimento e compromissione del sistema immunitario potessero aver favorito l'infezione da CMV e il

perpetuarsi della sintomatologia diarroica, è stata avviata la terapia con Ganciclovir e contestualmente terapia nutrizionale con nutrizione parenterale totale e multivitaminici. Per contrastare la severa ipoalbuminemia, è stata eseguita anche un'infusione di albumina.
Progressivamente il paziente ha mostrato un netto miglioramento con riduzione delle scariche di diarrea fino alla normalizzazione dell'alvo e riduzione edemi declivi e versamento pleurico e ascitico. È stata quindi riavviata la nutrizione orale associata a integratori proteici. Agli esami ematochimici si è assistito ad un progressivo aumento dei valori di emoglobina e albumina.
La diagnosi di enteropatia da Olmesartan con sovrapposta enterite da CMV è stata posta grazie all'anamnesi e all'esclusione di altre cause in quanto gli esami endoscopici sono stati eseguiti a distanza di oltre 4 settimane dalla sospensione del farmaco; non sono state quindi osservate le modifiche istologiche tipiche di questo processo patologico come l'atrofia dei villi e la linfocitosi intraepiteliale. Il significativo miglioramento della sintomatologia e delle condizioni generali del paziente si sono verificate dopo la sospensione del farmaco e l'avvio della terapia antivirale e nutrizionale.
Il caso clinico descrive una complicanza rara dovuta all'uso cronico di Olmesartan, l'enteropatia, complicata da infezione intestinale da CMV germe che colpisce tipicamente i pazienti immunocompromessi come il nostro paziente che presentava ormai da un anno diarrea e malassorbimento. Tale quadro ha determinato il peggioramento della sintomatologia. Vogliamo sottolineare l'importanza dell'anamnesi del paziente e di considerare l'enteropatia da farmaci nella diagnosi differenziale della diarrea cronica.
La sospensione del farmaco, insieme alla terapia antivirale e al supporto nutrizionale hanno determinato la risoluzione del quadro clinico.

FACIAL ERYSIPELAS HIDING ORBITAL CELLULITIS: A RARE PRESENTATION OF A COMMON INFECTION

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An 86-year-old male was admitted to our university hospital due to the recent onset of facial swelling and fever. Symptoms began several days prior to presentation and were not associated with any respiratory complaints. The patient denied any known drug allergies or recent initiation of new medications. He also reported no history of facial trauma, except for recent use of an electric shaver. The patient's medical history included metastatic prostatic cancer under active treatment with apalutamide, type 2 diabetes, and ischemic cardiomyopathy. Thus, the patient was admitted to our department for further diagnostic workup and initiation of appropriate therapy. Upon admission, vital signs were stable: blood pressure was 130/75 mmHg, heart rate 100 bpm, and oxygen saturation was 98% on room air. Physical examination revealed pronounced facial edema, particularly involving the eyelids, forehead, and earlobes. The overlying skin was warm and erythematous, displaying a malar rash distribution, with evidence of the characteristic "step sign." Cutaneous lacerations were especially prominent around the eyelids, where the swelling was most severe, and a mild serous exudate was noted. The remainder of the physical examination was unremarkable. The patient underwent laboratory testing, which revealed leukocytosis and elevated C-reactive protein (CRP) levels. Two sets of blood cultures were obtained. Given our clinical suspicion of facial erysipelas, empiric antibiotic therapy with ceftriaxone was initiated. An otolaryngologic evaluation with fibreoptic endoscopy was subsequently performed, confirming preservation of the airway and excluding infectious foci in the nasal and pharyngeal regions. Therefore, systemic antibiotic therapy was maintained, and adjunctive local treatment with chloramphenicol and tobramycin was continued. In the following days, blood culture results became available, identifying a multisensitive Streptococcus pyogenes. Based on this finding, the current antimicrobial regimen was confirmed. The patient showed partial clinical improvement, with progressive reduction of facial edema and erythema, and resolution of eyelid lacerations except on the right side. Fever subsided, and both white blood cell count and CRP levels returned to normal. Given the extent of ocular involvement, a computed tomography scan of the facial bones was performed, revealing radiological evidence of right-sided orbital cellulitis. A multidisciplinary discussion with the otolaryngology and ophthalmology teams was held, and surgical intervention was deemed unnecessary. The patient was subsequently discharged with instructions to continue oral cephalosporin therapy and to undergo close outpatient follow-up, including further otolaryngologic reassessment.
Erysipelas is a prevalent, acute bacterial infection of the skin, primarily involving the superficial dermis. Alongside cellulitis, these infections collectively affect approximately 19 to 24 individuals per 10,000 annually across European populations. The vast majority of cases are attributable to β-haemolytic Streptococci, particularly Group A strains. In contemporary clinical practice, erysipelas most frequently presents on the lower extremities, while facial involvement has become relatively uncommon. Disruption of the cutaneous barrier is recognized as a significant predisposing factor. Additionally, a substantial proportion of patients exhibit underlying co-morbidities, most notably cardiovascular disease and diabetes mellitus. Diagnosis is predominantly clinical, based on the presence of sharply demarcated, erythematous, warm, and tender skin lesions—often exhibiting the characteristic "step sign." Systemic manifestations, including fever, chills, malaise, and laboratory abnormalities such as leukocytosis and elevated CRP levels, are commonly observed. Although imaging studies are not diagnostic, they may be employed to assess for complications or to evaluate atypical or severe presentations. The prognosis is generally favorable when appropriate and timely treatment is initiated. However, facial erysipelas may carry a higher risk of complications. Management of uncomplicated cases typically involves empiric antibiotic therapy, most commonly with penicillins or cephalosporins, administered for 7 to 14 days.
This case illustrates an uncommon presentation of a common condition, underscoring the importance of recognizing atypical clinical manifestations. A thorough patient history and clinical evaluation are essential to rule out more prevalent differential diagnoses and to guide diagnostic reasoning toward the correct clinical suspicion. Only upon establishing an accurate diagnosis can appropriate treatment be initiated, thereby optimizing patient management and therapeutic outcomes.

CASE REPORT: PARANEOPLASTIC LEUKEMOID REACTION IN NON-SMALL CELL LUNG CANCER

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Introduction: and background: A white blood cell (WBC) count exceeding 50.000/μL with a marked neutrophilic shift, in the absence of a hematologic neoplasm, defines a leukemoid reaction. Common causes include infections, growth factor administration, corticosteroid therapy, hemophagocytic lymphohistiocytosis, and solid tumors. Paraneoplastic leukemoid reactions refer to a leukemoid reaction occurring in patients with solid malignancies, after excluding other potential causes. In rare cases, the WBC may exceed 100.000/μL, a condition known as hyperleukocytosis. Management of paraneoplastic leukemoid reactions is primarily supportive, with removal of the causative malignancy as the only curative option. Notably, paraneoplastic leukemoid reactions is associated with a poor prognosis.
Here we describe a case of paraneoplastic leukemoid reactions in a patient with non-small cell lung cancer (NSCLC).
Case report: An 81-year-old caucasian man presented to the emergency department with progressive chest pain and exertional dyspnea over the preceding month. His past medical history included arterial hypertension, type 2 diabetes, dyslipidemia, and prostate cancer treated surgically 7 years earlier, with documented complete remission. He was a former smoker (10 pack-year), consumed 1-2 alcohol units per week, and was fully independent in his daily activities. On examination, he had an increased respiratory rate and low peripheral oxygen saturation (89%), with abolished breath sounds in the left lung. Blood test showed leukocytosis (30,000 WBC/μL) with a neutrophilic shift. A chest computed tomography (CT) scan showed a massive pleural effusion in the left lung, associated with atelectasis and multiple subpleural nodules, the largest measuring 4 x 7cm. Through thoracoscopy, pleuric lesions were biopsied, and a pleural drainage was placed. Histopathological analysis subsequently confirmed the diagnosis of non-small cell lung carcinoma, TTF-1 and p40 negative, cytokeratin-6 positive, with 60% PD-L1 expression. PET-CT showed an enlarged ipsilateral pericardic lymph node, staging the cancer as rT4N2aM1a.
In the following days, the patient's WBC continued to rise, reaching a peak of 130,000 WBC/μl with a marked neutrophilic shift. Empiric antibiotic therapy was initiated for presumed hospital-acquired pneumonia with piperacillin/tazobactam, and vancomycin was added for Staphylococcus aureus coverage. However, the clinical and biochemical response was inadequate. Blood cultures, urinary antigens for Legionella and Streptococcus pneumoniae, and multiplex PCR for common respiratory viruses were all negative. A comprehensive infectious diagnostic work-up was conducted, excluding mycobacterial and fungal infections, human immunodeficiency virus, human herpes virus 8, Ebstein Barr Virus, cytomegalovirus, and Clostridioides Difficile. Bone marrow biopsy and fine-needle aspiration cytology ruled out both secondary invasion and primitive myeloproliferative neoplasms. BCR-ABL amplification was negative. Laboratory parameters including ferritin, triglycerides, fibrinogen,

and transaminases were assessed to rule out hemophagocytic lymphohistiocytosis. A final diagnosis of paraneoplastic leukemoid reactions determining hyperleukocytosis was established.
During hospitalization, the patient developed worsening respiratory failure, requiring non-invasive ventilation to maintain adequate oxygenation. He was deemed ineligible for chemotherapy due to clinical deterioration. Pulmonary function continued to decline rapidly, likely due to a combination of cancer progression and pulmonary leukostasis. Despite limited evidence supporting leukoreduction in the context of paraneoplastic leukemoid reactions, oral hydroxycarbamide was initiated alongside with allopurinol and adequate endovenous hydration to reduce the risk of tumor lysis syndrome. Although a gradual reduction in total WBC was observed, levels remained markedly elevated (> 80000 cells/µl) alongside with moderate increase in uric acid (from 7 to 9.6 mg/dl). The patient was evaluated for potential immunotherapy, but unfortunately died from worsening respiratory failure before treatment could be initiated.
Conclusion: Paraneoplastic leukemoid reaction is a rare complication of solid tumors, for which no specific treatment is currently established. Hyperleukocytosis in the context of paraneoplastic leukemoid reactions is uncommon and poses significant management challenges. Further research is needed to clarify the role of cytoreductive strategies in this setting. Diagnosis is made by excluding infectious causes and hematological malignancies, requiring a comprehensive diagnostic workup. paraneoplastic leukemoid reactions may serve as a surrogate marker of aggressive malignancy, as it is typically associated with high tumor burden, elevated systemic inflammation, and poor prognosis.

HYPERPYREXIA DUE TO INADEQUATE CORTISOL SECRETION

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Introduction: Fever of unknown origin (FUO) is classically defined as occasional body temperature ≥ 38.3°C without a certain diagnosis despite one week of appropriate in-hospital investigation. Main causes are infections, neoplasms and inflammatory diseases. However, a quarter of FUO remains undiagnosed. We report a case of a rare cause of FUO, in which the diagnosis could not be established through standard diagnostic work-up, but rather through an accurate review of the patient's medical history.
Case report: An 84 years-old man was admitted to our Internal Medicine Unit for dyspnea, fever, acute kidney injury and anemia. His relevant medical history included urothelial carcinoma treated surgically, right adrenalectomy for a hemorrhagic cyst, left adrenal lesion compatible with an adenoma, chronic kidney disease, atrial fibrillation, ischemic cardiomyopathy with ICD implantation, metasteroid diabetes and COPD. The patient was on treatment with clopidogrel, tamsulosin, carvedilol, pantoprazole, apixaban, hallopurinol, furosemide, insuline and inhaled corticosteroid. At the admission the patient presented with dyspnea, fever, acute renal failure (sCr 2.61 mg/dL), normocytic anemia (Hb 8.5 g/dL, MCV 89.2 fL) and high C-reactive protein (CRP 115.4 mg/L). Clinical presentation and chest X-ray supported the diagnosis of COPD exacerbation. Ceftriaxone and azithromycin were initiated, with improvement in respiratory symptoms and decrease of inflammatory markers. Fluids resuscitation restored renal function to baseline. Multifactorial anemia (due to kidney disease, vitamin deficiencies and chronic inflammation) required a single-unit blood transfusion. Pyrexia persisted despite antibiotic therapy, with increasing inflammatory markers (peak CRP 149.5 mg/L) and progressive psychomotor slowing and disorientation. Insulin therapy was tapered until discontinuation due to hypoglycemia. Blood and urine coltures tested negative in multiple occasions. Extended screening for autoimmunity was normal. Fungal and viral screening resulted negative for acute infections. Contrast-enhanced thoracic and abdominal CT scans were normal, except for a unilateral saccate pleural effusion previously detected on imaging. An attempted thoracentesis was unsuccessful. Persistent fever fulfilled both time-dependent and qualitative criteria for FUO, lasting a total of two-weeks from the admission. To further investigate, a PET-FDG was performed, showing focal enhancement on the left adrenal gland.Considering patient's clinical manifestation (fatigue, psychomotor slowing and hypoglycemia) adrenal insufficiency was suspected. A more detailed review of the patient's medical history revealed recent treatment for metastatic prostate cancer with a novel CYP11A1 inhibitor (ODM-208), with dexamethasone and fludrocortisone as replacement therapy, discontinued a month earlier due to dyspnea. Prednisone was continued until one week before admission. A review of the literature on ODM-208 revealed adrenal insufficiency as potential adverse drug reaction1. Given the known adrenal lesion and recent treatment with ODM-208, further evaluation of the hypothalamic-pituitary-adrenal pathway was performed. Low cortisol levels (2.46 µg/dL) and ACTH values (10.9 ng/L) confirmed the diagnosis of central hypoadrenalism. According to endocrinology consulting, immediate replacement therapy with cortisone acetate was initiated (50 mg die) leading to defervescence within two days and stable apyrexia. Interestingly, the patient's cognitive status improved significantly and regained psychomotor activity. The patient was discharged with cortisone supplementation therapy.
Discussion: and conclusionHyperpyrexia can result from inadequate suppression of proinflammatory cytokines due to insufficient cortisol secretion. Therefore, adrenal insufficiency represents a rare endocrine cause of FUO often overlooked by its nonspecific symptoms and misdiagnosed as infectious disease2. Clinical manifestations include fatigue, weight loss, vomiting, hypotension and fever. Hypoglycemia and hyponatremia are frequently observed. Risk factors are immunosuppressants or systemic steroids use. ODM-208 is an oral non-steroidal CYP11A1 inhibitor, with potential to treat endocrine regulated cancers by inhibiting the steroid hormone biosynthesis. As expected, adrenal insufficiency is a frequent treatment-related adverse event. However, data on prolonged adrenal suppression following discontinuation are currently lacking. Diagnosing adrenal insufficiency in this patient was challenging due to its nonspecific clinical features and its rare occurrence as a cause of FUO. In this case, an accurate revision of the patient's medical history was essential to detect risk factors associated to hypoadrenalism. The possibility of adrenal insufficiency should be considered in patients with fever of unknown origin and risk factors.
Bibliography: *et al. NEJM Evidence et al. Postgrad Med*

A CASE OF ATYPICAL NON-ALCOHOLIC WERNICKE ENCEPHALOPATHY

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Introduction: Wernicke encephalopathy (WE) is a neurological disorder secondary to thiamine (vitamin B1) deficiency. Although alcoholism is the most common predisposing factor, WE can occur in any patient with a nutritional deficiency state such as hyperemesis gravidarum, prolonged fasting, recurrent vomiting, gastric disorders or malignant disease1. The most common neurological findings include mental status changes, ophthalmoplegia and gait ataxia. However, this classical triad of symptoms presents in a low percentage of patients, which explain why WE is often underdiagnosed. Early diagnose and prompt treatment are necessary to prevent Korsakoff syndrome, which occurs in approximately 80% of untreated WE, with persistent neurocognitive impairments.
Case report: We present a case of a 70-years-old woman admitted to our Internal Medicine Unit for recurrent vomiting lasting almost three weeks. A week before the patient was discharged from our Emergency Department with a diagnosis of emesis reconducted to opioid abuse taken for polymyalgia rheumatica. Her medical history included hypercholesterolemia, a previous TIA, glaucoma and depressive anxiety syndrome. No history of alcohol consumption was detected. She was on treatment with allopurinol, atenolol, omeprazole, levosulpiride, acid acetylsalicylic and ezetimibe. The vomiting was not related to meals and was partially responsive to metoclopramide and haloperidol. During hospitalization oral feeding was poor. To investigate the cause of vomiting a contrast-enhanced abdominal CT scan was made and showed normal perfusion and caliber of intestinal loop, no free fluid was present. An esophagogastroduodenoscopy showed a hiatal hernia and a mucosal biopsy was suggestive of mild chronic gastritis. Magnetic resonance of the abdomen showed a dilatation of the main bile duct and a fibrotic stenosis of the Vater Papilla. An endoscopic ultrasonography was performed, showing normal caliber of explorable bile ducts and a normal aspect of the Vater Papilla. Brain CT scan did not reveal signs of intracranial hypertension that could be associated with vomiting. In addition, psychogenic or functional swallowing impairment were excluded. Blood tests and biochemistry results showed mild normocytic anemia (Hb 9.9 g/dL, MCV 86.6 fL) with iron deficiency, a slight elevation in C-reactive protein (CRP 10.37 mg/dL) which decreased spontaneously, but no sign of malabsorption. Blood and urine coltures tested negative. During the stay, the patient developed a progressive asthenia leading to a bedridden state. At the same time the patient's mental status was rapidly worsening, displaying apathy and disorientation, progressing to a persistent soporous condition. Simultaneously, the patient presented blurred vision and onset of scotomas. An emergency brain CT scan performed immediately was normal. Considering the neurological findings and suspecting metabolic encephalopathy, a nasogastric tube was placed for nutritional support and ex-adiuvantibus therapy with intravenous thiamine was started at the dose of 500 mg every 8 hours. A brain MRI revealed findings consistent with metabolic deficiency and confirmed the diagnosis of Wernicke encephalopathy. T2-weighted imaging showed hyperintensities in the tectal plate, dorsomedial thalamus, periventricular region and around the cerebral aqueduct, areas typically affected in thiamine-deficiency-related metabolic encephalopathy1. The patient regained consciousness the day after the initiation of intravenous thiamine, with a significant improvement in mental status. Vomiting immediately regressed, and oral feeding was rapidly resumed. Visual disturbances improved with return to pre-hospital baseline. At discharge, the patient's cognitive status had improved. Neurological

examination at the two-months follow-up was normal, except for mild memory impairment.
Conclusion: Wernicke encephalopathy is frequently underdiagnosed and suspected during life in only 6% of non-alcoholic patients. The diagnosis in non-alcoholic population is often challenging with considerable delay in treatment. Its recognition remains difficult due to lower prevalence and complex clinical presentation, especially when the classic triad is not fully detectable. In the case mentioned, the most consistent feature of the syndrome was the change in mental status. Interestingly, in this case, prolonged emesis also appeared a prodromal symptom of the syndrome preceding the onset of neurological manifestations, as described in some case reports2. After exclusion of organic, neurological or functional causes of emesis and an unsuccessful maximal and prolonged symptomatic therapy, we observed an immediate regression of the emesis after the initiation of thiamine replacement therapy. For these reasons prolonged emesis is not only an exacerbating factor of WE, as widely described in the literature, but appeared in this case as an atypical and early manifestation of encephalopathy.
Bibliography: *Mayo Clin Proc BMJ Case Rep*

IS COGNITIVE STIMULATION AND REORIENTATION AN EFFECTIVE THERAPEUTIC STRATEGY FOR DELIRIUM PREVENTION? RESULTS FROM A PILOT REAL LIFE STUDY IN AN INTERNAL MEDICINE SETTING

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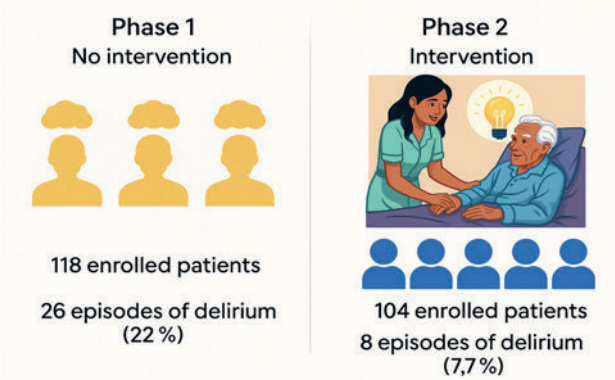
Background: Delirium is a mental disorder characterized by acute disturbance of consciousness, attention, and cognition tending to fluctuate during the day. The occurrence of delirium in non-critical medical setting is reported over 20%, including internal medicine settings characterized by frail patients, aged 70 and over, a large percentage with comorbidities and exposed to numerous risk factors for developing delirium during hospitalization. Regardless of the care setting, the occurrence of delirium has a huge clinical, social and economic burden on the healthcare systems across countries.
The aim of the study is to verify the effectiveness on the prevention of delirium of targeted and punctual actions based on cognitive stimulation and reorientation, delivered by medical student volunteers in the 3rd-6th year adequately trained through a structured theoretical-practical course for the acquisition of cognitive stimulation and reorientation skills.
Methods: A monocentric longitudinal study has been carried out in the Internal Medicine Unit 4 of the University Hospital of Careggi (Florence). The study has been divided in two phases.
Phase 1: Inpatients have been consecutively enrolled for three months if fulfilled the inclusion criteria (age > 65 years at the admission) and exclusion criteria. The exclusion criteria were dementia, the occurrence of delirium within 72 hours before hospitalizations and the inability to understand or take part in the study. Delirium incidence has been assessed via the administration of Four "A"s Test delirium screening tool (4-AT) by physicians of the Unit, every day for the whole duration of the hospitalization.
Phase 2: As for phase 1, inpatients have been consecutively enrolled for three months following the same inclusion and exclusion criteria, and the 4-AT has been used to detect the occurrence of delirium. The only variable differing from phase 1 was the targeted intervention of volunteers trained medical students, delivered every day for all the hospitalization, with a time session of 45 minutes, always under the supervision of clinical psychologists and physicians of the Unit.
Results: In phase one 118 patients have been enrolled, with an average age of 81.23 ± 8.84 years, average length of hospitalization 10.91 ± 6.05 days (47.5 % females). In 26 of the 118 patients enrolled (22%) the 4-AT showed the onset of a first episode of delirium.
In phase two 104 patients have been enrolled, with an average age of 815 ± 8.28 years, average length of hospitalization 10.29 ± 4.87 days (48.1 females). In 8 of the 104 patients enrolled (7,7%) the 4-AT showed the onset of a first episode of delirium.
In Figure 1, the study is presented in the form of a graphical flowchart.
Conclusions: In the literature there is a general agreement about the need of a multiprofessional approach to delirium prevention and management, in order to adopt a targeted strategy including pharmacological and not pharmacological interventions. In this context, the emerging role of trained volunteers, better if part of the medical word such as medical students, may play a pivotal role. These preliminary data seem to confirm the significative impact of a targeted intervention on cognitive stimulation and reorientation in reducing the delirium incidence in this clinical setting, at the same time offering to volunteers medical students the possibility to develop skills in medical-patient relationship.



EFFECT OF A SINGLE ZOLEDRONIC ACID ADMINISTRATION ON CIRCULATING BIOMARKERS OF LIPID METABOLISM IN WOMEN WITH POSTMENOPAUSAL OSTEOPOROSIS

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The mutual interaction between cardiovascular and metabolic bone disease is a current area of active research. In this context, one major topic is represented by the possible effect of bone-active drugs on cardiovascular disease and cardiovascular risk factors. As far as bisphosphonates, emerging evidence suggest a reduction in cardiovascular events and mortality in alendronate users. Few and inconsistent reports have been published on zoledronic acid (ZA) and cardiovascular risk. The primary outcome of this observational study was the assessment of the effect of a single intravenous administration of ZA on serum biomarkers of lipid metabolism in women with postmenopausal osteoporosis. We studied 34 women with postmenopausal osteoporosis (mean age ± SD, 72 ± 8.2 years) and indication to treatment with ZA, that was administered as a single 5 mg intravenous dose. Ten healthy postmenopausal women were recruited as control group among those referred by general practitioners for menopause-screening program. Subjects with disorders and/or on any drug potentially affecting bone metabolism were excluded from the study. Fasting blood samples were drawn between 8.00 and 10.00 a.m. at baseline, 3, 6 and 9 months. We measured serum ionized and total calcium (Ca++, Ca), phosphate (P), creatinine (Cr), total alkaline phosphatase (ALP), bone alkaline phosphatase (BALP), 25-hydroxy-vitamin D [25(OH)D], and parathyroid hormone (PTH); total and HDL cholesterol (C), triglycerides, homocysteine, apolipoprotein (APO) A and B. Serum LDL-C was calculated by the Friedewald formula.
Baseline data showed no between-group difference in demographic and anthropometric characteristics, serum levels of biomarkers of bone and lipid metabolism, except for higher ALP in the ZA group (168.7 ± 60.7 vs 79 ± 46 IU/L, $p < 0.05$, normal values 35-104). At 9 months, mean serum PTH levels were higher in the ZA (43.7 ± 20.5 pg/mL) compared to the control (34 ± 6) group ($p < 0.05$); serum BALP levels were lower in the ZA (15 ± 7 mg/L) compared to the control (21 ± 3.5) group ($p < 0.02$). No significant 9-month difference in all the other parameters were observed between the two groups. The within-group analysis showed no change in serum Ca, Cr and P levels, and a slight 3-month decline in serum Ca++ ($p<0.01$), with no cases of frank hypocalcemia in the ZA group (Figure 1A). Serum ALP and BALP significantly decreased over time ($p<0.05$), and a mean 17.5 ± 15% 9-month increase in serum PTH was observed ($p<0.01$) in the ZA group. Interestingly, the increase in serum PTH levels was significant as soon as 3 months ($p<0.05$) and declined afterwards (Figure 1B). Serum 25(OH)D levels were maintained above the threshold of > 30 ng/mL during the entire observation period with no change over time in the ZA group (Figure 1B). There were no significant changes in serum total C, HDL-C, LDL-C and triglycerides, APO-A, APO-B, and homocysteine at any time point in the ZA group (Figure 1C-D). No significant difference was observed in any of the metabolic parameters in the control group.
Our pilot study demonstrated that the administration of a single intravenous 5 mg dose of ZA has no relevant effect on the circulating biomarkers of lipid metabolism in women with postmenopausal osteoporosis.

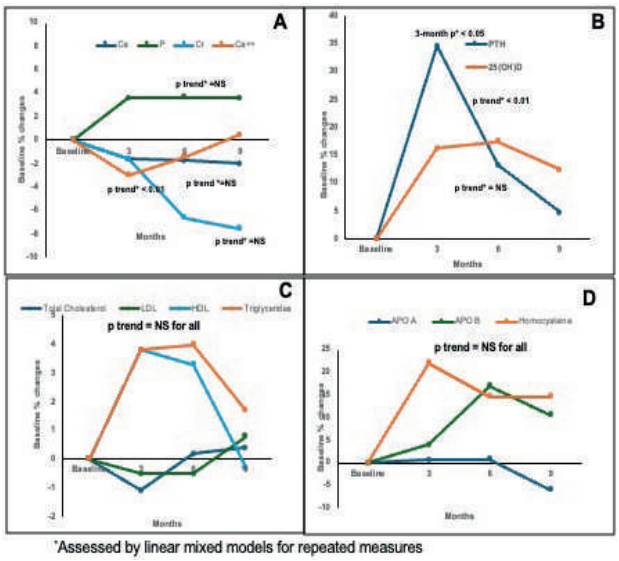

Figure 1. Time trend of serum biomarkers of bone and lipid metabolism after a single intravenous infusion of 5 mg zoledronic acid in postmenopausal women with osteoporosis

LONG-TERM SAFETY OF MRNA VACCINES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND LUPUS-LIKE DISEASES WITH A PREVIOUS HISTORY OF MYOCARDITIS

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Introduction: Patients with systemic autoimmune diseases can experience disease flares following immune stimuli, such as infections. Vaccination against common pathogens reduces infection rates and is associated with a lower risk of adverse events compared to natural infections. Therefore, vaccination is highly recommended by international guidelines. However, limited specific evidence exists about the long-term safety of the novel mRNA-based vaccine platforms developed to fight the recent COVID-19 pandemic. These vaccines are known to induce (though infrequently) myocarditis, raising concerns among patients with pre-existing history of myocardial inflammation in the setting of autoimmunity. To address these concerns, we have previously analysed the short-term impact of vaccination in a cohort of 13 patients with Systemic Lupus Erythematosus (SLE) and lupus-like connective tissue disorders and history of myocarditis. We now report on their long-term follow up.
Methods: We enrolled all consecutive patients who attended a scheduled follow-up visit in the Lupus Clinic of our hospital between April 2021 and January 2022 fulfilling the following criteria: diagnosis of SLE according to the 2019 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) and/or the 2012 SLE International Collaborating Clinics (SLICC) classification criteria for SLE, an UCTD diagnosis, or a MCTD diagnosis; history of virus-negative myocarditis; having received an anti-SARS-CoV-2 vaccination as per national protocols. Demographic and clinical data, including the occurrence of flare, were collected at baseline, after subsequent vaccination doses and in the regular follow-up visits for at least 24 months after the last post vaccination visit. Disease activity was quantitated through the SLE disease activity index 2000 (SLEDAI-2K) and the British Isles Lupus Assessment Group (BILAG) 2004. Damage was estimated through the SLICC/ACR damage index (SDI). Remission was defined according to the low disease activity status (LLDAS) and definition of remission in SLE (DORIS) criteria. Continuous variables are expressed in median and interquartile range, categorical variables as number and percentage. Chi square test was performed to compare categorical variable, while we used Wilcoxon's matched-pair signed rank test to assess interindividual changes in continuous variables
Results: Out of the original 13 patients, 12 (92%) received follow-up visit, while one patient moved to a different Region. Seven (58%) were female, 10 had SLE and 1 MCTD and 1 UCTD. The median observation time from first vaccination dose was 41 (35-45) months, while the median follow-up time from the last post-vaccination visit was 27 (26-32) months. No disease flare or sign of myocarditis recurrence were observed in the follow-up period. At last visit, all patients had a low disease status according to LLDAS definition and all but one remission according to DORIS. The median SLEDAI-2K was 0 (0-2) and no patient displayed activity in any BILAG dominion. The median SDI was 1 (0.8-2.3), with no significant variation from pre-vaccination visit. Cardiac enzyme testing was available for 9 (75%) of patients at follow-up. Median ProBNP levels were 67(43-232) pg/ml with no significant variation from baseline (median variation -49 [-92 - 5] pg/ml p=0.250). the median troponin T level was 8 (4 - 14) ng/ml with no significant variation from baseline (median variation 1 [0 - 3]). Of notice, two patients had a higher-than normal troponin level (14.5 and 27ng/ml respectively). Both patients had altered troponin level at baseline, and no significant variation was detected for both. Nine patients underwent new routine echocardiography (median time after first dose 35 (29-41) month), with no worsening findings detected. One patient underwent cardiac MRI, with no signs of active myocarditis.
Discussion: . mRNA-based vaccines do not associate with clinically relevant long-term signals of concern in patients with SLE and lupus-like disorders with a previous history of myocarditis both in terms of general disease activity and of cardiac safety. Validation of these data in an independent cohort is warranted to confirm their generalisability.

DIFFERENTIAL DIAGNOSIS OF HYPOPHOSPHATEMIA AND BONE PAIN IN ADULTS: A RARE CASE OF ENPP1-RELATED ARHR2

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Background: Hypophosphatemic syndromes are a heterogeneous group of disorders characterized by hypophosphatemia and impaired bone mineralization. Their clinical manifestations include abnormalities in skeletal development, fragility fractures, as well as bone and muscular pain. In the differential diagnosis of hypophosphatemic syndromes, both genetic and acquired forms must be considered (e.g., tumor-induced osteomalacia). Among the genetic forms, a particularly rare one is autosomal recessive hypophosphatemic rickets type 2 (AHRH2), which results from a mutation in the ENPP1 gene. This mutation leads to an overproduction of the phosphaturic hormone fibroblast growth factor 23 (FGF23). A distinctive feature of this gene is that its mutations can be associated with Generalized Infantile Arterial Calcification (GACI), which is characterized by widespread arterial calcifications, typically affecting the medium and large arteries. From a laboratory perspective, AHRH2 is characterized by hypophosphatemia, hyperphosphaturia, elevated serum FGF23 levels, and increased bone alkaline phosphatase (bALP) levels.
Case report: We report the case of a 36-year-old woman who presented to our clinic with hypophosphatemia and hyperparathyroidism. Her family history includes a miscarriage in the mother and a sister who passed away in infancy. She is short in stature (148 cm) and reports chronic pain localized to the spine and the joints of the upper limbs since the age of 18, without any evidence of a rheumatic disorder. At the age of 33, she underwent an orthopedic evaluation, which recommended arthroplasty for bilateral coxarthrosis. Laboratory findings showed hypophosphatemia (0.62 mmol/L) with normal calcium levels (2.25 mmol/L), hyperphosphaturia, hyperparathyroidism (PTH 65.7 ng/L), and evidence of increased bone turnover (bALP 37.9 µg/L), with inappropriately normal 1,25-dihydroxyvitamin D levels (104 pmol/L). Bone densitometry showed reduced bone mass compared to what is expected for her sex and age. Radiographs revealed reduced bone mass and calcific enthesopathy involving the sacroiliac and coxofemoral joints. To rule out the primary causes of hyperparathyroidism, she underwent a neck ultrasound, neck scintigraphy with 99mTc-sestamibi, and PET-CT with 11CCholine, all of which yielded negative results for parathyroid pathology. In the suspicion of a hypophosphatemic syndrome, serum intact FGF23 levels were measured and found to be elevated (107 pg/mL). At this point, given the onset of symptoms in young adulthood, an acquired form was considered less likely. Therefore, due to suspicion of a genetic disorder, Next Generation Sequencing (NGS) was performed and revealed a homozygous mutation (Cys241Arg) in the ENPP1 gene, confirming the diagnosis of ARHR2. The genetic testing extended to first-degree relatives identified the same mutation in heterozygosity. Given the association of this gene with GACI, Doppler ultrasound of multiple vascular districts was performed, with no evidence of arterial calcifications.
Conclusion: This is a complex case of very rare hereditary hypophosphatemic rickets, diagnosed in adulthood despite manifestations being present many years before. Although there is no direct evidence to support this, it could be hypothesized that the miscarriage in the mother and the early death of a sister

may be related to mutations in the same gene (present in heterozygosity in both parents), with subsequent progression to a GACI phenotype. Hypophosphatemic syndromes, although rare, should be included in the differential diagnosis of conditions involving unexplained bone fragility or bone pain. Early recognition of these syndromes can be facilitated by including serum phosphate measurement in the diagnostic work-up of these patients.

ELEVATED INTERLEUKIN-6 LEVELS ARE ASSOCIATED WITH AN INCREASED RISK OF QTC INTERVAL PROLONGATION IN A LARGE COHORT OF US VETERANS

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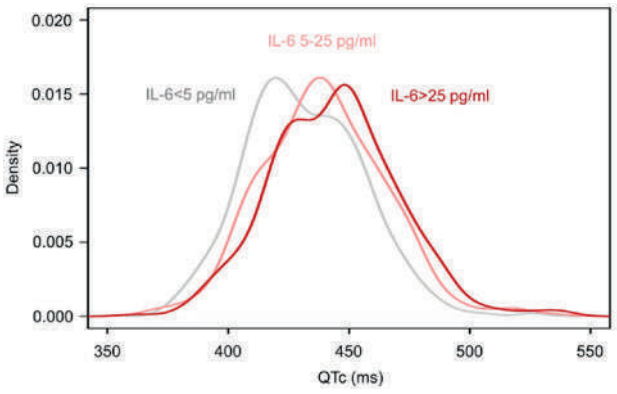
Background: Although accumulating data indicate that IL-6 (interleukin-6) can promote heart rate-corrected QT interval (QTc) prolongation via direct and indirect effects on cardiac electrophysiology, current evidence comes from basic investigations and small clinical studies only. Therefore, IL-6 is still largely ignored in the clinical management of long-QT syndrome and related arrhythmias. The aim of this study was to estimate the risk of QTc prolongation associated with elevated IL-6 levels in a large population of unselected subjects.
Methods: An observational study using the Veterans Affairs Informatics and Computing Infrastructure was performed. Participants were US veterans who had an ECG and were tested for IL-6. Descriptive statistics and univariate and multivariate regression analyses were performed to study the relationship between IL-6 and QTc prolongation risk.
Results: Study population comprised 1085 individuals, 306 showing normal (25pg/mL) IL-6 levels. Subjects with elevated IL-6 showed a concentration-dependent increase in the prevalence of QTc prolongation, and those presenting with QTc prolongation exhibited higher circulating IL-6 levels. Stepwise multivariate regression analyses demonstrated that increased IL-6 level was significantly associated with a risk of QTc prolongation up to 2 times the odds of the reference category of QTc (e.g. QTc >470 ms men/480 ms women ms: odds ratio, 2.28 [95% CI, 1.12–4.50] for IL-6 >25 pg/mL) regardless of the underlying cause. Specifically, the mean QTc increase observed in the presence of elevated IL-6 was quantitatively comparable (IL-6 >25pg/mL:+6.7 ms) to that of major recognized QT-prolonging risk factors, such as hypokalemia and history of myocardial infarction.
Conclusions: Our data provide evidence that a high circulating IL-6 level is a robust risk factor for QTc prolongation in a large cohort of US veterans, supporting a potentially important arrhythmogenic role for this cytokine in the general population.
References: 1. Tisdale JE. Prevalence and significance of acquired QT interval prolongation in hospitalized patients. Heart Rhythm. 2017;14:979–980. doi: 10.1016/j.hrthm.2017.03.036 5.
2. El-Sherif N, Turitto G, Boutjdir M. Acquired long QT syndrome and torsade de pointes. Pacing Clin Electrophysiol. 2018;41:414–421. doi: 10.1111/pace.13296 6.
3. Lazzerini PE, Capecchi PL, Laghi-Pasini F. Long QT syndrome: an emerging role for inflammation and immunity. Front Cardiovasc Med. 2015;2:26. doi: 10.3389/fcvm.2015.00026 7.
4. Lazzerini PE, Capecchi PL, Laghi-Pasini F. Systemic inflammation and arrhythmic risk: lessons from rheumatoid arthritis. Eur Heart J. 2017;38:1717–1727. doi: 10.1093/eurheartj/ehw208



UNCOMMON PATHOGEN, UNCOMMON CHALLENGE: A CASE OF LISTERIA ABDOMINAL ENDOGRAFT INFECTION

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Background: Aortic endograft infection is a rare but potentially life-threatening complication of endovascular abdominal aortic repair (EVAR), with mortality rates ranging from 3% to 50%. Common pathogens include Staphylococcus spp. and Salmonella spp. for native aortic infections, while Escherichia coli and Pseudomonas aeruginosa are more frequent in endograft infections. Listeria monocytogenes is an exceptionally rare cause of endograft infections, with only isolated cases reported. Listeria is a gram-positive, foodborne pathogen known to cause listeriosis. In immunocompetent individuals, listeriosis is often presented as a self-limited gastrointestinal illness. In contrast, in elderly or immunocompromised patients, Listeria can disseminate hematogenously, causing severe invasive diseases such as bacteremia, or, more rarely, vascular infections. In Italy, invasive listeriosis was observed in 0.4-0.5 cases per 100,000 inhabitants. Once ingested, Listeria can spreads hematogenously , adhering to aortic wall or prosthetic material, and endograft infection is associated with a mortality rates ranging from 25% to 100%. Endograft explantation is the "gold standard" treatment, but its risk in elderly or comorbid patients have prompted alternative approaches with prolonged targeted antibiotic therapy, occasionally in combination with percutaneous or surgical drainage. Case Report: An 82-year-old Caucasian man presented to the Emergency Department (ED) in February 2025 for abdominal pain partially responsive to paracetamol. His medical history included EVAR in 2019 with fenestrated endograft involving the renal arteries, superior mesenteric artery (SMA), and celiac tripod. In 2023, he underwent urgent SMA thrombectomy and stent relining for the occlusion of the stent. Surveillance imaging was performed biannually. In January, he visited another ED twice for abdominal pain and fever. An abdominal CT scan revealed a significantly dilated aorta, with an intramural hematoma along the left aortic wall, and mild heterogeneity of the adjacent adipose tissue; that raised suspicion of endograft infection, but he declined admission. One month later, he presented to our ED with persistent symptoms. Laboratory tests showed elevated C-reactive protein (CRP) levels, measuring 97 mg/L. He was admitted to our Internal Medicine department and, given the suspicion of endograft infection, a 18F-FDG PET scan was conducted, revealing a lesion with increased glucose metabolism located at the profile of a hematoma noted on the co-registered CT. Additionally, air bubbles were found in the aneurysmal sac on the baseline CT, which had not been present in previous radiological assessments, and suggestive of an infectious etiology. Blood cultures turned positive for Listeria monocytogenes, with concurrent fever, elevated CRP, and mild leukocytosis. Other microbiological tests, including beta-D-glucan, rectal swab, and nasal swab for MRSA, returned negative. As part of the diagnostic process, a transthoracic echocardiogram and a fundus examination were conducted, and excluded concomitant endocarditis or septic emboli. Following the identification of Listeria, a retrospective anamnesis revealed the ingestion of unpasteurized cheese in Sardinia, identified as the likely source of infection. Radiological and clinical data supported a diagnosis of endograft infection. However, due to the type of endoprosthesis, patient's age, and technical complexity of the initial aortic repair, the surgical explantation of the endograft through thoraco-phreno-laparotomic approach— requiring reconstruction of the thoraco-abdominal aorta and visceral vessels—was discussed collegially among internist, vascular surgery, infectious disease specialist, and anesthesiology team. Surgical treatment was excluded due to prohibitive perioperative risks, and conservative management with intravenous amoxicillin therapy was initiated, followed by transition to oral amoxicillin 1g every 6 hours after the conversion to negative of the blood cultures. The patient was discharged on this antibiotic regimen, with a three months treatment plan and reassessment to determine whether to extend therapy to six months or transition to chronic suppression regimen (amoxicillin 1g every 12 hours). Conclusions: This clinical case illustrates a rare presentation of Listeria monocytogenes endograft infection in an elderly patient following complex aortic repair. While in cases of prosthetic-related infections, surgical removal of the prosthesis remains the gold standard treatment, it is not always feasible, particularly in fragile patients. In such scenarios, the internist plays a key role in guiding diagnostic evaluation, integrating clinical and instrumental data, and balancing therapeutic options based on patient-specific risk. Although antibiotic therapy alone may not eradicate the infection, it can achieve infection control, prevent systemic complications, and maintain clinical stability. This case underscores the importance of individualized and patient-centered management strategies, particularly when dealing with rare and high-risk infectious complications in frail patients.

WALDENSTRÖM'S DISEASE, UNUSUAL DISEASE SITES: BING-NEEL SYNDROME

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Introduction: Waldenstrom macroglobulinemia (WM) is a clinicopathological entity characterized by the infiltration of the bone marrow by B cells with a lymphoplasmacytic phenotype and the presence of monoclonal IgM gammopathy in the bloodstream. WM is a rare oncohematological disease, with an incidence of three patients per million persons per year. The MYD88 gene is mutated in 90% of cases. Clinical presentation depends on neoplastic cell infiltration in hematopoietic organs or IgM clone effects in the bloodstream. Therapy is recommended for symptomatic patients. First-line therapy consists of cycles of bendamustine and rituximab; second-line option consists of the continuous administration of BTK inhibitors (e.g. ibrutinib).
Bing-Neel syndrome (BNS) is a rare complication of WM caused by the infiltration of the central nervous system by the lymphoplasmacytic clone. The exact incidence is unknown, but it is estimated to occur in 1% of WM cases. Furthermore, one-third of patients develop this syndrome during active treatment for WM. Clinical suspicion arises in the presence of balance and gait disturbances, cranial nerve involvement, cognitive status changes, headache, sensory deficits, paresthesia, alterations in vision and hearing, and psychiatric symptoms. The diagnosis is complex and relies on performing brain/spinal MRI and studying cerebrospinal fluid (chemical-physical analysis, cell count, flowcytometry, MYD88 mutation). The gold standard would be brain or meninges biopsy. In symptomatic patients the preferred treatment is ibrutinib.
Case Study: An 85-year-old woman presented to the Emergency Department (ED) with worsening dyspnea and a chest X-ray showing bilateral pleural effusion, significantly more pronounced on the right side. The patient also reported chronic leg pain and worsening hearing, both recently aggravated. The patient had a history of Waldenström's disease and had been on second-line active therapy with ibrutinib for six years.
Given the high suspicion of neoplastic disease (due to her hematologic history and serosanguineous pleural fluid on thoracentesis), a total-body CT was performed, revealing bilateral paravertebral extrapleural tissue, sacral spinal canal involvement, and a left iliac bone lesion. The percutaneous biopsy of the right paravertebral lesion showed massive lymphoplasmacytoid B-cell infiltration (CD20+, bcl2+, MUM1+, CD138-, CD5-, CD3-, CD10-, Cyclin D1-, bcl6-, CD38+, IgM+, CD23-/+; with a proliferative index ki67+ of approximately 10%), confirming Waldenström's localization. Flow cytometry of the pleural fluid identified cells with the same immunophenotype.
To further investigate the suspected spinal and bone involvement, an MRI of the pelvis and spine was performed, confirming extensive occupation of the sacral and lumbar spinal canal by vascularized pathological tissue, which appeared hypointense on long TR sequences. This tissue enveloped the nerve roots of the cauda equina and the spinal conus medullaris. Additionally, two small pelvic bone lesions of suspected progressive significance were described. A lumbar puncture with chemical-physical and flow cytometric analysis of cerebrospinal fluid (CSF) confirmed spinal involvement of Waldenström's disease, consistent with Bing-Neel syndrome. An off-label treatment with pirtobrutinib was undertaken upon hematologic recommendation.
Conclusions: BNS is highly heterogeneous in its clinical presentation, radiologic features, and treatment options. Prognosis data is limited, with variable study results. This syndrome should be considered in all WM patients with atypical neurological symptoms to prevent the risk of permanent neurological damage and establish appropriate therapy. This condition must be differentiated from IgM-mediated polyneuropathy, which typically presents with symmetric distal sensory loss. In contrast, BNS is characterized by asymmetric radicular symptoms with predominant motor deficits.

THE CEREBRAL GLUCOSE UPTAKE AS A MARKER OF CENTRAL INSULIN RESISTANCE: A SYSTEMATIC REVIEW.

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Introduction: Recent evidence in the literature indicates a significant relationship between the glucose metabolism and Alzheimer's disease (AD), with an increased risk of dementia in both prediabetes and type 2 diabetes (DM2). It has been proposed to consider AD as a cerebral diabetes or DM3, due to the important role of the insulin resistance in the pathogenesis of neurodegeneration. It is known that: - insulin receptors (IR) are present in the central nervous system (CNS), in particular in the typical cognitive areas (such as the hippocampus and the cerebral cortex); - insulin crosses the blood brain barrier via a transport process; - a local production of insulin in the CNS is possible; - the glucose uptake into the CNS (and cerebral metabolic rate of glucose, CMRglu) relies mainly on insulin-independent glucose transporter 1 and 3 (GLUT1 in astrocytes and GLUT3 in neurons), while insulin facilitates glucose uptake into the synapse via GLUT4. According to the amyloid cascade in AD, the deposition of amyloid beta (Aβ) plaques precedes the neuronal dysfunction with neurofibrillary tangles (tau protein). The neuroradiological tests that can commonly support the diagnosis of AD are: positron emission tomography (PET) with tracers (for example florbetapir) for fibrillar Aβ beta-amyloid (for the extent of the plaque load); PET with the tracer (flortaucipir) for tau (for neurofibrillary tangles); PET with the tracer 18F-fluorodeoxyglucose (18FDG) (for the evaluation of regional glucose metabolism); magnetic resonance imaging (MRI) and functional MRI (for brain atrophy and blood oxygen level-dependent, or BOLD, changes).
Aim of the study: The aim of this systematic review is to evaluate the relationship between the cerebral glucose uptake (and CMRglu) by 18FDG-PET, in subjects without substantial brain atrophy, and the presence of insulin resistance.
Materials and methods: The online medical literature database (via PubMed) was searched from 2003 to 2025, covering the 22-year period that marked the use of 18FDG-PET, using the search strategy to address the following: (1) problem (Alzheimer's disease), (2) diagnostic support (18FDG-PET), comparisons (different methods for assessing glucose metabolism), (3) outcome (accuracy), (4) article type (experimental studies) and (5) study design (any). The following string was used in the PubMed database search: Alzheimer's disease [Title/Abstract] AND glucose PET [Title/Abstract] AND insulin resistance [Title/Abstract]; cerebral glucose uptake [Title/Abstract] AND insulin [Title/Abstract]. The exclusion criteria were: studies not in English, inability to obtain the full text, type of articles (e.g. expert opinions, editorials, tutorials, case reports, abstracts, commentaries, book chapters, reviews or systematic reviews), no relationship with Alzheimer's disease (surrogate endpoints such as disability, dementia or other medical conditions related to cognitive dysfunction other than AD), no reported assessment of insulin resistance (surrogates such as metabolic syndrome), intervention studies (not related to purpose of the study), studies not applied to human subjects (studies on animal models). The selection of articles involved a two-stage screening process by two independent researchers: in the first stage, studies were assessed in terms of their relevance for assessing the relationship between insulin resistance and 18FDG-PET and, in the second stage, full texts were selected for inclusion. If necessary, any disagreements were resolved by a third independent reviewer.
Results: Six articles were selected and a total of n.92 studies were evaluated. In the first phase, we excluded n.2 systematic reviews and meta-analyses, n.15 reviews, n.1 practice guideline, n.40 studies with animal models (rat, mouse, primate, mammals) and n.18 in vitro cellular models. In the second phase, we excluded n.2 pharmacological studies, n.7 studies without 18FDG-PET scanning and n.6 studies without insulin resistance index.
The insulin resistance was assessed by using the "homeostasis model assessment-insulin resistance" (HOMA) index. The selected studies showed an average fasting blood glucose level between 75.6-107.1 mg/dl, an average fasting insulin 2.0-17.1 mcU/ml, a glycosylated hemoglobin (HbA1c) 5.0-5.5% and HOMA index 1.2-4.5. All the experimental studies reported a significant inverse correlation between the glucose uptake or consumption (CMRglu) in brain areas and the HOMA index.
Conclusions: The present systematic review supports the evidence of a significant relationship between the systemic insulin resistance and the cerebral glucose metabolism.
According to the recent guidelines, the evaluation of the cognitive functions of the patients with DM2 can be useful in order to personalize the targets of the antidiabetic treatments and to use the optimal pharmacological combinations.

PLATYPNEA-ORTHODEOXIA SYNDROME: A RARE CAUSE OF POSITIONAL HYPOXEMIA IN AN ELDERLY PATIENT

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Introduction: Platypnea-Orthodeoxia syndrome (POS) is a rare clinical entity characterised by positional dyspnea and arterial desaturation, defined as a drop in PaO2>4mmHg or SaO2>5% when transitioning to the upright position. The hypoxemia results from the admixture of deoxygenated venous blood with oxygenated arterial blood through a shunt. Based on the location of the shunt, the mechanisms of hypoxemia in POS are classified as either intracardiac or extracardiac. Intracardiac causes include patent foramen ovale (PFO) - the most common - atrial septal defect and atrial septal aneurism. Extracardiac causes include intrapulmonary arteriovenous malformation and hepatopulmonary syndrome.
Case report: An 86-year-old woman with a history of kyphosis and multiple thoracic vertebral fractures due to osteoporosis and no home medications, presented to the Emergency Department (ED) with dyspnea and hypoxemia occurred in the last few days (SpO_2 85% on room air, confirmed by arterial blood gas – pH 7.47, pCO2 28 mmHg, pO2 51 mmHg, HCO3- 20 mmol/L, lactates 0.9 mmol/L, electrolytes within limits) and no other symptoms. She required oxygen via Venturi mask with FiO2 of 60% to correct hypoxemia. Two days earlier, she had presented to another ED with similar symptoms and was discharged with a diagnosis of heart failure and advised to undergo further evaluation.
In our ED, no history of cardiac or pulmonary disease emerged; the patient was a non-smoker and had no cardiovascular risk factors. On physical examination, there was no heart murmur or peripheral edema, only fine bibasilar crackles. Electrocardiogram (ECG) was normal, as was a chest X-ray; lung ultrasound revealed focal B-lines (but fewer than three per field) bilaterally in the basis. Cardiac ultrasound showed normal left ventricular ejection fraction, no significant valvular disease, normal right heart, normal inferior vena cava, and mildly dilated ascending aorta (28 mm/m2). Compression ultrasonography (CUS) resulted negative for deep vein thrombosis. Complete blood count, liver and renal function tests, electrolytes, and coagulation were all within normal limits; NT pro-BNP was 650 pg/ml. A diagnosis of heart failure with preserved ejection fraction was made, thus the patient was treated with diuretics and admitted to the internal medicine ward.
During hospitalization, the patient developed acute tachypnoea and worsening hypoxemia, despite receiving oxygen therapy via Venturi mask FiO2 60%. Consequently, high-flow nasal cannula with FiO2 80% was initiated. Cardiac findings remained within normal limits and repeat CUS was negative for deep vein thrombosis. A contrast-enhanced chest CT scan excluded pulmonary embolism and other significant parenchymal lung diseases.
On physical examination, a marked improvement in oxygenation - approximately a 10% increase in SaO2, as confirmed by blood gas analysis showing a rise in pO2 from 50 to 83 mmHg - was observed in the supine position, with rapid desaturation upon sitting upright, raising suspicion of POS. The patient first underwent transthoracic echocardiography, followed by transthoracic echocardiography with bubble contrast, which demonstrated a right-to-left shunt through a PFO within the first three cardiac cycles. A definitive diagnosis of PFO was established. In the catheterization lab, under fluoroscopic and transesophageal echocardiographic guidance, the PFO was successfully closed via femoral vein access using a 30/25 mm Amplatzer Talisman device. Following the procedure, the patient's orthostatic hypoxemia resolved. She was discharged on dual antiplatelet therapy for one month, followed by aspirin monotherapy.
Conclusion: The diagnosis of POS can be challenging and requires a high index of suspicion. In the study of patients with dyspnea of unknown cause, a thorough medical history and careful physical examination are essential - particularly the assessment of oxygen saturation in both orthostatism and clinostatism positions, ideally confirmed by arterial blood gas analysis. In patients with otherwise unexplained dyspnea and evidence of platypnea-orhodeoxia, contrast-enhanced echocardiography (bubble study) should be performed. If a right-to-left shunt appears within the first three cardiac cycles, an intracardiac cause such as PFO or atrial septal defect is likely. If the shunt is detected after three cardiac cycles, a CT pulmonary angiogram is recommended to evaluate for intrapulmonary arteriovenous malformations. If this is negative, hepatopulmonary syndrome should be considered. Other potential differential diagnoses include pulmonary interstitial or alveolar diseases. Finally, in some patients—especially the elderly—POS may become clinically apparent due to secondary anatomical or functional factors that alter intracardiac blood flow. These include ascending aortic aneurysm, aortic valve replacement, prominent Eustachian valve, or severe kyphosis, as seen in our case.

DIFFERENT SEX HORMONE PROFILES ARE ASSOCIATED WITH TORSADE DE POINTES VENTRICULAR TACHYCARDIA IN MALES AND FEMALES: A CLINICAL-ELECTROPHYSIOLOGICAL STUDY

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Background: Female sex is a well-recognized risk factor for long-QT-syndrome(LQTS) and Torsades de Pointes(TdP), likely reflecting the influence of sex hormones on ventricular repolarisation. Overall, estradiol prolongs, while progesterone and testosterone shorten heart ratecorrected QT-interval. However, no studies have comprehensively evaluated sex hormone levels in male and female LQTS patients developing TdP, nor their implications in terms of clinical outcomes and electrophysiological changes.
Methods: We investigated: (1)the levels of sex hormones in a prospective cohort of male and female patients who developed TdP; (2)the relationship between sex hormones and arrhythmia outcome in TdP men and women; (3)the in-vitro impact of sex-specific TdP hormone profiles on guinea-pig ventricular myocyte APD and its modulation by sex-specific hormonal interventions.
Results: Over 13 years, 68 TdP patients(42 females) were consecutively enrolled. Compared to controls, a differential sex hormone profile was observed in TdP men and women, primarily reduced testosterone in males, and increased 17β-estradiol in females. Within the TdP cohort, lower testosterone in men and higher 17β-estradiol in women were associated with a worse short-term arrhythmia outcome. In-vitro reproduction of sex-specific TdP hormone profiles prolonged APD in sex-matched guinea-pig ventricular myocytes, an effect reversed by the addition of testosterone in males and progesterone in females, respectively.
Conclusions: Different sex hormone profiles, primarily low testosterone in males and high 17βestradiol in females, are associated with TdP occurrence and outcome in men and women. These endocrine milieus act, at least in part, via direct and reversible effects on cardiac electrophysiology, thereby supporting the antiarrhythmic potential of sex-specific hormonal-modulating therapies.
1. Drew BJ, Ackerman MJ, Funk M, Gibler WB, Kligfield P, Menon V, Philippides GJ, Roden DM, Zareba W, American Heart Association Acute Cardiac Care Committee of the Council on Clinical Cardiology tCoCN, and the American College of Cardiology Foundation. Prevention of torsade de pointes in hospital settings: a scientific statement from the American Heart Association and the American College of Cardiology Foundation. Circulation. 2010;121:1047-1060. doi: 10.1161/CIRCULATIONAHA.109. 192704
2. Salem JE, Waintraub X, Courtillot C, Shaffer CM, Gandjbakhch E, Maupain C, Moslehi JJ, Badilini F, Haroche J, Gougis P, et al. Hypogonadism as a Reversible Cause of Torsades de Pointes in Men. Circulation. 2018;138:110-113. doi: 10.1161/CIRCULATIONAHA.118.034282
3. Lazzerini PE, Cantara S, Bertolozzi I, Accioli R, Salvini V, Cartocci A, D'Errico A, Sestini F, Bisogno S, Cevenini G, et al. Transient Hypogonadism Is Associated With Heart Rate-Corrected QT Prolongation and Torsades de Pointes Risk During Active Systemic Inflammation in Men. J Am Heart Assoc. 2022;11:e023371. doi: 10.1161/JAHA.121.023371
4. Lazzerini PE, Bertolozzi I, Acampa M, Cantara S, Castagna MG, Pieragnoli L, D'Errico A, Rossi M, Bisogno S, El-Sherif N, et al. Androgen Deprivation Therapy for Prostatic Cancer in Patients With Torsades de Pointes. Front Pharmacol. 2020;11:684. doi: 10.3389/fphar.2020.00684

ADALIMUMAB VS. IXEKIZUMAB EFFECTIVENESS IN PATIENTS WITH PSORIATIC ARTHRITIS: A REAL-WORLD MULTICENTER STUDY WITH MATCH-ADJUSTED COMPARISONS

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Scolo del lavoro: Adalimumab (ADA) e Ixekizumab (IXE) sono risultati efficaci nel trattamento di diversi domini dell'Artrite Psoriasica (PsA) sia in studi controllati randomizzati (RCT) che in setting "real-world".
In questo studio multicentrico, l'obiettivo principale è stato confrontare l'efficacia

"real-world" di ADA vs. IXE, utilizzando un propensity score-matching per equilibrare gli outcomes di efficacia sulla base delle caratteristiche cliniche dei pazienti.

Mteriali e metidi: I dati dei pazienti (caratteristiche cliniche, comorbidità, punteggi di attività di malattia ed eventi avversi) sono stati raccolti retrospettivamente ed analizzati al baseline, ed a 3, 6 e 12 mesi. Gli outcome principali erano: 1. la proporzione di pazienti in MDA e VLDA, oltre che in remissione (REM) e bassa attività di malattia (LDA), utilizzando il DAPSA; 2. l'effetto medio del trattamento (ATE) sulla coorte di studio stimato con analisi di regressione dopo propensity-score matching.

Risultati: Sono stati arruolati un totale di 278 pazienti (68,3% ADA, 31,7% IXE). Al basale, i gruppi di pazienti ADA e IXE differivano significativamente (Tab. 1), soprattutto nelle comorbidità (più rappresentate nel gruppo IXE), nel precedente utilizzo di bDMARD (39,2% vs 56,7% rispettivamente), nell'attività di malattia secondo DAPSA (24,2±8,1 vs 30,0±11,5 rispettivamente), ASDAS-CRP (2,75±0,91 vs 3,01±0,49 rispettivamente) e PCR elevata (33,5% vs 67,5% rispettivamente).

Sia ADA che IXE sono risultati efficaci nel migliorare l'attività di malattia a livello articolare, cutaneo e funzionale ad 1 anno (Δ DAPSA: -12,8 e -14,9 rispettivamente p<0,0001; Δ PASI: -0,43 e -0,89 rispettivamente p<0,01; Δ HAQ: -0,34 e -0,49 rispettivamente p<0,0001).

La MDA è stata raggiunta nel 46% e 22% dei pazienti nei gruppi ADA e IXE, la VLDA nel 10% e 6%, la DAPSA LDA nel 53% e 44%, e la DAPSA REM nel 20% e 10% rispettivamente. Le retention-rates di entrambi i farmaci sono risultate simili.

Quando aggiustato in base alle caratteristiche basali dei pazienti, l'ATE stimato per IXE ha mostrato un rischio relativo per il raggiungimento di MDA a 1 anno di 0,577 (p<0,001) indicando che i pazienti IXE avevano una minore probabilità di raggiungere MDA rispetto a ADA. Tuttavia, nessuna differenza tra i due trattamenti è stata osservata per quanto riguarda l'efficacia clinica valutata da DAPSA e PASI.

Conclusioni: Questo studio riporta dati clinici rilevanti nel confronto dell'efficacia clinica di ADA vs. IXE nella real-life, e sia ADA che IXE hanno dimostrato un'efficacia simile nel migliorare attività di malattia e stato funzionale dei pazienti affetti da PsA. ADA è risultato più efficace nel raggiungimento dell'MDA, ma è necessaria una più ampia numerosità campionaria per rendere maggiormente affidabile il metodo statistico di matching ed ottenere una valutazione comparata più bilanciata nella composizione dei gruppi di trattamento.

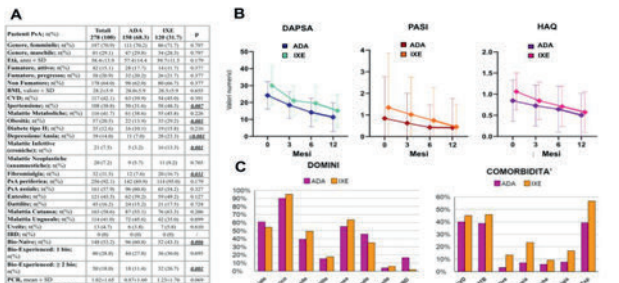

Figura 1. A. Caratteristiche della popolazione di studio al basale. **B.** Efficacia clinica valutata mediante DAPSA, PASI e HAQ (da sinistra a destra) dal baseline a 12 mesi per ADA e IXE a confronto (confronto solo visuale, non statisticamente aggiustato e quindi non statisticamente significativo). **C.** Distribuzione dei domini di PsA e delle comorbilità rilevamenti nei gruppi ADA ed IXE a confronto.
Abbreviations. ADA: Adalimumab; IXE: Ixekizumab; PsA: Artrite Psoriasica; PsO: Psoriasi; BMI: Body Mass Index; CVD: Malattie Cardiovascolari; MTB: Malattie Metaboliche; An: PsA assiale; Per: PsA periferica; IBD: Infiammatory Bowel Disease; PCR: Proteina C Reattiva; PASI: Psoriasis Area Severity Index; DAPSA: Disease Activity in Psoriatic Arthritis; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score with the C-reactive protein; HAQ: Health Assessment Questionnaire; SD: Deviazione Standard; IQR: Range Interquartile. Analisi statistiche condotte mediante software "Stata" – test Chi-quadro per valori nominali, T-test di Student "two-tailed" per a test di Mann-Wjitney U per valori a distribuzione normale e dati numerici non parametrici, rispettivamente. P significative (in grassetto) se <0.05.

SCURVY MIMICKING DERMATOMYOSITIS: A DIAGNOSTIC CHALLENGE

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Case presentation: A 47-year-old woman was admitted at out Internal Medicine ward to be treated for dermatomyositis NXP2. Her past medical history was remarkable for breast cancer (surgically treated), asthma, microcytic anemia, fibromyalgia, Raynaud's phenomenon, thalassaemic trait and panic attack disorder. She developed progressive food and medication avoidance after her son's birth at around thirty years old due to fear of fatal allergic reactions. She reported one anaphylactic shock following IV iron infusion.

Four years earlier, she was referred for rheumatologic evaluation for purple diffused lesions at the legs, myalgias and distal edema limiting mobility, suspected of erythema nodosum. She also presented gingivitis without aphthae but with tooth loss and arthralgias. Corticosteroids at moderate doses gave limited relief for leg pain and partial improvement of skin lesions. She remained on steroids therapy at moderate dosage for four years. Positive anti-NXP2 antibodies led to a diagnosis of dermatomyositis, and methotrexate (7.5 mg/day) was initiated but worsened anemia, likely due to marrow suppression, requiring chronic transfusions.

Due to poor control, she was referred to immunology/dermatology. NXP2 positivity was confirmed. Additional workup showed ANA 1:160 (speckled), HLA-B27+, mild anticardiolipin/beta-2-glycoprotein positivity; normal TSH, C reactive protein, erythrocyte sedimentation rate, reumatoid factor, creatin-kinase, creatinine, C3, C4, protein electrophoresis. Cryoglobulins, hepatitis panel, anti-Jo1 negative. MRI revealed leg muscle edema; muscle biopsy showed lobular panniculitis; gingival biopsy suggested vasculitis. Total body CT excluded malignancy/sarcoidosis.

Anemia was attributed to thalassemic trait, bone marrow suppression for methotrexate and possible gastro-intestinal (GI) bleeding. She reported black stools, but iron therapy complicated interpretation.

With dermatomyositis suspected, steroid pulses and Intravenous ImmunoGlobulins (IVIG) were indicated. Methotrexate was discontinued.

Hospital Stay: She was treated with methylprednisolone 500 mg/day for 3 days and IVIG 30 g/day for 5 days in a monitored setting. For anemia work-up esophagogatroduodenoscopy was made. It didn't show upper GI bleeding. The patient refused colonoscopy fearing allergic reactions to bowel preparation, so GI bleeding source remained unidentified.

Dietary history revealed intake limited to milk, dairy, and select flours. Given panniculitis, gingival disease, anemia, possible GI bleeding and **ecchymoses, vitamin C deficiency (scurvy)** was suspected and confirmed since ascorbic acid blood levels were undetectable. Vitamin levels were mostly normal except for low zinc. Supplementation was started with ascorbic acid 500 mg/day, vitamin B complex and folic acid, with a significant clinical improvement. Allergy testing confirmed only PR10 protein sensitization. Psychiatric follow-up was arranged.

Post-Discharge: At one-month follow-up: anemia was resolved with emoglobin rising to 12.9 g/dL from 8.2 gr/dL without transfusions. Gingival lesions improved, leg edema resolved, panniculitis lesions disappeared, mobility was restored with walker

Discussion: This case highlights how **scurvy**, though rare, can still occur in industrialized nations. In this patient, the trigger was a psychiatric disorder—**Avoidant/Restrictive Food Intake Disorder (ARFID)**—a diagnosis recently included in **DSM-5**. ARFID causes restrictive eating not related to body image concerns and can result in severe nutritional deficiencies, notably of **vitamins C and A**, as documented in recent literature [2,3].

The clinical presentation was complicated by autoimmune markers suggestive of **NXP2-positive dermatomyositis**, a rare variant that may involve distal myositis, cancer risk, and peripheral edema [4]. However, classic symptoms of **scurvy—ecchymoses, leg edema, muscle and joint pain, gingival inflammation with bleeding, and tooth loss**—were all present [5].

Scurvy, once suspected, is **easily diagnosed and rapidly treated**.

Conclusion: It remains difficult to determine whether the patient's improvement was due to immunosuppressive therapy or to the correction of scurvy. However, normalization of haemoglobin, disappearance of gingival and leg lesions, and regained mobility—all occurring despite prior long-term steroid and methotrexate use—suggest that **vitamin C deficiency was the main contributor**. This underscores the importance of considering **nutritional deficiencies in atypical presentations**, particularly in the context of restrictive eating patterns and psychiatric comorbidities

Ecchymosis and leg panniculitis

TAKOTSUBO SYNDROME: UNDERSTANDING THE COMPLEXITIES OF A RARE CARDIAC SYNDROME

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Background: Takotsubo syndrome is characterized by a transient, and sometimes severe, systolic dysfunction of the left ventricle, presenting with features similar to those of acute coronary syndrome, accompanied by chest pain or dyspnea, electrocardiographic changes, and a modest release of myocardial necrosis enzymes. The primary cause of this cardiomyopathy is an acute, intense emotional or physical stress, which triggers a massive release of catecholamines, causing a temporary toxic effect on the heart muscle. The electrocardiogram (ECG) shows ST-segment elevation in multiple leads, while coronary angiography does not reveal significant stenosis. Laboratory tests show an alteration of myocardial necrosis markers, but the levels never reach high values. Treatment consists of rest and supportive therapy, based on the administration of beta-blockers, ACE inhibitors, acetylsalicylic acid, and diuretics. Recovery is spontaneous, and normal myocardial function is restored within a few weeks.
Clinical Case: A 52-year-old Caucasian woman was admitted to the Emergency Department (ED) due to diffuse abdominal pain, a single episode of food vomiting, and psychomotor agitation. Her medical history included a diagnosis of Type 2 Diabetes Mellitus at the age of 40, initially treated with metformin, then managed with diet and physical activity, with good compensation. In the ED, the patient appeared agitated and was unresponsive. Arterial blood gas (ABG) showed a picture compatible with diabetic ketoacidosis (pH 7.05, glucose 507 mg/dL, lactate 5 mmol/L, bicarbonate (HCO3-) 1.9 mEq/L, BE -29). Laboratory tests revealed normal blood counts, no evidence of inflammation, and normal liver and renal function. Troponin T (cTnT) was 16 ng/L. The ECG showed sinus tachycardia (114 bpm). Intravenous hydration was administered, along with potassium supplementation, sodium bicarbonate, and intravenous insulin therapy. The acute diabetic ketoacidosis resolved, and the patient was admitted to our department.
A few hours after admission, the patient complained of worsening diffuse abdominal pain, radiating to the dorsal-lumbar region, associated with tachypnea and cold sweating. Arterial blood gas showed a recurrence of diabetic ketoacidosis (pH 7.21, glucose 299 mg/dL, lactate 3.97 mmol/L, bicarbonate (HCO3-) 4.9 mEq/L, BE -20). The ECG showed T-wave inversion in V2-V3 and ST-segment elevation in V3-V4. Bedside echocardiography revealed akinesia of the middle and apical myocardial segments. Troponin T (cTnT) was 181 ng/L. After intravenous morphine bolus administration, urgent CT of the chest and abdomen, with and without contrast, was negative for pulmonary embolism, acute pancreatitis, and aortic dissection. Regarding the ECG changes associated with regional wall motion abnormalities, urgent coronary angiography was performed, revealing patent coronary arteries. A diagnosis of suspected Takotsubo syndrome in diabetic decompensation with severe metabolic acidosis was established.
Following further investigations, the patient was admitted to the Intensive Care Unit for clinical monitoring and continued treatment. After an improvement in the acute cardiac condition and stabilization of the metabolic state (initiation of a basal-bolus insulin regimen), the patient was transferred to the Internal Medicine department. As per cardiology guidelines, heart failure therapy was optimized by introducing a low-dose beta-blocker and ACE inhibitor. Cardiac MRI confirmed a mid-ventricular Takotsubo syndrome with a left ventricular ejection fraction (LVEF) of 33%. Given the heart failure syndrome (mild peri-malleolar edema and bilateral pleural effusion on cardiac MRI), intravenous diuretic therapy was introduced, followed by oral diuretic therapy. A 24-hour Holter-ECG and a resting Doppler echocardiogram of the supra-aortic trunks were normal. The patient was discharged with instructions to continue heart failure therapy and follow-up with a cardiology visit and echocardiogram one month later. Suspecting Type I Diabetes Mellitus, anti-glutamic acid decarboxylase (GAD) antibodies were requested, which were positive. A basal-bolus insulin regimen was continued at discharge.
Conclusion: Diabetic ketoacidosis may act as a triggering or contributing factor for Takotsubo cardiomyopathy through metabolic stress, catecholamine release, electrolyte imbalances, and acidosis. Although rare, this association is documented in the literature and should be considered in patients presenting with diabetic ketoacidosis and cardiac symptoms.

RELATIVE FAT MASS INDEX PREDICTS NUTRITIONAL STATUS AND BODY COMPOSITION IN HOSPITALIZED FRAIL ELDERLY PATIENTS

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Background: La prevalenza della fragilità è particolarmente elevata tra i pazienti anziani ospedalizzati, dove si associa ad una serie di outcomes clinici sfavorevoli. Elementi determinanti della fragilità sono la malnutrizione e la sarcopenia, entrambe associate a cambiamenti sfavorevoli della composizione corporea, come la riduzione della massa magra e l'aumento della massa grassa. Risulta quindi fondamentale poter individuare precocemente e rapidamente tutti quei fattori di rischio strettamente legati alla fragilità, come lo stato nutrizionale e le alterazioni della composizione corporea. Per questo motivo, sono stati sviluppati numerosi metodi per valutare la massa magra e la massa grassa, tra cui, recentemente, l'indice di massa grassa relativa (Relative Fat Mass, RFM). Il RFM stima la percentuale di massa grassa corporea basandosi su tre parametri rapidamente disponibili: circonferenza vita, altezza e sesso. Questo lo rende ideale nel contesto per acuti. Tuttavia, esistono pochi dati sulla sua applicazione nei pazienti anziani fragili.
Scopo dello Studio: Valutare la relazione tra RFM, stato nutrizionale e composizione corporea in una popolazione di pazienti anziani fragili ospedalizzati.
Materiali e metodi: Sono stati reclutati consecutivamente 50 pazienti fragili ricoverati presso il reparto di Medicina Interna e dell'Invecchiamento del Policlinico Riuniti di Foggia, con età ≥ 65 anni. La fragilità è stata diagnosticata in presenza di almeno tre dei cinque criteri di Fried. All'ingresso è stato eseguito un prelievo su sangue venoso per l'esecuzione della routine ematochimica e sono stati rilevati i parametri antropometrici quali altezza, peso, BMI e circonferenza vita. La forza muscolare è stata valutata attraverso l'hand grip test. La stima della composizione corporea è stata fatta attraverso la bioimpedenziometria, utilizzando la BIA101 (Akern, Florence Italy). L'RFM è stato calcolato secondo la formula di Woolcott e Bergman. Lo stato nutrizionale è stato valutato tramite il Mini Nutritional Assessment (MNA) e la popolazione è stata divisa in due gruppi in base al punteggio ottenuto: malnutriti se MNA < 17 (26 pazienti, 52%), ben nutriti se MNA ≥17 (24 pazienti, 48%).
Risultati: L'età media della popolazione era 78.84 (± 6.7) anni, di cui 22 (44%) erano donne. Il 52% dei pazienti risultava malnutrito. I due gruppi non differivano per età e valore di emoglobina, uricemia, assetto lipidico, albumina, PCR, forza muscolare, circonferenza vita, percentuale di massa grassa e massa magra. Nei pazienti con malnutrizione risultavano valori significativamente superiori di età, piastrine ed eGFR, mentre valori significativamente inferiori si osservavano per il numero di globuli bianchi. I dati sono riassunti nella tabella 1. All'analisi di correlazione, il RFM risultava correlare in maniera significativamente positiva con la FM%, mentre correlava in maniera significativamente inversa con hand grip, MNA, FFM% e MM% (tabella 2). Al fine di valutare la capacità predittiva della FM% da parte della RFM nella popolazione in studio, è stata eseguita un'analisi di regressione lineare multipla utilizzando come variabile dipendente la FM% (valutata con la BIA) e come variabile indipendente la RFM corretta per l'età. Il modello spiega una varianza della FM% del 98.4% (F 105, p < 0001).
L'equazione predittiva della FM% per la popolazione in studio risulta essere: FM%=56,7 + 1,0RFM − 0,8 Età.

Conclusion: I risultati mostrano come la RFM correli significativamente sia con lo stato nutrizionale che con la percentuale di massa grassa, valutata con la bioimpedenziometria. L'equazione ricavata per il calcolo della FM% utilizzando la RFM evidenza un elevato valore predittivo che, se confermato su popolazioni più ampie e considerando ulteriori fattori confondenti come le comorbidità, potrebbe essere un affidabile strumento alternativo per la valutazione della massa grassa di rapida esecuzione soprattutto nel contesto dei pazienti acuti ospedalizzati. Nel complesso, i risultati supportano l'uso della RFM per stimare la percentuale di grasso corporeo totale in una popolazione fragile.

Tab. 1. Caratteristiche baseline della popolazione in base alla presenza o meno di malnutrizione.

Tab. 1	MNA ≥ 17	MNA < 17	*p value*
Età, anni	78.8 ± 6.03	79 ± 9.36	0.934
BMI, kg/m^2	27.30±3.47	24.50±1.37	**0.016**
Hb, g/dl	11.64±2.43	11.50±1.03	0.860
WBC, n/mm^3	9934.12±4240.18	5228.00+1750.70	**0.001**
PTL, µL	212000±77.14	378000±0	**0.007**
eGFR, ml/min	48.43±32.67	96.50±37.08	**0.003**
Uricemia, mg/dL	5.95±1.96	6.31 ±31	0.648
Colesterolo totale, mg/dl	155.88±42.89	137.40±47.78	0.254
LDL, mg/dl	99.88±30.47	81.80±27.96	0.103
HDL, mg/dl	40.13±16.34	43.40±14.58	0.574
Trigliceridi, mg/dl	125.87±78.75	76±20.85	0.057
Albumina, g/dL	3.08±0.40	3.08±0.21	0.993
PCR, mg/L	79.35±81.45	41,94±53.42	0.180
Hand-grip	17.19±8,62	14,65±3.65	0.422
Circonferenza vita	86.68±9.20	87.67±11.18	0.819
MNA	23.12±3.88	14.10±2.39	0.000
FM_pct	32.17±8.19	37.60±0.00	0.368
FFM_pct	67.83±8.19	62.40±0.00	0.368
MM_pct	33.02±7.16	30.60±0.00	0.644
Metabolismo basale	1271,61±99.85	1266.70±0.00	0.946
RFM	28.20±7.14	47.40±4.51	0.000

Abbreviazioni: BMI, body mass index; Hb, haemoglobin; WBC, white bood cells; PTL, platelets; LDL, low density lipoprotein; HDL, high density liproprotein; PCR, C rective protein; MNA, mini nutritional assessment; FM_pct, fat mass percentage; FFM_pct, free fat mass percentage; MM_pct, muscle mass percentage, RFM, relative fat mass .

Tab. 2. Analisi di correlazione tra lo stato nutrizionale e le variabili antropometriche con il RFM.

Tab. 2	*r*	*p value*
BMI, k/m^2	-0.198	0.261
Hb, g/dl	-0.183	0.333
PTL, µL	0.590	0.073
eGFR, ml/min	0.410	0.072
Uricemia, mg/dL	0.416	**0.022**
Colesterolo totale, mg/dL	0.004	0.984
Trigliceridemia, mg/dL	-0.294	0.115
Albumina, g/dL	-0.195	0.319
Hand-grip	-0.558	**0.001**
MNA	-0.456	**0.007**
FM%	0.696	**0.025**
FFM%	0.696	**0.025**
MM%	-0.851	**0.002**
Metabolismo basale	-0.552	0.122

Abbreviazioni: BMI, body mass index; Hb, haemoglobin; PTL, platelets; MNA, mini nutritional assessment; FM%, fat mass percentage; FFM%, free fat mass percentage; MM%, muscle mass percentage.

PREVALENCE OF HEART OVERLOAD/FAILURE ACCORDING TO NT-PROBNP LEVELS AND ROLE OF SINGLE-INHALER TRIPLE THERAPY IN OLDER PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A MULTICENTER LONGITUDINAL STUDY

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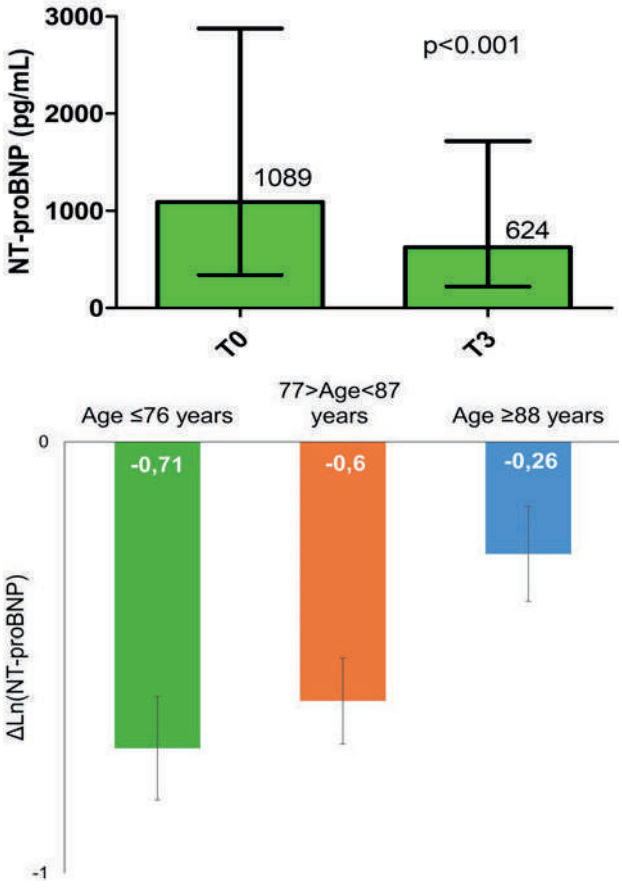
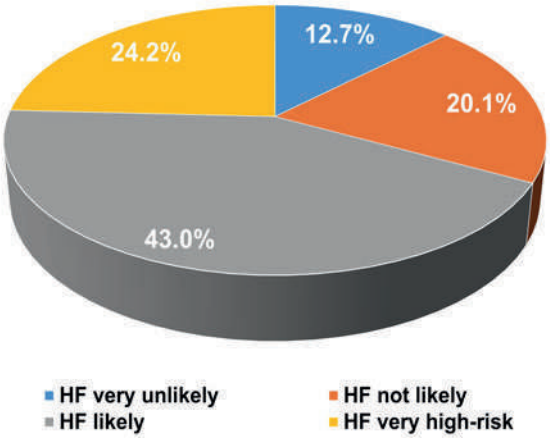
Background: and aim: Chronic obstructive pulmonary disease (COPD) and its acute exacerbations (AECOPD) are associated with increased total and cardiovascular (CV) mortality that might be reduced by single-inhaler triple therapy (SITT), as highlighted in some randomized clinical trials.

Heart failure (HF) is often unrecognized in older COPD patients, given the similar symptoms, but may play an important role in the outcome. Our study aimed at evaluating the prevalence of HF risk using N-terminal pro-B-type natriuretic peptide (NT-proBNP) assay, as endorsed by the 2023 Clinical Consensus Statement of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC), in older COPD patients eligible for SITT. Moreover, we explored the impact of SITT on NT-proBNP levels after a 3-month follow-up.
Methods: An observational multicenter longitudinal study was conducted on 165 consecutive older COPD outpatients, eligible for SITT according to the 2023 Global Obstructive Lung Disease (GOLD) recommendations. Patients with an overt or known HF history were excluded. Patients were classified according to age-comorbidity-adjusted NT-proBNP cut-points. Plasma for NT-proBNP assay was collected before the SITT initiation and after 3 months (n=116 patients).
Results: Mean age was 80.7±9.7 years with female prevalence (52.1%). Mean body mass index (BMI) was 26.8±5.6 kg/m 2 . Hypertension was the most prevalent comorbidity (83.3%). Age-comorbidity-adjusted NT-proBNP levels indicative of "HF likely" and "HF very high-risk" were found in 43.0% and 24.2% of patients, respectively. The presence of HF risk was associated with AECOPD in the previous 30 days, lower hemoglobin levels and higher number of anti-hypertensive drugs taken. After 3 months of SITT, NT-proBNP levels were significantly reduced [from 1088.5 (338.5-2876.5) pg/mL at baseline to 624.0 (220.0-1716.3) pg/mL at 3-month follow-up, p<0.001], with a greater decrease in younger patients (p for interaction between ΔLn(NT-proBNP) and age tertiles=0.020).
Conclusion: We found a remarkable prevalence of heart overload and failure according to NT-proBNP levels in the initial clinical workup of older outpatients with recent AECOPD. The early detection of "HF likely" and "HF very high-risk" appears to be crucial in the management and prognosis of COPD patients, leading to echocardiographic evaluation and referral to a specialist for appropriate HF phenotyping and treatments. Moreover, SITT may help reduce cardiac overload, as highlighted by the significant reduction of NT-proBNP levels and might be directly involved in reducing CV mortality.





THE CHALLENGE OF SCLERODERMA IN OLD AGE

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Nel febbraio del 2025 è giunta a visita una paziente A.A. (donna, 74 anni) per comparsa di ulcere alle punte delle mani e dei piedi. La donna presentava inoltre anche un fenomeno di Raynaud insorto da 12 mesi. Interrogata la paziente, inoltre, riferiva fibrillazione atriale in terapia con bisoprololo e apixaban, e pregressa infezione da HBV. La paziente riporta inoltre calo ponderale di circa 20kg in circa due anni.
L'esame obiettivo mostra unicamente polsi periferici iposfigmici ed asimmetrici. La paziente viene ricoverata per iniziare terapia con Iloprost 500mg in Soluzione fisiologica a infusione continua. Durante il ricovero vengono praticati esami ematochimici che mostrano reattività per gli anticorpi Antinucleo ed anticentromero con valori superiori alla massima diluizione (maggiore di 640,00 ua/ml).
Nel sospetto di una sclerodermia secondaria a sindrome paraneoplastica, viene praticata tomografia computerizzata total-body che mostra: formazione ipodensa endoluminale a ridosso della parete laterale del cieco, multiple lesioni disomogeneamente ipodense ed a margini sfumati del fegato, areola di incrementata impregnazione contrastografica corticale encefalica in regione parietale sinistra, multiple linfoadenomegalie toraco-addominali, tutte necessarie di approfondimenti specialistici.
Viene praticata in elezione colonscopia con endoscopio flessibile. La lesione del cieco viene identificata e bioptizzata.
Contemporaneamente la paziente viene sottoposta a PET-TC con 18-FDG e RMN encefalica. Dai risultati degli esami strumentali, viene confermato che le sopracitate sedi interessate da neoformazioni, risultano altamente captanti il tracciante radiometabolico somministrato ed identificate come lesioni metastatiche epatiche ed encefaliche.
Successivamente, dall'analisi istopatologica, viene posta diagnosi di adenocarcinoma del colon stadio Tx N4 M1 (stadiazione TNM).
Si procede quindi all'attivazione del gruppo oncologico multidisciplinare (GOM) il quale esclude trattamenti chirurgici a causa dell'elevato numero di sedi interessate da metastasi. Inoltre risulta controindicato l'utilizzo di terapie biotecnologiche chemioterapiche a causa della possibile reattività autoimmune data dalla sclerodermia paraneoplastica. Si pone quindi indicazione alla chemioterapia convenzionale.
A.A. nel corso del ricovero continua terapia con Iloprost, alla dimissione, riceve terapia specialistica con Sildenafil 20mg 1cp ogni 8 ore. A distanza di due mesi, si osserva regressione totale delle ulcere digitali e riduzione della frequenza degli episodi di Raynaud.
Allo stato attuale, la paziente ha accettato di sottoporsi a terapia chemioterapica che al momento risulta essere ancora in corso.

ANTI-RO/SSA ANTIBODIES BLOCKING CALCIUM CHANNELS AS A POTENTIALLY REVERSIBLE CAUSE OF ATRIOVENTRICULAR BLOCK IN ADULTS

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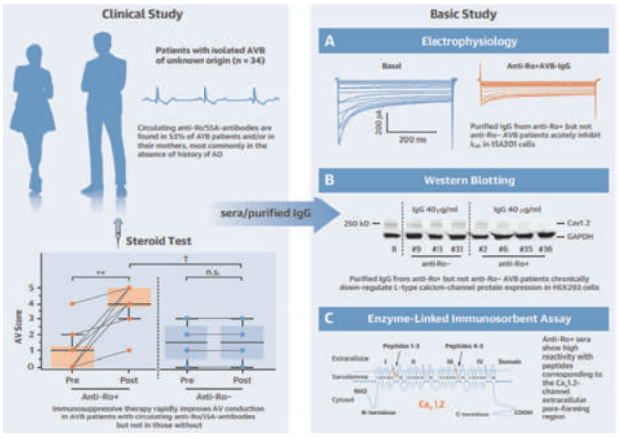
Background: In ~50% of severe atrioventricular blocks (AVBs) occurring in adults <50 years, the underlying etiology remains unknown. Preliminary evidence from case reports suggests that autoimmunity, specifically the presence of circulating anti-Ro/SSA antibodies in the patient (acquired form), in the patient's mother (late-progressive congenital form), or in both (mixed form), could be involved in a fraction of idiopathic AVBs in adults by possibly targeting the L-type calcium channel (Cav1.2) and inhibiting the related current (ICaL).
OBJECTIVES The purpose of this study was to evaluate whether anti-Ro/SSA antibodies are causally implicated in the development of isolated AVBs in adults.
Methods: Thirty-four consecutive patients with isolated AVB of unknown origin and 17 available mothers were prospectively enrolled in a cross-sectional study. Anti-Ro/SSA antibodies were assessed by fluoroenzyme-immunoassay, immuno-Western blotting, and line-blot immunoassay. Purified immunoglobulin-G (IgG) from anti-Ro/SSA-positive and anti-Ro/SSA-negative subjects were tested on ICaL and Cav1.2 expression using tSA201 and HEK293 cells, respectively. Moreover, in 13 AVB patients, the impact of a short course of steroid therapy on AV conduction was evaluated.
Results: Anti-Ro/SSA antibodies, particularly anti-Ro/SSA-52kD, were found in 53% of AVB-patients and/or in their mothers, most commonly an acquired or mixed form (two-thirds of cases) without history of autoimmune diseases. Purified IgG from anti-Ro/SSA-positive but not anti-Ro/SSA-negative AVB patients acutely inhibited ICaL and chronically down-regulated Cav1.2 expression. Moreover, anti-Ro/SSA-positive sera showed high reactivity with peptides corresponding to the Cav1.2 channel pore-forming region. Finally, steroid therapy rapidly improved AV conduction in AVB- patients with circulating anti-Ro/SSA antibodies but not in those without.
Conclusions: Our study points to anti-Ro/SSA antibodies as a novel, epidemiologically relevant and potentially reversible cause of isolated AVB in adults, via an autoimmune-mediated functional interference with the L-type calcium channels. These findings have significant impact on antiarrhythmic therapies by avoiding or delaying pacemaker implantation.
References:
1. Rudbeck-Resdal J, Christiansen MK, Johansen JB, Nielsen JC, Bundgaard H, Jensen HK. Aetiologies and temporal trends of atrioventricular block in young patients: a 20-year nationwide study. Europace. 2019;21:1710–1716.
2. Dideriksen JR, Christiansen MK, Johansen JB, Nielsen JC, Bundgaard H, Jensen HK. Long-term outcomes in young patients with atrioventricular block of unknown aetiology. Eur Heart J. 2021;42: 2060–2068.
3. Lazzerini PE, Capecchi PL, El-Sherif N, LaghiPasini F, Boutjdir M. Emerging arrhythmic risk of autoimmune and inflammatory cardiac channelopathies. J Am Heart Assoc. 2018;7:e010595.
4. Lazzerini PE, Capecchi PL, Laghi-Pasini F, Boutjdir M. Autoimmune channelopathies as a novel mechanism in cardiac arrhythmias. Nat Rev Cardiol. 2017;14:521–535.



GUILLAIN-BARRÉ SYNDROME AND RESTLESS LEGS SYNDROME: RARE ASSOCIATION OR MERE COINCIDENCE?

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Introduzione: La sindrome di Guillain-Barrè (GBS) è una polineuropatia infi-

ammatoria acuta a patogenesi immunomediata, innescata da un evento infiammatorio, che coinvolge gli assoni e la mielina dei nervi periferici, con conseguenti alterazioni della conduzione nervosa e della funzionalità muscolare. Il quadro clinico è caratterizzato da paralisi flaccida, spesso associata a parestesie e dolori muscolari, che esordisce agli arti inferiori e progredisce in senso ascendente, fino a coinvolgere, nei casi più gravi, la muscolatura respiratoria. La diagnosi si basa sulla presentazione clinica, supportata da indagini strumentali e confermata dall'analisi del liquor cerebrospinale (CSF) e dallo studio elettromiografico.
La sindrome delle gambe senza riposo (RLS), nota anche come sindrome di Willis-Ekbom, è una condizione neurologica caratterizzata dall'incontrollabile bisogno di muovere le gambe. I sintomi di questa particolare patologia si manifestano la sera, durante il riposo notturno. Alcune evidenze suggeriscono che la RLS sia dovuta a uno squilibrio nei livelli di dopamina la cui riduzione fisiologica la sera potrebbe spiegare la comparsa dei sintomi serotini e notturni. In particolare, anche la carenza di ferro incide sui livelli di dopamina.
Esistono una forma primaria idiopatica e una forma secondaria. La più comune fra le condizioni cliniche associate alla forma secondaria di RLS è la carenza di ferro, che è presente in poco più del 20% dei casi di RLS, confermata dal rilievo di bassi livelli di ferro nella substantia nigra dei soggetti affetti.
In letteratura sono descritti pochi casi di associazione della GBS con la RLS.
Caso Clinico: Una donna di 49 anni si presentava al Pronto Soccorso per astenia e melena. In anamnesi un'anemia sideropenica cronica, secondaria a frequenti metrorragie. Nelle due settimane precedenti il ricovero, la paziente riferiva un episodio simil-influenzale, trattato con farmaci antinfiammatori non steroidei (FANS). L'esofagogastroduodenoscopia (EGDS) metteva in evidenza erosioni multiple localizzate nel digiuno prossimale, verosimilmente attribuibili a danno gastrointestinale da FANS. Durante la degenza, la paziente ha cominciato a manifestare parestesie ingravescenti agli arti inferiori, associate a movimenti afinalistici, inizialmente limitate agli arti inferiori. Il quadro neurologico, alla luce degli esami ematochimici che mostravano grave anemia sideropenica (Hb 4.9 g/dL; sideremia 19 µg/dL; ferritina 14.7 ng/mL, transferrina 160 mg/dL, TSAT 8%), veniva attribuito in prima ipotesi alla RLS da disfunzione dopaminergica, secondaria alla carenza marziale. Ma, nonostante il ripristino di normali valori di sideremia ed emoglobina dopo terapia trasfusionale e infusione endovenosa di carbossimaltosio ferrico, si assisteva ad un peggioramento della sintomatologia neurologica con significativa limitazione funzionale della deambulazione, riflessi osteotendinei ipoelicitabili agli arti inferiori e progressione delle parestesie ad andamento ingravescente con successivo coinvolgimento degli arti superiori. La RMN encefalo-rachide evidenziava ispessimento e impregnazione patologica delle radici nervose della cauda equina, reperto suggestivo di polineuropatia infiammatoria, l'esame del liquor cefalorachidiano mostrava dissociazione albumino-citologica (cellule 21/mm3, polimorfonucleati 4.7%; mononucleati 95.3%, proteine totali 94.6 mg/dL, albumina 54.8 mg/dL) e l'esame elettromiografico confermava il quadro neurologico compatibile con la GBS. La paziente veniva quindi sottoposta a trattamento con immunoglobuline endovena (IVIG) alla dose di 0.4 gr/Kg per cinque giorni, con progressivo miglioramento del deficit motorio e sensoriale degli arti e con recupero della deambulazione autonoma.
Conclusioni: I: La sintomatologia iniziale ha fatto porre inizialmente diagnosi di RLS secondaria ad anemia sideropenica. La mancata risposta al trattamento marziale e il peggioramento progressivo della sintomatologia neurologica, hanno richiesto ulteriori indagini orientando verso la diagnosi di GBS concomitante. La coincidenza delle due condizioni patologiche insorte acutamente, pur non potendo escludersi una coincidenza, solleva l'ipotesi di una potenziale associazione fisiopatologica, ad oggi raramente ipotizzata in letteratura. Si potrebbe ipotizzare che la GBS amplifichi la disfunzione sensitivo-motoria periferica, procrastinando la scomparsa della RLS anche dopo la correzione dell'anemia sideropenica. Sono necessari nuovi studi per chiarire la prevalenza e il nesso fisiopatologico tra R.L.S e GBS.

TIME IS SPINE: A CASE REPORT OF LUMBAR PAIN MASKING A SPINAL EMERGENCY

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Case report: An 80-year-old Caucasian man presented to the emergency department (ED) with non-specific left flank pain, exacerbated by movement, without fever, urinary symptoms, or trauma. His medical history included hypertension, type 2 diabetes, cerebrovascular events, CAD, PAD and CKD (baseline creatinine 1.6-1.7 mg/dL). Laboratory tests showed elevated C-reactive protein (CRP) (7 mg/dL), normal leukocyte count, and creatinine at 1.9 mg/dL. He was discharged with a presumptive diagnosis of renal colic and started on empirical antibiotics. However, the persistence and progressive worsening of bilateral lumbar pain led to a second ED within a month. Laboratory analysis confirmed elevated CRP (6.4 mg/dL), with normal leukocytes. A contrast-enhanced abdominal CT scan was performed, revealing perirenal fat stranding and iliac and inguinal lymphadenopathies. The patient was admitted to our Internal Medicine ward with a suspected diagnosis of acute pyelonephritis and treated with Ceftriaxone (after a single dose of gentamicin), while urine culture resulted negative. Serial laboratory tests showed persistently fluctuating CRP levels, with normal leukocytes, and elevated lactate dehydrogenase (LDH) (700-800 U/L). Despite analgesic therapy with Paracetamol, Tramadol and Paracetamol/codeine, bilateral lumbar pain persisted. Given the atypical features, such as persistent back pain, elevated CRP and LDH, and inconclusive cultures, a total-body 18F-FDG PET scan was performed. It revealed widespread marrow-replacing disease involving multiple osteomedullary sites and adjacent soft tissues, including the thoracic spine (D8–D12), several lymph nodes, right prostatic lobe, and ipsilateral perirenal fascia, findings suggestive of an aggressive infiltrative process. After Haematology consultation, a bone marrow biopsy was performed.
Before diagnostic confirmation, the clinical picture suddenly evolved. In fact, the patient developed painless acute urinary retention, followed later the same day by sudden onset of weakness and hypoesthesia of the right lower limb. An urgent contrast-enhanced spinal MRI showed extensive epidural pathological tissue from C4 to L1, circumferentially encasing the spinal cord, with critical compression at the D8–D9 level and multiple vertebral lesions. Prompt neurosurgical intervention with posterior decompression and removal of the D8-D10 lesion was performed.
Bone marrow biopsy confirmed the diagnosis of Diffuse Large B-cell Lymphoma (DLBCL), centroblastic/immunoblastic variant with a germinal center B-cell-like phenotype, and double-expressor status (Bcl-2 and c-Myc). Due to widespread skeletal involvement, the disease was staged as IVa.
The patient began R-miniCOMP chemotherapy (cyclophosphamide – doxorubicin – vincristine – rituximab), completing five cycles, with four intrathecal administrations. After four cycles, follow-up PET and MRI showed significant reduction in disease burden, with resolution of epidural mass. After a period of neuromotor rehabilitation, patient regained bladder function and partial mobility.
Background: DLBCL is the most common subtype of non-Hodgkin lymphoma, known for its aggressive course and heterogeneity. Extranodal involvement occurs in approximately one-third of cases, most commonly in gastrointestinal tract, skin and soft tissues, bone, or genitourinary tract. Central nervous system (CNS) involvement, although rare, is classically observed during disease relapse, and remains a feared complication due to its significant prognostic implications. The risk of CNS recurrence is estimated at 2–5% and has decreased after introduction of rituximab-based immunochemotherapy. Risk factors for CNS spread include advanced tumor stage, high international prognostic index (IPI), high LDH, bone marrow or testicular or paranasal sinuses involvement, and specific molecular features such as translocations involving MYC, BCL-2 or BCL-6 genes ("double-hit" lymphomas), and germinal center B-cell-like phenotype.
Acute spinal cord compression as the initial manifestation of DLBCL is extremely rare and may mimic non-hematologic conditions.
The therapy of DLBCL is the combination of a chemotherapy with immunotherapy. In selected high-risk cases, CNS prophylaxis or treatment with intrathecal chemotherapy is indicated.
Conclusion: This case illustrates an uncommon and clinically significant presentation of DLBCL with early CNS involvement manifesting as spinal cord compression. The initial symptoms were non-specific, mimicking renal pathology, and the absence of B symptoms or leukocytosis could delay the diagnosis. The timely recognition of red flags such as progressive neurological deficits and elevated LDH in the context of persistent back pain, especially with the concomitant presence of systemic inflammatory markers without clear infectious etiology, enabled us to perform a prompt diagnostic workup and initiation of appropriate therapy. This case highlights both the role of internist in the early detection of atypical presentation of aggressive lymphomas, and the value of multidisciplinary collaboration to ensure the optimal management and patient outcomes of a complex lymphoma presentation.

OPTIMIZING VASCULAR ACCESS DEVICE SELECTION IN INTERNAL MEDICINE WARDS: DOES EXPERT OPINION STILL MATTER IN THE AGE OF ALGORITHMS?

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Background: Placing a vascular access device (VAD) is one of the most

frequently performed invasive procedures in hospitalized patients. Despite technological advancements that offer a wide range of devices, selecting the most appropriate VAD remains a complex process influenced by various clinical and organizational factors such as therapy duration, physicochemical properties of drugs, patient-specific factors and clinical setting.Inappropriate VAD selection can lead to complications, catheter failure, reduced therapy effectiveness and prolonged hospital stay. Therefore, standardized protocols, decision-making algorithms, and the involvement of a specialized Vascular Access Team (VAT), composed of trained nurses and physicians, are essential for improving selection processes. This study aimed to analyze the appropriateness of VAD selection in internal medicine wards and to identify discrepancies between actual clinical practice and best-practice recommendations.
Methods: A descriptive observational study was conducted at L. Sacco Hospital in Milan between October 2024 and January 2025. Adult patients hospitalized in three different internal medicine units who required a VAD were included. Data were collected at 72 hours and 10 days after admission through electronic health record reviews, staff and patient interviews, and bedside assessments. Clinical VAD choices were compared with algorithm-based recommendations (DAV-Expert and MAGIC), decisions made by the treating team (physician and nurse) and evaluations made by VAT members (physician and nurse). Agreement was evaluated using the weighted Cohen's kappa coefficient.
Results: At 72 hours, 291 patients were assessed. At 10 days, 156 remained hospitalized due to discharges, transfers, or deaths. The median patient age was 82.0 (73.0-87.0), with balanced gender distribution (female 50%), a tendency toward overweight with a median BMI of 24.5 (21.5-27.5), and a high incidence of Difficult Intravenous Access (DIVA) risk factors (60%). The primary indication for VAD placement was intravenous (IV) therapy (89.3%). Although therapy duration initially seemed suitable for peripheral access (expected duration of IV therapy 6.8±2.6 days), 39.8% of patients at 72 hours were receiving medications requiring central access. By day 10, 52.4% of the therapies were incompatible with peripheral devices, indicating increased clinical complexity.
At 72 hours, short peripheral catheters (SPC) remained the most commonly used devices (90%). However, this choice did not always align with the recommendations provided by DAV-Expert (k=0.12), MAGIC (k=0.08) or the VAT (physician k=0.32 and nurse k=0.22). The algorithms recommended at least 80% more central VADs than were placed in clinical practice, while the VAT took a more intermediate position, suggesting approximately twice as many central VADs as those used in practice (5% at 72 hours), but still fewer than those recommended by the algorithms.By day 10, SPC use declined slightly (78%), with a modest increase in midline (17%) and central devices (9%), reflecting a partial adaptation to evolving clinical complexity. However, an evident discrepancy persisted between clinical practice, DAV-Expert (k=0.18), and MAGIC (k=0.06), which favored using more stable devices. The VAT displayed internal consistency and a stronger evidence-based approach (physician and nurse agreement k=0.63).Whereas alignment between the treating team's choices and actual clinical needs improved by day 10, concordance with VAT recommendations remained limited (physician k=0.45 and nurse k=0.35), underscoring the need for greater expert integration. VAT evaluations remained stable over time, demonstrating their ability to consistently identify the correct VAD and maintain that recommendation (physician 72h vs 10 days k=0.86 and nurse 72h vs 10 days k=0.96). DAV-Expert and MAGIC evaluations changed considerably between the two checkpoints (DAV-Expert 72h vs 10 days k=0.11 and MAGIC 72h vs 10 days k=0.16). This issue arose from a glitch during the 10 day evaluation when the algorithms lost accuracy due to the shortened therapy duration.
Conclusions: The study highlighted a persistent gap between evidence-based recommendations and clinical practice in VAD selection. Algorithms alone proved insufficient to fully capture patient complexity and dynamic clinical needs. Conversely, VAT members consistently identified the most appropriate devices early and maintained their recommendations over time. These findings suggest that a multidisciplinary, expert-led approach, initiated with early VAT involvement, can optimize VAD selection, thereby likely reducing complications and enhancing the quality of patient care.

DIETARY CARBOHYDRATE RESTRICTION AFFECTS HEPATIC GLUCOSE PRODUCTION AND INTESTINAL GLUCOSE ABSORPTION INDEPENDENTLY OF BODY WEIGHT LOSS

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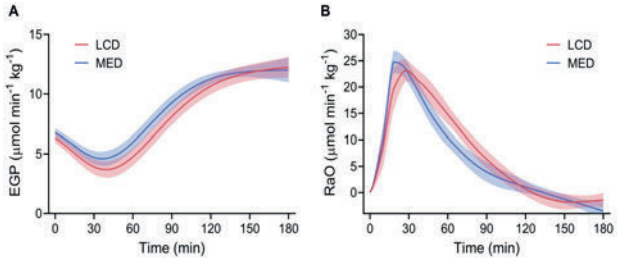
Background: and aims: Low-carbohydrate diets (LCD) have demonstrated short-term benefits in body weight and plasma glucose management. Preliminary evidence suggests that carbohydrate restriction may modulate hepatic glycogenolysis, duodenal glucose absorption, and peripheral glucose disposal. However, how LCD distinctly influences organ-specific glucose handling independently of body weight loss remains unclear. This study evaluated the impact of LCD compared to an energy-matched Mediterranean diet (MED) on postload glucose metabolic fluxes in individuals with overweight.Materials and methods: In this randomized cross-over study, 20 volunteers with BMI>27 kg/m2 and without diabetes (age 53.5±7.4 years, 11 [55%] women, BMI 30.8±3.5 kg/m2) were assigned to a 4-week mild hypocaloric LCD (20% carbohydrate, 50% fat, 30% protein) and an energy-matched 4-week MED (50% carbohydrate, 20% fat, 30% protein). After each diet, an oral glucose tolerance test (OGTT) with two stable glucose isotopes (intravenous [6,6-2 H2] glucose and oral [U-13C] glucose) was performed to measure glucose metabolic fluxes, including endogenous glucose production (EGP), rate of appearance of oral glucose (RaO), and glucose clearance (GCl). Insulin secretion rate (ISR) was estimated by modelling C-peptide concentrations. Adherence to dietary prescriptions was evaluated by food diaries and continuous glucose monitoring (CGM).Results: By design, LCD and MED led to a similar small weight reduction (-2.8±2.3 and -2.7±2.4 kg, respectively, p=0.398) but differed in self-reported daily carbohydrate intake (29.7±5.3% and 47.2±6.3%, p<0.0001) and CGM-derived average glucose levels (p=0.033). Plasma glucose, insulin and ISR profiles during OGTT were similar after the two diets. EGP was more suppressed by the oral glucose load after LCD than MED (AUC 1437±341 and 1553±250 µmol min-1kg-1xmin, p=0.041), showing reduced hepatic resistance to portal insulin (EGP×ISR AUC 113±43 and 125±41 µmol min-1kg-1× nmol/m2×min, p=0.026). Furthermore, RaO was significantly delayed by the LCD compared with MED (time to peak 30±12 and 21±7 min, p=0.001), although not reduced over the 180-min observation (AUC 1334±580 and 1149±557 µmol min-1 kg-1×min, p=0.303). There were no differences in postload GCl (327±93 and 339±56 ml min-1 kg-1× min, p=0.134) between the two diets, even after adjustment for plasma insulin levels (GCl/Ins 5.5±3.0 and 5.2±2.2 l min-1 kg-1 pmol-1 l×min, p=0.804).Conclusion: Dietary carbohydrate restriction potentiates the physiologic suppression of hepatic glucose production following an oral glucose load and delays intestinal glucose absorption in overweight individuals, without affecting peripheral glucose disposal. These adaptations may contribute to the glucometabolic benefits of LCD by mitigating postprandial glycaemic excursions.



177. BASELINE CHARACTERISTICS, CLINICAL PRESENTATION, ECHOCARDIOGRAPHIC DATA AND OUTCOMES AMONG THE BODY MASS INDEX CATEGORIES

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Background: Obesity is a common, multifactorial disease, increasingly widespread globally in recent decades, defined and classified by Body Mass Index (BMI) categories. Although previous reports suggest that a higher BMI might be associated with an increased risk of cardiovascular diseases, there is currently limited information available for patients hospitalised due to acute heart failure (AHF).
Methods: In this single centre, observational study, data on patients admitted due to AHF from 1st January 2016 and 31st December 2023 were retrospectively collected. Patients were divided in BMI categories. Baseline characteristics, clinical presentation, blood tests and echocardiographic data were classified across BMI categories. The association between BMI categories and outcomes was assessed using Cox's proportional hazard analysis. Outcomes: in-hospidal death, 90-day all-cause mortality and 90-day composite outcome of all-cause mortality or readmission due to AHF across BMI categories. Study population:

Of the 5,965 patients enrolled (median age 79 years, of whom 58% were men), 2,551 (43%) had normal weight, 2,226 (37%) were overweight and 1,188 (20%) were obese.
Results: Patients with higher BMI were younger and had higher proportion of hypertension, diabetes and chronic obstructive pulmonary disease (COPD). Similar prevalences were observed across the BMI groups for atrial fibrillation, history of coronary artery disease and kidney failure. Individuals with higher BMI were more likely to present dyspnoea, orthopnoea and bilateral peripheral swelling, compared to those with normal weight. No differences were found in haemoglobin measurements and inflammatory biomarkers such as red blood cell distribution width and the neutrophil/lymphocyte ratio. N-terminal pro brain natriuretic peptide (NT-proBNP) concentrations were higher in participants with normal weight (6,215 pg/ml) and in those who were overweight (4,920 pg/ml), compared to the obese group (3,518 pg/ml) (p = 0.001). Left atrial (LA) and left ventricular (LV) indexed volume as well as pulmonary arterial systolic pressure were similar across the BMI categories.
Conclusions: Our study demonstrated that patients with higher BMI were younger, presented an increased prevalence of diabetes and hypertension but lower NT-proBNP concentrations. Our findings did not confirm an association between BMI and outcomes but, conversely, they suggested a paradoxical protective effect of weight on prognosis which is still to be confirmed by further studies.

DIFFERENCES IN CLINICAL PRESENTATION AND OUTCOMES BETWEEN DE NOVO HEART FAILURE AND ACUTE DECOMPENSATED CHRONIC HEART FAILURE: A RETROSPECTIVE OBSERVATIONAL STUDY

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Background: Patients with heart failure (HF) frequently may be hospitalized due to the sudden onset of signs and symptoms. Recent findings suggest differences in clinical characteristics and outcomes between acute decompensated chronic heart failure (ADCHF) and de novo heart failure (DNHF). A better understanding of these two distinct entities may represent an opportunity to tailor treatments and improve outcomes.
Methods: This is a single-center, retrospective, observational study. The study was conducted on patients hospitalized for heart failure from January 1, 2001 to December 31, 2019. The presence or absence of heart failure in the medical history was assessed, as well as demographic data, symptoms, blood tests and echocardiographic data. The outcomes chosen were rehospitalization for heart failure at 90 days and 1 year after discharge.
Results: A total of 9169 patients were enrolled, of which 4903 (53%) were in the ADCHF group and 4293 (47%) in the DNHF group. The mean age was 81 years and 53% of patients were male.Compared to DNHF, patients with ADCHF were more frequently men (57% vs 48%; p<0.01) and showed a higher prevalence of coronary artery disease (41% vs 14%; p<0.01), as well as other comorbidities including hypertension (48% vs 39%), chronic kidney disease (30% vs 24%), diabetes mellitus (28% vs 20%), and atrial fibrillation (36% vs 24%) (all p<0.01). At presentation, clinical manifestations were similar among the cohorts with dyspnea (48%), peripheral oedema (19%) and chest pain (15%) being commonly reported in both the groups. Patients with ADCHF showed significantly higher concentrations of NT-proBNP compared to those with DNHF (5,638 pg/mL vs 4,399 pg/mL; p<0.01). Moreover, echocardiographic evaluation revealed worse structural remodeling in the ADCHF group, with increased indexed left atrial (49 mL/m2 vs 44 mL/m2; p<0.01) and left ventricular volumes (110 mL/m2 vs 105 mL/m2; p<0.01).Within 90 days post-discharge, almost 10 % of patients were rehospitalized for HF, with similar rates between DNHF and ADCHF cohorts. However, at one-year of follow-up, patients with ADCHF had about 30% increased risk to be rehospitalized compared to those with DNHF (p<0.001).Conclusions: Compared to DNHF, patients with ADCHF had more comorbidities, higher NT-proBNP measurements, increased LA and LV indexed volumes. At 90 days post discharge, the rate of HF rehospitalization was similar between the two cohorts, however it differs in the one-year prolonged follow up. Distinction between ADCHF and DNHF may enhance our understanding of worsening heart failure, improving prognosis by the adoption of tailored approaches.

RED BLOOD CELL DISTRIBUTION WIDTH AND NEUTROPHIL-TO-LYMPHOCYTE RATIO: BOTH POTENTIAL PREDICTORS FOR ADVERSE OUTCOMES IN PATIENTS WITH ACUTE HEART FAILURE

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Background: Red blood cell distribution width (RDW) and neutrophil-to-lymphocyte ratio (NLR) have both recently been recognized as markers of systemic inflammation and associated with the occurrence of adverse events in chronic heart failure (HF). Since RDW and NLR are both easily accessible through routine blood cell count assessments and, inexpensive when acquired, they may serve as promising biomarkers for predicting outcomes also in the context of acute HF (AHF). Therefore, we aim to determine the prognostic utility of RDW and NLR in a cohort of inpatients with AHF.
Methods: This is a monocentric, retrospective, observational study. Patients hospitalized for acute heart failure from January 1, 2016 to December 31, 2023 were enrolled. The threshold value for RDW was > 14.6% while the threshold for NLR was > 2. The demographic, clinical, laboratory and echocardiographic data of the enrolled patients were collected, dividing them through the RDW/NLR categories. The primary outcome was the composite of death from any cause or readmission due to AHF within 90 days from discharge.
Results: 7,452 patients (median age 81 years, 53% men) fullfilled diagnostic criteria for AHF and were divided into 4 groups based on RDW and NLR values. Age significantly differed among the four cohorts, with patients showing increase in both biomarkers being older compared to those with normal values. Echocardiographic variables did not show any significant difference among the groups, whereas NT-proBNP measurements were higher in the RDW+/NLR+ compared to the RDW−/NLR−.RDW (HR: 1.22; 95% CI: 1.11-1.38) and NLR (HR: 1.36; 95% CI: 1.19-1.59) were both independent predictors of the composite of death from any cause or readmission due to AHF. Individuals with normal measurement both for RDW and NLR (reference group) reported the lowest risk of the composite of all-cause mortality or hospitalisation due to AHF. Patients with only increased RDW (HR: 1.78; 95% CI: 1.23-2.21) and those with only elevated NLR (HR: 1.83; 95% CI: 1.31-2.19) reported a similar risk profile, in both cases higher when compared with reference. Participants with both increased RDW and NLR (HR: 2.45; 95% CI: 1.89-2.88) were at greatest risk of adverse events.
Conclusions: RDW and NLR are frequently elevated in patients with AHF and are associated with other well-established prognostic markers. Both are independent predictors of poor outcomes, with patients exhibiting increased values for both markers being at the highest risk of poor prognosis.

IMPACT OF BEMPEDOIC ACID ON HEPATIC STEATOSIS, NON-ALCOHOLIC STEATOHEPATITIS, AND FIBROSIS: A CLINICAL EVALUATION USING ADVANCED ELASTOSONOGRAPHY TECHNIQUES

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Introduction: Bempedoic acid is an innovative oral drug that lowers LDL cholesterol levels and also provides benefits in glycometabolic control and systemic inflammation. While its impact on cardiovascular risk is well-documented, the effects of bempedoic acid on liver diseases, such as hepatic steatosis, non-alcoholic steatohepatitis, and hepatic fibrosis, remain under investigation. Recent studies, including those published in Cell in [2025], have begun exploring the potential of bempedoic acid in treating hepatic steatosis. These studies suggest that bempedoic acid may suppress diet-induced hepatic steatosis independently of ATP-citrate lyase (ACL), an enzyme crucial for fatty acid and cholesterol synthesis in the liver. This mechanism implies that bempedoic acid could reduce hepatic steatosis by targeting specific metabolic processes beyond its effect on LDL cholesterol levels. Our study aims to evaluate the effects of bempedoic acid on hepatic steatosis and fibrosis using advanced techniques like hepatic elastosonography, which will monitor liver stiffness and correlate elastosonographic parameters with traditional biomarkers.
Study Objectives: The primary objective of this study is to assess the impact of bempedoic acid on hepatic steatosis, steatohepatitis, and hepatic fibrosis. This

will be achieved through abdominal ultrasonography and hepatic elastosonography performed "blind" by two separate radiologists. Liver stiffness will be measured using parameters like Shear Wave Elastography (SWE), Shear Wave Dispersion (SWD), and Attenuation Imaging (ATI), which will be correlated with traditional biomarkers such as GOT, GPT, GammaGT, and FIB-4 and FLI indices. Secondary objectives include evaluating changes in lipid levels, inflammatory markers, and glycometabolic function.
Methodology: This study will involve 100 patients with dyslipidemia, metabolic syndrome, and familial hypercholesterolemia, treated with either bempedoic acid or statins. Patients will be enrolled at the Ambulatory Unit of Metabolic Disease Pathophysiology of the University Hospital of Siena. Each patient will undergo a comprehensive clinical evaluation, including monitoring lipid levels, hepatic enzymes and glycometabolic parameters, inflammation markers. The instrumental part of the study will include abdominal ultrasonography and TSA color Doppler echography performed at baseline, six, and twelve months. Regarding hepatic elastosonography, measurements will be conducted in a "blind" manner, so that operators will not be informed of whether the patient is receiving bempedoic acid or statins, minimizing potential biases associated with knowledge of the treatment. Each operator will independently take measurements of SWE, SWD, and ATI parameters. Subsequently, the quality and accuracy of the measurements will be assessed by comparing the operators' readings to ensure the reliability of the results.
Impact and Data Transferability: Bempedoic acid could significantly impact the management of hepatic steatosis, steatohepatitis, and fibrosis by potentially reducing the progression to advanced liver disease. Hepatic elastosonography, using advanced parameters like SWE, SWD, and ATI, will allow precise monitoring of liver stiffness and correlate changes with traditional biomarkers. These data will help clarify the potential role of bempedoic acid in managing non-alcoholic liver diseases and preventing cardiovascular events, particularly in patients with metabolic syndrome and liver comorbidities. Moreover, bempedoic acid has a favorable economic profile compared to injectable therapies like PCSK9 inhibitors, making it a potentially cost-effective therapeutic option for primary prevention and management of dyslipidemia.
Expected Results: We expect that treatment with bempedoic acid will lead to a significant reduction in hepatic steatosis, steatohepatitis, and hepatic fibrosis, as measured by abdominal ultrasonography and hepatic biomarkers. Hepatic elastosonography should reveal a reduction in liver stiffness, measured by SWE, SWD, and ATI parameters, which will be correlated with fibrosis (FIB-4) and steatosis (FLI) scores. Additionally, we anticipate improvements in glycometabolic parameters and a reduction in cardiovascular risk, monitored through CRP. The results of this study could provide valuable evidence on the efficacy of bempedoic acid in treating non-alcoholic liver diseases and preventing cardiovascular complications.
Conclusions: This study will explore the efficacy of bempedoic acid in treating hepatic steatosis, steatohepatitis, and hepatic fibrosis using advanced methodologies such as hepatic elastosonography and FIB-4 and FLI indices. While studies on the drug in this context are still under development, preliminary data suggest potential benefits. The "blind" design with two separate operators will ensure the reliability of the results, minimizing potential biases from treatment knowledge. The data collected could support the adoption of bempedoic acid as a therapeutic option for managing liver and cardiovascular comorbidities, while also providing a valuable tool for the prevention and management of dyslipidemia in patients with metabolic syndrome.

PROGNOSTIC IMPORTANCE OF TAPSE/PASP RATIO AMONG OLDER PATIENTS WITH ACUTE HEART FAILURE WITH PRESERVED EJECTION FRACTION

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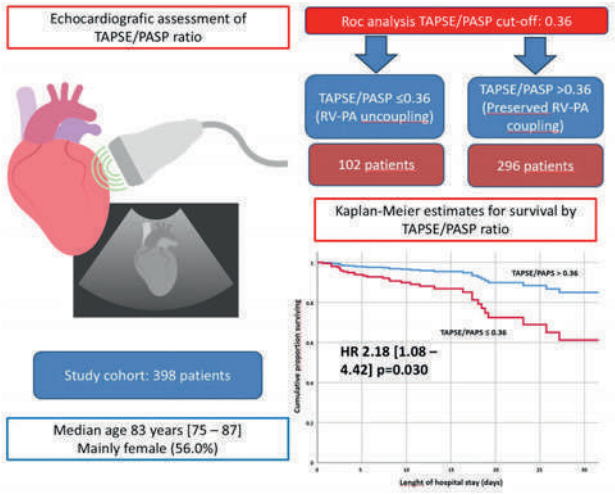
Background: Right ventricular (RV)-pulmonary artery (PA) uncoupling is associated with poor outcome in patients with Heart Failure with Preserved Ejection Fraction (HFpEF). Tricuspid annular plane systolic excursion (TAPSE) and pulmonary artery systolic pressure (PASP) ratio is simple echo-derived indicator of RV-PA uncoupling. This study aimed to investigate the prognostic impact of TAPSE/PASP ratio among patients with HFpEF hospitalized for acute heart failure (AHF).
Materials and methods: Single-centre, retrospective study including patients hospitalized for AHF over a 4-year period. Receiver operating character (ROC) curves for the TAPSE/PASP ratio were used to identify the cut-off value for the composite outcome of all-cause in-hospital mortality and hospital readmission.
Results: Overall, 398 patients were included (median age 83 years, 56.0% females). According to ROC curve analysis, we calculated an ideal cut-off of 0.36 mm/mmHg for TAPSE/PASP ratio. Patients were divided into two categories, preserved RV-PC coupling (TAPSE/PASP ratio > 0.36) and RV-PC uncoupling (TAPSE/PASP ratio ≤ 0.36). Overall, both in-hospital mortality and readmission rate were higher among HFpEF patients with TAPSE/PASP ratio ≤ 0.36 compared to those with TAPSE/PASP ratio > 0.36 (31.4 % vs 20.3%; p=0.008). At multivariate analysis, TAPSE/PASP ratio ≤ 0.36 emerged as an independent risk factor both for death (HR 2.18 [1.08 – 4.42]; p=0.03) and the composite outcome (HR 1.95 [1.22 – 3.12]; p=0.005).
Conclusion: Among older patients with HFpEF and hospitalized for AHF, the RV-PA uncoupling was associated with a nearly two-fold increased risk of in-hospital mortality.
Keywords: heart failure with preserved ejection fraction, acute heart failure, TAPSE/PASP ratio, right ventricular dysfunction.



STATIN-INDUCED IMMUNE-MEDIATED NECROTIZING MYOPATHY (IMNM): A PHARMACOVIGILANCE ANALYSIS

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Introduction: Immune-mediated necrotizing myopathy (IMNM) is a rare, still undefined disease that causes asthenia and muscle weakness predominantly in the proximal muscles of upper and lower limbs with increased myocytonecrosis. Most cases of IMNM are associated with myositis-specific autoantibodies, namely anti-SRP or anti-3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR), although approximately 20% of patients with IMNM remain seronegative. Muscle biopsy of IMNM typically shows necrosis and degeneration of muscle cells in the absence of significant inflammatory infiltrates. Treatment involves the administration of different classes of drugs, e.g. methotrexate and steroids or rituximab associated with immunoglobulins (along with physiotherapy and speech therapy in patients with dysphagia) depending on the antibody profile. Objective: The aim of this study is to investigate the iatrogenic component of IMNM by analyzing international databases of spontaneous reporting of adverse drug reactions.Materials and Methods: Spontaneous reports of adverse reactions to statins were obtained from the FAERS (FDA Adverse Event Reporting System) archive evaluated up to December 31, 2024 and de-duplicated based on sex, age, weight, country of origin of the report, suspected drugs, adverse drug reactions (ADR) and date of the event. These reports were subsequently processed in order to eliminate possible duplicates and low-quality data. The following terms (preferred terms) were used to characterize the adverse reaction: immune-mediated myositis, necrotizing myositis, autoimmune myositis, myocarditis-myositis-myasthenia gravis overlap syndrome.Results: The male sex with 57.29% of total cases was the most affected. The affected

patients had a mean age between 50 and 74 years. A subset of the subjects (4.48%) died following the adverse reaction to statins, i.e. because of IMNM occurrence, and approximately 9% reported permanent disability. Specifically, distinguishing the results for each preferred term used, in the "immune-mediated myositis" the number of reports in which the drug and the adverse event were both present mainly concerned atorvastatin (n= 830 cases; CI: 6.3 [6.19-6.38]). No reports were attributed to the myocarditis-myositis-myasthenia gravis overlap syndrome, while for necrotizing myositis atorvastatin (n= 256 cases; CI: 6.28 [6.08-6.43]) and simvastatin (n= 51 cases; CI: 4.71 [4.25-5.05]) were the mainly responsible drugs. IMNM was mainly associated to atorvastatine (n= 106 cases; CI: 5.87 [5.55-6.1]) and rosuvastatin (n= 23 cases; CI: 4.18 [3.48-4.67]).Conclusion: The results of this pharmacovigilance analysis confirmed the association between the use of statins and the development of immune-mediated myopathies, some of which, such as IMNM, with potential fatal outcome.

ACCURACY OF URINARY GLUTEN-IMMUNOGENIC PEPTIDES IN COELIAC DISEASE PATIENTS: A CROSS-SECTIONAL MONOCENTRIC STUDY

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Background and aims: Urinary gluten immunogenic peptide (GIP) testing has emerged as an effective, non-invasive method for monitoring adherence to a gluten-free diet (GFD) in patients with coeliac disease (CD) [1]. This test directly detects gluten contamination in the GFD and is recommended by gastroenterology societies in the "Best Practice Advices" and guidelines on CD as part of the evaluation of patients with persistent or recurrent symptoms, alongside serologic testing, dietary review, and small bowel biopsies [2,3]. A negative urinary GIP result is considered a reliable non-invasive indicator of intestinal mucosal healing in CD patients adhering to a GFD [1].
This study aimed to evaluate the presence of urinary GIP in CD patients on a GFD and to explore its relationship with clinical and histological responses, as well as epidemiological and clinical factors.
Methods: Between April and December 2024, CD patients following a GFD for at least one year were randomly selected during routine visits to undergo urinary GIP testing. Patients were not informed about the test beforehand. The "IvyCheck GIP Urine Test" commercial kit was used according to the manufacturer's instructions, capable of detecting gluten ingestion within 3 to 15 hours at a minimum threshold of 50 mg.
Epidemiological and clinical data, including symptom persistence, were retrospectively extracted from medical records. Dietary adherence was assessed using the Biagi's score questionnaire. Data on anti-tissue transglutaminase IgA and anti-endomysial antibodies in GFD were collected when available. Data from duodenal biopsies performed while patients were on a GFD were also collected; routine endoscopic follow-up was usually omitted in younger patients with optimal clinical and biochemical responses.
Statistics was performed using Student's T-test calculator for parameters expressed as mean (+SD), Mann-Whitney for parameters not normally distributed, expressed as median (IQR), and Chi square for percentages.
Results: A total of 50 samples from CD patients (37 females, mean age 40.40 ± 15.20 years, mean age at diagnosis 32.98 ± 17.32 years) were analyzed. The urinary GIP test was positive in 20 patients (40.00%) and negative in 30. There was no significant difference in GIP positivity rates between females and males (36.59% vs. 55.56%, p=0.98). Patients with negative GIP results were slightly older at follow-up (40.93±15.53 vs. 39.80±14.34 years, p=0.38) and with a longer period in GFD (4.5 (IQR 1.45-12.41) vs. 2 (IQR 1.31-8.91)years, p=0.19). Self-reported adherence to the GFD, as measured by the Biagi's score, was higher in GPI-negative patients than positives, but without statical difference (85.71% of GIP-negative vs. 75.00% of GIP-positive patients reporting scores of 3-4, k=0.11). The time elapsed since the last control did not differ [1 (1-1.5) year in GPI-negative vs. 1 (1-2) years in positive patients, p=0.23]. Similarly, there was nosignificant difference between GPI-negative and positive patients in anti-transglutaminase IgA levels [2 (1-14) vs. 5 (1-19) U/L, p=0.19], anti-endomysial antibody positivity (27.38% vs 35.50%, p=0.55), or the presence of persistent symptoms [46.67% vs. 35.00% (p=0.67)]. Persistence of villous atrophy (Marsh 3a) was detected in 4 out of 19 GIP-negative patients and 1 out of 14 GIP-positive patients (p=0.36).
There was no difference in the nutritional parameters between the two groups at the time of GPI test: in GPI-negative versus positive patients, BMI was 22.43+2.80 vs. 21.56+2.13 (p=0.31); ferritin levels were 43 (18-69) ng/mL vs. 46 (22-125) (p=0.65); folates were 4.7 (4.1-8.5) ng/mL vs. 5.3 (3.2-9.9) (p=0.73); and albumin levels were 4.25+0.38 g/dL vs. 4.40+0.14 (p=0.29).
Conclusions: The prevalence of positive results from the random urinary GPI test in CD patients from the outpatient clinic of a referral center for CD was notable, even among those reporting excellent adherence to GFD, consistent with previous reports [1]. These patients generally report well-being and show good clinical and biochemical parameters. Moreover, the persistence of villous atrophy was not significantly related to the ingestion of minimal amounts of gluten, as demonstrated by this test.
We suggest that the GPI test is not strictly necessary in well-being, compliant CD patients, but a negative GPI test could be useful in specific setting of patients, as persistently symptomatic patients, slow responders, or suspected refractory CD.

A CASE OF SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS: CLINICAL PRESENTATION AND DIAGNOSTIC CONSIDERATIONS

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Introduzione: La linfoistiocitosi emofagocitica è una sindrome grave e pericolosa per la vita caratterizzata da un'importante infiammazione che spesso porta all'insufficienza multiorgano e alla morte se non trattata prontamente e in modo appropriato. La sindrome emofagocitica è stata classificata in forme primarie (genetiche) e forme secondarie (acquisite). La diagnosi è particolarmente complicata e molto spesso sottodiagnosticata. Una rapida diagnosi e un contestuale repentino avvio di trattamento specifico è essenziale per ridurre la mortalità e le complicanze. In questo case report descriviamo un caso di sindrome emofagocitica da forme secondarie, con lo scopo di sensibilizzare il clinico all' iter diagnostico da seguire.
Caso Clinico: Donna di 38 anni di origine ucraina, stabilmente in Italia da circa 3 anni. Anamnesi patologica remota muta. Da febbraio 2024 comparsa di sintomatologia respiratoria cronica caratterizzata da tosse secca e dispnea persistenti. Da luglio 2024 comparsa di dermatopatia eritemato-pruriginosa al tronco con anche lesioni maculari e nodulari. Da settembre 2024 associata inoltre cefalea ricorrente e febbricola. Da ottobre 2024 la febbre è diventata continuativa e molto elevata (T 39.5) associata a brivido, vomito, astenia, calo ponderale, peggioramento della tosse secca e della dispnea cronica. Per persistenza di tale sintomatologia la paziente giungeva in Pronto Soccorso a novembre 2024 e ricoverata presso il reparto di Medicina Interna. All'arrivo in reparto paziente prostrata, ipotesa (PA 80/60 mmHg, FC 130 bpm), tachipnoica (FR 25 atti/minuto, spO2 98% in aria ambiente). Febbrile (T 39.9°C), brividante. Sintomatica per intensa tosse secca e dispnea a riposo. Obiettività cardiotoracica nella norma, paziente tachicardica; evidenza di epatosplenomegalia. Al laboratorio quadro di pancitopenia ingravescente, minimo incremento degli indici di flogosi, marcatissimo incremento del D-Dimero, dei valori di ferritina (> 12.000) e della LDH (> 1000), transaminasite, lieve incremento dei trigliceridi. Eseguita TC torace-addome con evidenza di polmonite interstiziale, epatosplenomegalia e linfogranulia diffusa. Quadro clinico "sepsis-like" con evidenza laboratoristica di "iperinfiammazione": pancitopenia febbrile, severa linfocitopenia. Quadro fortemente sospetto per sindrome emofagocitica (HScore 252 punti). Eseguiti estesi accertamenti microbiologici: sierologie virali (HIV, HBV, HCV), emocolture, urocolture, striscio di sangue periferico. Nelle successive 48 ore peggioramento del quadro clinico per ipotensione e picchi febbrili persistenti, comparsa di insufficienza respiratoria acuta e alterazione del sensorio. Al laboratorio rapidissimo peggioramento della pancitopenia e rapido incremento degli indici di flogosi. Considerato l'elevato sospetto di sindrome emofagocitica avviata empiricamente terapia steroidea sistemica e trattamento per la polmonite interstiziale con terapia antibiotica (cotrimossazolo) e antivirale (ganciclovir) per presenza di CMV su sangue periferico. Discreto, rapido miglioramento clinico. Eseguita biopsia osteomidollare che confermava il sospetto di sindrome emofagocitica. La paziente successivamente veniva trasferita presso il reparto di Malattie Infettive dove ha proseguito la terapia steroidea ed è stata sottoposta alla terapia antiretrovirale per riscontro di positività ad HIV.
ConclusionI: Le forme secondarie della sindrome emofagocitica sono largamente sottodiagnosticate in tutto il mondo. Nel trial HLH-2004 viene descritto un algoritmo diagnostico basato sull'evidenza della presenza di almeno cinque tra i seguenti criteri: febbre, splenomegalia, bicitopenia, ipertrigliceridemia o ipofibrinogenemia, emofagocitosi, iperferritinemia, bassa o assenza di attività delle cellule NK ed elevati livelli di CD25. Un'alternativa è l'utilizzo dell'HScore basato su nove variabili: febbre, organomegalia, immunosoppressione, ematofagocitosi, citopenie, ferritina, trigliceridi, fibrinogeno e AST. Tale score permette di calcolare la probabilità di sindrome emofagocitica. Entrambi gli score hanno una buona accuratezza diagnostica: HLH-2004 presenta il 95% di sensibilità e 93.6% di specificità, mentre un valore ≥ 168 nel HScore è fortemente sospetto per sindrome emofagocitica. Pertanto una attenta analisi dei segni e sintomi

dei pazienti e l'utilizzo dei corretti score diagnostici potrebbe aiutare a fare diagnosi di tale sindrome, ancora così sottodiagnosticata.

THINK OUTSIDE THE LIVER IN A CASE OF PORTAL HYPERTENSION

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Case report: A 61-year-old man with no relevant medical history presented to the Emergency Department (ED) with progressive bilateral lower limb edema and abdominal distension over the past months. He denied fever, weight loss, or dyspnea. Vital signs were unremarkable. Physical examination and bedside ultrasound showed bilateral pitting edema, massive grade 3 ascites and splenomegaly (22 cm), in the absence of signs suggestive of chronic liver disease. Laboratory results revealed normocytic anemia (Hb 8.7 g/dL; MCV 89 fl), neutrophilic leukocytosis, elevated LDH and alkaline phosphatase (LDH 850 U/L; ALP 325 U/L), with preserved renal and liver function. Notably, thrombocytopenia was present (PLT 78'000/μL). The patient was admitted to our Internal Medicine department for further evaluation.
After admission, intravenous furosemide led to gradual reduction in weight and ascites. The patient denied alcohol intake, and screening for viral hepatitis (HBV and HCV) and liver autoantibodies (ANA, AMA, ASMA, LKM) was negative. A diagnostic paracentesis was performed, revealing a serum-ascites albumin gradient (SAAG) > 1.1 g/dL, along with an elevated protein concentration. Malignancy and infections were excluded.
Total-body CT showed hepatomegaly with no focal lesions, patent splenoportal and suprahepatic circulation, portal vein dilation (20 mm), and severe splenomegaly (26 cm), raising suspicion for non-cirrhotic portal hypertension. Given the absence of hepatic parenchymal disease, together with hematologic abnormalities, a haematological etiology was suspected. A 18F-FDG PET/CT was performed, revealing diffuse hypermetabolic activity in the osteomedullary compartment, and hepatosplenomegaly with normal uptake in liver or spleen. A bone marrow biopsy showed marked megakaryocytic hyperplasia (CD61+), with giant and dysplastic forms and increased reticulin fibrosis. Molecular testing confirmed the presence of JAK2V617F mutation in peripheral blood, establishing the diagnosis of primary myelofibrosis (PMF) in the fibrotic phase. Given the clinical picture of portal hypertension, an esophagogastroduodenoscopy (EGDS) was performed, revealing grade 1 esophageal varices without active bleeding. Prophylaxis with non-selective beta-blocker (carvedilol) was started. The patient was referred to hematology for prognostic stratification (intermediate-1 risk according to DIPSS) and treatment planning, including the possible initiation of JAK inhibitor therapy.
The absence of cirrhosis, together with massive splenomegaly, preserved liver architecture, and ascitic fluid with high SAAG but elevated protein content, supported a pre-hepatic mechanism of portal hypertension, likely secondary to myeloproliferative infiltration and splanchnic congestion. Hepatology follow-up was arranged.
Background: Primary myelofibrosis (PMF) is a chronic myeloproliferative disorder characterized by clonal proliferation of megakaryocytes and granulocytes, variably associated with bone marrow fibrosis, cytopenias, hepatosplenomegaly and extramedullary hematopoiesis. It typically affects middle-aged or older adults and is the least common and most prognostically unfavorable among myeloproliferative neoplasms. Patients are at risk of premature death due to disease progression, leukemic transformation, thrombo-hemorrhagic events, and infections. The most frequent mutation is JAK2V617F in the JAK2 gene; CALR and MPL mutations are also described. These mutations are diagnostically and therapeutically relevant, guiding the use of JAK inhibitors.
Diagnosis requires three major criteria (megakaryocytic proliferation with grade 2–3 fibrosis; JAK2/CALR/MPL mutation; exclusion of other myeloid neoplasms) and at least one minor criterion (e.g., anemia, leukocytosis, elevated LDH, leukoerythroblastosis). Additionally, PMF may rarely present with presinusoidal portal hypertension, typically in the absence of underlying liver disease. This can result from massive splenomegaly and extramedullary hematopoiesis, which contribute to increased portal flow and vascular resistance.
Conclusions: PMF may be asymptomatic or present with vague constitutional symptoms. In rare cases, it can mimic advanced liver disease by manifesting with signs of portal hypertension such as ascites, variceal bleeding, or portal hypertensive gastropathy, despite the absence of underlying hepatopathy. Moreover, in PMF, ascitic fluid analysis revealed high SAAG, indicative of portal hypertension, along with an elevated protein concentration due to splenomegaly and neoplastic infiltration.
This case highlights the need to consider myeloproliferative neoplasm like PMF in the differential diagnosis of portal hypertension, especially in the absence of liver disease.
Beyond disease-modifying treatments aimed at controlling progression and reducing leukemic transformation risk, a multidisciplinary approach is essential to manage the complications related to portal hypertension.
Patients showing signs of portal hypertension should undergo hepatological evaluation to exclude additional causes and ensure appropriate long-term monitoring.

MALNUTRITION AFFECTS INFECTION RATES AND QUALITY OF LIFE IN PATIENTS UNDERGOING PRIMARY HIP AND KNEE ARTHROPLASTY: A RETROSPECTIVE STUDY

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Background: Although malnutrition is globally associated with incremental morbidity, mortality, and cost, there has been a fundamental lack of consensus on diagnostic criteria for application in clinical settings. The study aims were: (i) to identify Malnutrition role as independent risk factors for complications in Total Joint Arthroplasty context; and (ii) to analyze malnutrition impact on treatment success, specifically in terms of patient-reported Quality of Life.
Methods: The study retrospectively analyzed 1,070 patients undergoing total hip or knee arthroplasty between January 2019 and July 2022. Before the surgery patients' nutritional status were assessed through Nutritional Risk Screening 2002 (NRS 2002) and Controlling Nutritional Status (CONUT) score. Patients were classified in two different group: patients with NRS≥3 were included in Malnutrition group, and patients with NRS<3 in the Control group, instead.
Results: A total amount of 682 patients were included in the Study. Mean age was 70.1±9.6, 53% women ratio, BMI 28.1±4.8 Kg/m2. A univariate regression, adjusted for age and sex, was performed. Both NRS 2002 and CONUT score were significant risk factors in infectious complications and in EQ5 domains of Quality-of-life assessment ($p<0.05$).
Conclusions: Malnutrition, as identified by both the NRS 2002 and CONUT score, emerges as an independent risk factor, contributing to worse postoperative outcomes and increased complications, thereby decreasing the potential benefits of TJAs. Preoperative nutritional assessment and targeted intervention to address malnutrition can play a crucial role in improving clinical outcomes, quality of life, and complication rates.

REAL-WORLD SAFETY AND EFFECTIVENESS OF LOMITAPIDE IN HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLAEMIA OVER TEN YEARS: DATA FROM THE LOMITAPIDE OBSERVATIONAL WORLDWIDE EVALUATION REGISTRY (LOWER)

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Aim: To report ten-year safety and efficacy data from the LOWER registry of lomitapide use in patients with homozygous familial hypercholesterolaemia.
Methods: ntre, prospective, observational registry investigating long-term safety and effectiveness of lomitapide in clinical practice. Data has been collected over 10 years since enrolment of the first patient in March 2014. We summarize participant characteristics and clinical data collected until 29th February 2024.
Results: A total of 234 patients (57.7% female) have enrolled in LOWER; 121 (51.7%) had ongoing cardiac disorders at baseline. The mean ±SD [range] age of participants and baseline low-density lipoprotein-cholesterol level (LDL-C) were 51.1 ±15.19 [18–83] years and 243.1 ±110.7 [71–672] mg/dL, respectively. Post-lomitapide data were available for 233 patients (99.6%). Lomitapide doses ranged from 2.5–50 mg/day, with a global mean dose of 12.1 mg/day (16.1

mg/day in Europe). Duration of lomitapide exposure ranged from 9 days to ≥10 years (mean 42.06 months). Approximately one-third of patients received lomitapide for 2 to <5 years (n=73; 31.3%), with around one quarter receiving it for 5 to <10 years (n=58; 24.8%). The most common events of special interest (ESI) were gastrointestinal and hepatic; 19.3% of patients experienced at least one hepatic ESI. Asymptomatic aminotransferase levels ≥3–<5x and ≥5x the upper limit of normal were observed in 10.7% and 8.6% of patients, respectively, and were manageable by dose reduction. 157 patients (67.4%) experienced a reduction in LDL-C by ≥50% from baseline at any timepoint after lomitapide initiation, with 168 (72.1%), 113 (48.5%) and 84 (36.1%) reaching LDL-C <100 mg/dL, <70 mg/dL and <55 mg/dL, respectively.
Conclusions: Ten-year LOWER registry data support the long-term lipid-lowering effect and safety of lomitapide. Around half of patients achieved LDL-C <70 mg/dL and over one third reached LDL-C <55 mg/dL at least once.

SHEAR WAVE DISPERSION IN THE LIVER AND SPLEEN: REFERENCE VALUES IN THE HEALTHY POPULATION AND CLINICAL APPLICATION OF SHEAR WAVE IMAGING IN PATIENTS WITH PORTAL HYPERTENSION

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Background e obiettivi: negli ultimi anni sono state sviluppate numerose tecnologie per la valutazione ultrasonografica multiparametrica (multiparametric ultrasound, MPUS) dei pazienti con malattia epatica. La tecnologia di imaging Shear Wave Dispersion (SWD) permette la misura della pendenza del gradiente frequenza-dipendente della velocità delle shear waves per la stima indiretta della viscosità tissutale, possibilmente correlata a fenomeni di necro-infiammazione e congestione parenchimale secondo diversi studi preclinici e clinici. Gli studi per la determinazione dei valori di riferimento di SWD a livello epatico (L-SWD) e splenico (S-SWD) nella popolazione sana sono ad oggi scarsi. Gli obiettivi di questo studio sono stati: i) stabilire i valori medi di L-SWD and S-SWD nei soggetti adulti sani; ii) valutare in uno studio clinico pilota eventuali variazioni dei valori di Shear Wave Elastography e Dispersion a livello epatico (L-SWE, L-SWD) e splenico (S-SWE, S-SWD) in un gruppo di pazienti con ipertensione portale (portal hypertension, PH) prima (T0) e dopo (T1) posizionamento di shunt porto-sistemico intraepatico transgiugulare (trasnjujular intrahepatic porto-systemic shunt, TIPSS).
Materiali e metodi: per la standardizzazione di L-SWD e S-SWD sono stati arruolati su base volontaria rispettivamente 91 (33 maschi, 42 ± 14 anni) e 36 (12 maschi, 49 ± 13 anni) soggetti adulti sani. Sono stati raccolti inoltre i dati antropometrici di indice di massa corporea (IMC) e circonferenza vita (CV). Per lo studio pilota sono stati arruolati tre pazienti con PH ed indicazione al posizionamento di TIPSS. I pazienti sono stati sottoposti alla misura invasiva intraprocedurale del gradiente pressorio venoso epatico (hepatic venous pressure gradient, HVPG) ai tempi T0 e T1. Tutti i partecipanti sono stati sottoposti a MPUS con il sistema ultrasonografico Canon Aplio i800 (trasduttore i8CX1) per la misura di L-SWE, L-SWD, S-SWE e S-SWD e del coefficiente di attenuazione epatico mediante Attenuation Imaging (ATI). Per lo studio pilota i pazienti sono stati sottoposti a MPUS ai tempi T0 e T1.
Risultati: i valori medi di L-SWD e S-SWD ± deviazione standard sono risultati rispettivamente pari a 11.5 ± 1.3 (m/s)/kHz e 13.0 ± 1.9 (m/s)/kHz. I valori di L-SWD hanno presentato una distribuzione normale, quest'ultima non osservata per la distribuzione dei valori di S-SWD. I valori di L-SWD e S-SWD non hanno presentato significative differenze tra i soggetti di sesso maschile e femminile, né significative correlazioni con età, IMC, CV o altri parametri ultrasonografici. Nei tre pazienti dello studio clinico pilota è stata osservata una riduzione dei valori di L-SWE, S-SWE e S-SWD a seguito del posizionamento di TIPSS ed è stata rilevata una correlazione statisticamente significativa tra i valori di S-SWE e HVPG (coefficiente di correlazione di Spearman 0.812, p = 0.050).
Conclusione: il valore medio di L-SWD nella popolazione sana può essere utilizzato come riferimento in futuri studi clinici, mentre un aumento della numerosità campionaria è auspicabile per la determinazione dei valori di riferimento di S-SWD. La MPUS si mostra promettente per la valutazione non invasiva delle componenti dinamiche strutturali e di emodinamica splancnica nei pazienti con malattia epatica, in particolare per la stima di HVPG.

PLASMATIC EXTRACELLULAR VESICLES AT THE INTERSECTION OF IMMUNE AND METABOLIC DYSREGULATION IN OBESITY AND TYPE 2 DIABETES

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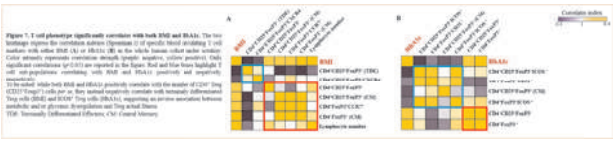
Purpose: Type 2 diabetes (T2D) and its cardiovascular complications represent a major biomedical challenge due to their high individual and societal burden. Understanding the pathological mechanisms underlying T2D development is therefore a research priority. Obesity and chronic inflammation are major drivers of the current T2D epidemic. Identifying the cellular and molecular mediators that connect these conditions has enormous clinical relevance. In this context, we hypothesize that plasmatic extracellular vesicles (EVs) may reflect endogenous dysmetabolic states and impair the function of CD4+CD25 high regulatory T (Treg) cells - key players in maintaining immune tolerance - thereby promoting inflammation and increasing T2D susceptibility.
Methods: We recruited lean healthy individuals (BMI <25) and overweight/obese subjects (BMI >25) with: (i) normal glucose sensitivity, (ii) impaired glucose tolerance, and (iii) diagnosed T2D. In all participants, plasmatic EVs were isolated by size-exclusion chromatography and characterized for concentration, size distribution, and molecular cargo (protein and microRNA profiles). In parallel, circulating Treg cells were analyzed ex vivo by flow cytometry (FACS) to assess their phenotype and proliferative capacity. Furthermore, functional assays are ongoing to evaluate the effects of isolated EVs on Treg cell activation, gene expression profiles, and effector functions in vitro.
Results: By integrating metabolic, immunological, and environmental data, we are mapping the specific intersections between the plasmatic EV molecular signatures, cytokine/adipokine profiles, and Treg cell fitness across different subject groups. Preliminary results indicate that the characteristics of plasmatic EVs are significantly modulated by the individual's metabolic status. Specifically, EVs appear to act both as targets and modulators during T2D progression, contributing to alterations in Treg cell suppressive function in conditions of dysmetabolism and chronic inflammation.
Conclusion: A deeper understanding of the interplay between plasmatic EV dysregulation and Treg cell impairment in obesity and T2D is crucial not only for improving patient stratification but also for elucidating fundamental disease mechanisms. These insights may pave the way for novel therapeutic strategies aimed at preventing or slowing T2D onset and progression.



SiRNA VERSUS MABS FOR PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 (PCSK9) INHIBITION: REAL WORLD EVIDENCE SINGLE-CENTER STUDY ON LIPID PROFILE IN FAMILIAL HYPERCHOLESTEROLEMIA PATIENTS

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Background: and aim: PCSK9 inhibitor (PCSK9i) mAbs showed a dramatic effect on low-density lipoprotein cholesterol (LDL-C) reduction. A double-stranded small-interfering RNA (siRNA) therapeutic agent that suppresses PCSK9 translation (inclisiran) has been recently licensed. RCTs showed that inclisiran administered every 6 months is associated to a similar LDL-C reduction compared to every 14 days PCSK9i mAb treatment. The aim of our study is to compare in real world evidence lipid lowering effect of siRNA versus mAbs.
Methods: We perfomed a prospective cohort study. Familial hypercholesterolemia (FH) patients with a stable treatment (>6 month) with PCSK9i mAbs were included. Group1 was switched to treatment with PCSK9i siRNA (inclisiran) and Group2 continued the treatment with PCSK9i mAbs (Alirocumab or Evolocumab). Lipid profile [total cholesterol (TC) and LDL-C] and % of LDL-C target achievement were evaluated at the baseline (TO) and at 6-months fol-

low-up (T1).
Results: 52 FH patients were enrolled. Group1 (n=26) 56% males, average age of 56.1÷14.8years; 50% in secondary prevention. At TO, TC was 179.61+67.5mg/dl, LDL-C was 105.7+62.2mg/dl. At T1, TC was 175.4+53.1 mg/dl and LDL-C value was 97.6+47.9 mg/di. Group2 (n=26) 42% males, average age of 61.5+12.4years; 46% in secondary prevention. At T0, TC was139.8+54.8 mg/dl, LDL-C was 65.8+51.0mg/dl. At T1, TC was 137.6+35.0mg/d| and LDL-C was 63.132.2mg/dl. No significant difference between T1-TO LDL-C A mean % reduction was found comparing the 2 groups (10% for Group1 vs 35% for Group2 p=0,260). No significant difference in % of target achievement at T1 was found (31% for Group 1 and 50% for Group 2; OR: 95%CI:36.4-61.9, p=0.131).
Conclusions: Our preliminary results showed that no significant difference in efficacy were found between treatment with PCSK9i mAbs and siRNA, confirming siRNA a promising option mainly in low-adherent patients.

CRITICAL ILLNESS MYOPATHY-NEUROPATHY WITH TETRAPARESIS SECONDARY TO LEGIONELLA PNEUMONIA

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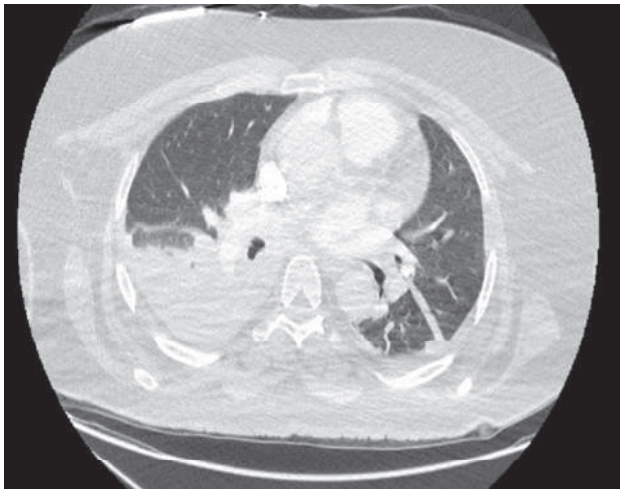
Ospedale Pierantoni

La malattia dei legionari è un'infezione batterica sistemica acuta che si verifica come una grave polmonite lobare associata a manifestazioni extrapolmonari. Qualsiasi specie della famiglia delle Legionellace può causare una polmonite sia in ospiti immunocompetenti che immunocompromessi. La specie patogenetica più frequente è la Legionella pneumophila. I pazienti con malattia dei legionari si presentano con febbre, brividi e sintomi sistemici. La radiografia del torace mostra una polmonite lobare mentre i test di laboratorio possono dimostrare un concomitante coinvolgimento renale ed epatico. L'antigene urinario della legionella è comunemente usato per diagnosticare l'infezione. Diverse manifestazioni neurologiche sono frequentemente osservate nei soggetti con legionellosi e sono per lo più rappresentate da un'encefalopatia reversibile. Altre anomalie neurologiche, tra cui l' interessamento del tronco cerebrale e la disfunzione cerebellare non sono comuni e tendono a persistere oltre la malattia acuta. Ma è il coinvolgimento dei nervi periferici con la polineuropatia sensoriale-motoria, la quale porta all'ipotonia o alla paralisi in entrambe le braccia e/o alle gambe, ad essere un evento eccezionalmente. Queste anomalie neurologiche di solito non sono evidenti al neuroimaging nè ai risultati biochimici di laboratorio. La patogenesi delle complicanze neurologiche in corso di Legionellosi rimane ancora incerta: l'esame del liquido cerebrospinale è di solito normale il che suggerisce che non si tratta di una meningoencefalite batterica secondaria ad una vera e propria invasione diretta del sistema nervoso centrale quindi la spiegazione più plausibile è che la patogenesi sia dovuta all'azione delle tossine batteriche rappresentate dell'antigene lipopolisaccaride il quale scatena veri e propri fenomeni immunologici associati a disturbi metabolici. Essendo la Legionella pneumophila un patogeno intracellulare gli antibiotici per un trattamento efficace sono: macrolidi, chinoloni, tetracicline e rifampicina, questo perchè hanno la capacità di accumularsi nello spazio intracellulare e di essere quindi bioattivi. La durata abituale del trattamento per la malattia del legionario è di circa 7, fino a 14 giorni se presenti complicanze. Noi descriviamo il caso clinico di un uomo di 55 anni autonomo, autosufficiente, non immunocompromesso, che accede in PS per febbre, tachipnea con insufficienza respiratoria e tachicardia, alterazione dello stato cognitivo con afasia ed ipostenia inizialmente al solo arto superiore destro successivamente degenerato in una tetraparesi. Nel sospetto di evento neurovascolare acuto è stato sottoposto a angioTAC+ TAC encefalo con mezzo di contrasto che non ha confermato eventi cerebrovascolari acuti. Per il quadro di grave insufficienza respiratoria con P/F 79 e lo stato settico, è stato necessario il ricovero in Terapia Intensiva. Tra gli accertamenti inziale: ALT 1280 (v.n. <41), bilirubina 2.4 (v.n.0.3-1.2), creatinina 2.3 (v.n. 0.7-1.2) , procalcitonina 96, emocolture negativa ma positività per l' antigene urinario per legionella. Il paziente è stato sottoposto a TAC torace, EMG e ecodoppler cardiologico per tachicardia trattata con cardioversione elettrica. E' stata effettuata la terapia antibitoica con Levofloxacina con dose di carico 750mg poi 500mg ogni 12h con remissione del quadro infettivo. Durante il ricovero in Medicina Interna il paziente ha proseguito la fisioterapia: il recupero neuro-motorio è ancora incompleto per il persistere della neuropatia motoria. La diagnosi di Critical Illness myopathy-neuropathy è stata posta sulla positività microbiologica dell' antigene urinario per legionella , sulla clinica e sull' elettromiografia (EMG). Con il nostro case report si vuole portare l' attenzione sulle possibili rare complicanze della malattia dei Legionari : oltre alle più frequenti presentazioni cliniche, esistono complicanze neurologiche incomuni come la neuro-miopatia critica che possono persistere oltre la risoluzione dello stato infettivo. I danni neurologici contemplano quasi certamente dei meccanismi autoimmuni o la combinazione di molteplicità di diversi meccanismi patogenetici concomitanti. La sfida per i clinici è dovuta al fatto che in corso di Legionellosi, gli eventi neurologici possono essere incomuni e difficili da diagnosticare perchè non vi è l' evidenza dell'infezione al neuroimaging e/o all'analisi del liquido cerebrospinale. Il nostro caso clinico è rappresentativo perchè dopo aver diagnosticato tempestivamente la Polmonite da Legionella, è stata iniziata subito la terapia antibiotica mirata è questo è stato l' outcome più favorevole per il paziente, l' EMG ha consentito di confermare il sospetto diagnostico di critical illness myopathy-neuropathy secondario ad infezione da Legionella.



TAC torace: si osserva ampio addensamento che impegna quasi completamente il lobo inferiore destro,il segmento dorsale e parte del segmento apicale del lobo superiore omolaterale con conservato broncogramma aereo. Altra componente addensata con alterazioni disventilatorie si osserva nelle porzioni basali del lobo inferiore di sinistra ed in parte il segmento apico-dorsale lobo superiore di tale lato.

HIGH PLASMA LEVELS OF LIPOPROTEIN (A) ARE ASSOCIATED WITH INCREASED COAGULANT ACTIVITIES OF FACTOR V: PRELIMINARY RESULTS FROM AN ANGIOGRAPHICALLY-CONTROLLED STUDY

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Background: Lipoprotein (a) [Lp(a)] is an established risk factor for cardiovascular disease. Beyond its proatherogenic and proinflammatory properties, a prothrombotic role has also been proposed, but the link between Lp(a) and haemostatic balance remains controversial so far.
Aims: To perform an overall assessment of the activities of coagulation factors according to Lp(a) plasma levels in a cardiovascular cohort of subjects with or without coronary artery disease (CAD).
Methods: The coagulant activities of factors II, V, VII, VIII, IX, X, XI and XII by one-stage clotting method, as well as plasma levels of Lp(a), apolipoproteins A1 (ApoA1) and B (ApoB), were assessed in clinically stable subjects undergoing elective coronary angiography. Subjects taking anticoagulant therapies were excluded. Lp(a) threshold values were defined according to the European Atherosclerosis Society consensus statement: normal <30 mg/dL, intermediate 30-50 mg/dL, and high >50 mg/dL.
Results: The laboratory data were available for 383 subjects (males 75.2%; mean age 68.2±9.7 years): 65 subjects had normal coronary arteries (CAD-free), 52 subjects had coronary lesions with stenosis <50% (CAD-borderline), and 266 subjects had coronary lesions with stenosis ≥50% (CAD). The main clinical characteristics of the study population according to the coronary angiography classification are shown in Table 1. A progressive and significant increase of FV coagulant activity (FV:C) from low to high Lp(a) plasma levels was found, while there was no difference for the other coagulation factors. Subjects with high Lp(a) plasma levels had also higher levels of ApoB (Table 2). The association of Lp(a) levels with FV:C (standardized beta-coefficient=0.107, P=0.033) was confirmed by linear regression models after adjustment for sex,

age, CAD diagnosis, serum creatinine, ApoA1 and ApoB levels.
Conclusions: In this pilot study within a cardiovascular cohort high Lp(a) plasma levels were associated with increased FV:C.

Table 1: Main clinical characteristics of the study population according to the coronary angiography classification.

	Total (n = 383)	CAD-free (n = 65)	CAD-borderline (n = 52)	CAD (n = 266)
Male sex (%)	75.2	55.4	71.2	80.8
Age (years)	68.2 ± 9.7	63.4 ± 9.8	70.4 ± 8.3	69.0 ± 9.7
BMI (kg/m²)	26.4 ± 3.9	26.6 ± 4.0	26.4 ± 3.7	26.3 ± 4.0
Creatinine (mg/dl)	0.93 (0.90 – 0.95)	0.89 (0.85 – 0.94)	0.91 (0.87 – 0.96)	0.96 (0.91 – 0.99)
Hypertension (%)	70.8	61.5	63.5	74.5
Diabetes (%)	21.9	17.0	19.2	23.7
Smoking (%)	39.7	35.4	38.5	41.0
Dyslipidemia (%)	84.3	69.2	73.1	90.2
Apolipoprotein A1 (g/L)	1.29 ± 0.22	1.39 ± 0.23	1.35 ± 0.23	1.29 ± 0.21
Apolipoprotein B (g/L)	0.71 ± 0.20	0.74 ± 0.21	0.74 ± 0.20	0.70 ± 0.20
Lp(a) < 30 mg/dL (%)	66.6	73.8	71.2	63.9
Lp(a) 30-50 mg/dL (%)	12.0	7.7	17.3	12.0
Lp(a) > 50 mg/dL (%)	21.4	18.5	11.5	24.1

Table 2: Coagulant activities of coagulant factors, traditional coagulation parameters, serum creatinine, apolipoprotein A1 and B levels according to lipoproten (a) [Lp(a)] plasma levels.

	Lp(a) <30 mg/dL (n = 255)	Lp(a) 30-50 mg/dL (n = 46)	Lp(a) >50 mg/dL (n = 82)	p*
FII:C (%)	90.1 ± 11.9	88.3 ± 13.8	91.3 ± 13.0	0.612
FV:C (%)	84.4 ± 18.7	88.8 ± 18.3	90.1 ± 18.7	**0.011**
FVII:C (%)	88.9 (86.2-91.7)	87.0 (80.8-93.8)	93.8 (89.7-98.1)	0.130
FVIII:C (%)	98.5 (94.7-102.4)	95.8 (88.4-103.9)	98.0 (90.5-106.1)	0.826
FIX:C (%)	117.5 ± 19.7	111.6 ± 19.6	114.7 ± 19.3	0.143
FX:C (%)	96.2 (94.2 – 98.3)	89.9 (85.7 – 94.9)	94.1 (90.7 – 97.7)	0.148
FXI:C (%)	104.1 ± 19.5	99.8 ± 21.4	102.9 ± 19.1	0.459
FXII:C (%)	102.3 ± 24.9	94.3 ± 27.5	100.6 ± 25.8	0.379
PT	1.02 ± 0.07	1.03 ± 0.07	1.00 ± 0.06	0.054
aPTT	1.00 ± 0.09	1.03 ± 0.09	1.02 ± 0.09	0.213
Fibrinogen (mg/dL)	330 (320 – 341)	337 (317 – 358)	351 (330 – 373)	0.061
Creatinine (mg/dL)	0.92 (0.90 - 0.95)	0.90 (0.84 - 0.95)	0.96 (0.91 – 0.99)	0.280
ApoA1 (g/L)	1.30 ± 0.23	1.24 ± 0.18	1.29 ± 0.22	0.171
ApoB (g/L)	0.69 ± 0.20	0.70 ± 0.20	0.76 ± 0.18	**0.012**

*: by ANOVA with polynomial contrasts for linear trend

SWEET DREAMS ARE MADE OF THIS: AN UNCOMMON ADVERSE EFFECT OF SGLT2-INHIBITORS

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Background: Sodium-glucose co-transporter-2 inhibitors (SGLT2-i) are a relatively new class of drugs used in the management of type 2 diabetes mellitus (T2DM), heart failure and chronic kidney disease. They act by inhibiting SGLT2 proteins located in the proximal tubules of the nephrons. By blocking these transporters, they induce glycosuria and natriuresis, resulting in lower plasma glucose levels. While generally well tolerated, SGLT2-i are associated with an increased incidence of urinary tract and genital infections and more rarely with severe metabolic complications.
Case report: A 65-year-old Saudi tourist initially presented to the emergency department (ED) following an accidental fall with head trauma. A head CT scan was unremarkable and the patient was discharged. The following night, he returned to the ED due to repeated episodes of vomit, appearing dehydrated and drowsy and was admitted to our medical intermediate care unit. He spoke only broken English and was unable to provide his medical history or therapy. He complained of nausea and dysuria. Vital signs were within normal limits. Physical examination revealed confusion but no focal neurological deficits. Laboratory tests showed mild neutrophilic leukocytosis (neutrophils 12,890/mmc) and mild hyperglycemia (175 mg/dL). Arterial blood gas analysis revealed a pH of 7.12 and a bicarbonate level of 9 mmol/L. Blood alcohol level, urine toxicology screen and a repeat head CT were all negative. Urinalysis was positive for glycosuria and ketonuria, although capillary blood glucose levels remained only mildly elevated. The patient was started on lactated Ringer, IV bicarbonate and empiric antibiotic therapy with ceftriaxone. Despite initial treatment, both neurological and metabolic status showed no significant improvement.
Upon questioning hotel staff, some medications were found in the patient's room, including a blister of empagliflozin and vitamin B supplements. In light of this finding, euglycemic diabetic ketoacidosis (EDKA) was suspected and the patient was started on IV dextrose and insulin. After 24 hours of appropriate therapy, blood pH normalized and neurological conditions improved. The patient never showed any clinical or biochemical sign of infection or other causes of glycaemic decompensation.
To complete the diagnostic work-up, further tests were performed to evaluate the patient's diabetes status: autoantibodies (anti-islet cell antibodies [ICA], glutamic acid decarboxylase antibodies [GAD], and anti-insulin antibodies) were negative, C-peptide was within normal range, endogenous insulin was decreased and HbA1c was 83.0 mmol/mol. The patient's son confirmed that he had diabetes and had recently discontinued insulin, as recommended by his general practitioner. Four days after presentation, the pH remained consistently normal, urine ketones had cleared and the patient was fully oriented. At that point, he was transitioned to subcutaneous insulin and discharged with an absolute contraindication to restarting SGLT2-i.
Discussion: SGLT2 inhibitors are an innovative oral drug class used in the management of T2DM, heart failure and chronic kidney disease. Genitourinary infections and hypotension are the most commonly reported adverse effects associated with their use. Less frequently, they can lead to a particular form of diabetic ketoacidosis known as EDKA. This condition is characterized by metabolic acidosis and ketonemia, with blood glucose levels that remain below 250 mg/dL. Due to this atypical presentation and its rarity, EDKA is often underrecognized, resulting in diagnostic delay. EDKA is more common in type 1 diabetes and latent autoimmune diabetes in adults (LADA), however it can occur in long-standing DM2. Therefore clinicians must be aware of this condition.

SEVERE DELAYED HEMOLYTIC TRANSFUSION REACTION (DHTR) IN SICKLE-B-THALASSEMIA: WHEN ECULIZUMAB BECOMES THE ONLY OPTION

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Background: Sickle-β-thalassemia is a rare inherited hemoglobinopathy caused by co-inheritance of abnormal hemoglobin S (HbS) and β-thalassemia mutations, combining features of both sickle cell disease and thalassemia. The clinical phenotype is heterogeneous, characterized by erythrocyte sickling, vaso-occlusion, chronic hemolysis, and progressive organ damage. While erythrocytes transfusion therapy remains a mainstay in disease management, it may rarely lead to delayed hemolytic transfusion reaction (DHTR), a potentially life-threatening complication involving alloimmunization, macrophage activation, and complement-mediated hemolysis. Standard therapeutic strategies to DHTR include high-dose corticosteroids, intravenous immunoglobulins (IVIg), erythropoiesis-stimulating agents, and avoidance of further transfusions whenever possible. In refractory cases, eculizumab - an anti-C5 monoclonal antibody - has emerged as a promising option by inhibiting terminal complement activation and mitigating ongoing hemolysis. To date, the use of eculizumab in hemoglobinopathies remains off-label and has been primarily reported in patients with sickle cell disease. No cases of its use in patients with sickle- β -thalassemia have been documented so far.
Case report: A 22-year-old male with sickle-β-thalassemia was admitted to our Internal Medicine department for acute chest pain. Since childhood, he had experienced recurrent vaso-occlusive crises (VOC) and had been treated with hydroxyurea, discontinued due to lack of efficacy. He had since been undergoing automated erythrocytapheresis every 40 days. His clinical history was also notable for multiple episodes of acute chest syndrome (ACS), prior splenectomy and cholecystectomy, and a recent hip replacement due to femoral avascular necrosis.
At presentation, vital signs, clinical examination, electrocardiogram, arterial blood gas analysis and chest X-ray were unremarkable. Laboratory tests revealed elevated inflammatory markers (C-reactive protein 63 mg/L), leukocytosis (WBC 14.6x10^3/μL), and stable hemoglobin (Hb 10.4 g/dL) with an HbS of 39.4%. Initial management included intravenous hydration, analgesia, and empiric ceftriaxone. Antithrombotic prophylaxis with heparin was also initiated. The patient also underwent a manual exchange transfusion (1 unit of packed red blood cells -PRBC- and 400 mL phlebotomy).
Within 48 hours, despite negative cultures, the patient remained febrile with persistent chest pain and rising CRP levels (165.5 mg/L). A chest CT scan revealed bilateral consolidations consistent with ACS, prompting escalation to

piperacillin/tazobactam and a second exchange transfusion. Despite initial improvement, the patient developed mild respiratory insufficiency, worsening pain, progressive anemia (Hb 6.6 g/dL), and rising hemolysis markers (LDH 826 U/L, indirect bilirubin 9.69 mg/dL), requiring a third exchange transfusion and two additional PRBC units, without clinical benefit. Immunohematologic testing confirmed DAT positivity (IgG, IgM, anti-C3d) and anti-e/anti-I autoantibodies, supporting a DHTR diagnosis. High-dose steroids and IVIg were started, but both of them proved ineffective. The patient's condition deteriorated dramatically, developing hypotension, hypoperfusion (lactate 7.5 mmol/L), critical anemia (Hb 1.8 g/dL, HbS 15.4%, HbA 78%), marked reticulocytopenia, and mild complement consumption (normal C3, C4 0.09 g/L). Following the failure of all conventional therapies, off-label eculizumab (900 mg) was administered, followed by transfusion of two PRBC units, resulting in rapid clinical stabilization, allowing the continuation of supportive care including corticosteroids and erythropoietin. Despite persistent anemia (Hb 2–4 g/dL), no further transfusions were required. Due to sustained reticulocytopenia, a bone marrow biopsy was performed, showing no significant abnormalities. Eculizumab was administered weekly for 3 additional doses. The patient was discharged after 30 days with Hb of 4.9 g/dL, and completed the fourth and final infusion as outpatient, with Hb increasing to 6.4 g/dL.

Conclusions: this case describes a rare and severe presentation of DHTR in a patient with sickle-β-thalassemia, marked by rapid clinical and hematologic deterioration despite intensive standard treatment. In this context, off-label administration of eculizumab was undertaken. Although its use has been described in anecdotal cases of DHTR in sickle cell disease, this is, to our knowledge, the first reported case in a patient with sickle- β -thalassemia. The prompt clinical stabilization and progressive recovery observed after eculizumab administration support the role of complement activation in the pathogenesis of DHTR, particularly in patients with sickle cell disease and related hemoglobinopathies.

With the increasing complexity and longevity of patients with hemoglobinopathies, internists are increasingly involved in the management of rare but severe complications such as DHTR, where early recognition and multidisciplinary management are critical to improving outcomes.

FROM SUSPECTED METASTASIS TO HCC DIAGNOSIS ON MASLD: THE VALUE OF AN INTEGRATED CLINICAL AND ULTRASOUND APPROACH IN INTERNAL MEDICINE

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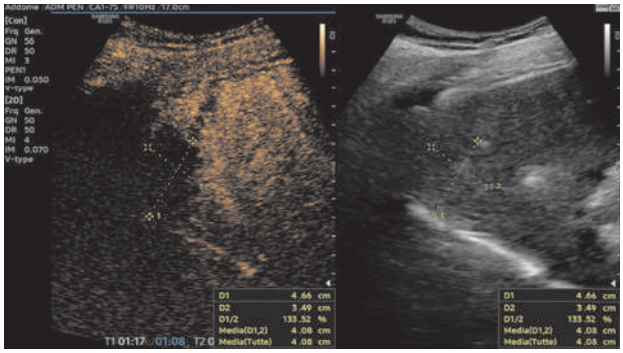
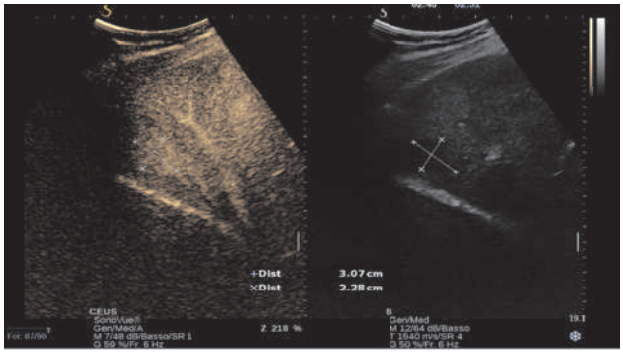
Evaluation of focal liver lesions in patients with multiple comorbidities is a clinical challenge, as MASLD (Metabolic dysfunction-associated steatotic liver disease) is now the main cause of chronic liver disease and hepatocellular carcinoma (HCC) in Western countries. Increasing evidence indicates that MASLD-related HCC may develop even in the absence of overt cirrhosis, especially in those with type 2 diabetes mellitus and features of the metabolic syndrome. This non-cirrhotic hepatocarcinogenesis pathway complicates early detection, as typical signs of advanced liver disease may be lacking and hepatic dysfunction can be subclinical. In oncologic patients, with active or recent cancer, metabolic liver diseases such as MASLD or MASH (metabolic dysfunction-associated steatohepatitis) often go unrecognized, as clinical attention is primarily directed toward cancer management. A systemic approach is essential to avoid delays and misdiagnosis.We describe the case of a 68-year-old male patient with longstanding type 2 diabetes mellitus, initially poorly controlled and recently optimized through insulin therapy. The patient also had a history of bladder cancer, previously treated with intravesical Bacillus Calmette-Guérin (BCG) instillations, and was in routine cancer follow-up. A contrast-enhanced total-body computed tomography (CT) scan revealed a solid hepatic lesion measuring approximately 28 mm in segment VII. The radiologist's initial interpretation was suggestive of a secondary metastatic deposit, given the cancer history. To investigate further, a fluorodeoxyglucose (FDG) positron emission tomography (PET) scan was done; however, the examination showed no areas of increased metabolic uptake, including within the liver. This discrepancy raised questions regarding the nature of the hepatic lesion and prompted referral to our internal medicine ultrasound unit for advanced diagnostic evaluation.At presentation, we conducted a comprehensive clinical assessment, focusing on metabolic risk factors. He reported a 15-year history of type 2 diabetes mellitus. Historical laboratory data confirmed prior poor glycemic control (HbA1c 7.7%), with recent improvement (HbA1c 6.2%) following the initiation of insulin. Anthropometric parameters included a BMI of 29.69 kg/m² and a waist circumference of 105 cm. A baseline abdominal ultrasound revealed a coarse echotexture of the liver with increased echogenicity consistent with severe steatosis and irregular liver margins. Suspecting fibrosis, we proceeded with two-dimensional shear-wave elastography (2D-SWE), showing elevated liver stiffness (11 kPa), indicative of advanced fibrosis (F3–F4).Focused sonographic evaluation of the previously identified lesion in segment VII revealed a hypoechoic, well-demarcated lesion. We then performed contrast-enhanced ultrasound (CEUS) to better characterize the vascular behavior of the lesion. The CEUS study showed rapid and intense arterial phase enhancement with persistent isovascularity in the portal and late venous phases, without definite washout (Figure 1). These findings matched a CEUS LI-RADS 4 lesion, suggesting probable HCC. The integration of imaging findings, the metabolic profile, the absence of FDG avidity on PET scan, and the context of previously undiagnosed metabolic liver disease, suggested HCC arising in the setting of MASLD with advanced fibrosis, rather than a secondary metastatic lesion.Given the high suspicion for primary liver malignancy, we proceeded with an ultrasound-guided percutaneous liver biopsy. Histological examination confirmed the presence of a poorly differentiated (WHO grade 3) hepatocellular carcinoma, arising on liver tissue with severe steatosis and significant fibrosis. The lack of FDG uptake at PET imaging aligned with the known low sensitivity of FDG-PET for well to moderately differentiated HCC.Considering the lesion's location, size, and the absence of extrahepatic disease or contraindications, the patient was deemed suitable for locoregional treatment. He underwent ultrasound-guided radiofrequency ablation (RFA) performed by trained internists at the Centralized Medical Area Day Hospital of the University Hospital of Sassari. The procedure was carried out using a 17G electrode needle, delivering radiofrequency energy for a total of 17 minutes. Post-procedural CEUS at 0 and 24 hours confirmed complete coagulative necrosis of the lesion with no evidence of residual viable tissue (Figure 2).The patient entered tailored oncology-hepatology follow-up. This case underscores the critical value of a systemic, integrative approach—hallmarks of Internal Medicine—in complex diagnostic settings. The ability to combine clinical reasoning with advanced imaging techniques and procedural skills enables internists to play a pivotal role in early diagnosis and management of oncologic and chronic liver diseases. As supported by the SIMI training program, the acquisition of advanced ultrasound skills is essential in modern Internal Medicine and contributes to improved patient outcomes.





SURVEY OF NONRESOLVING PNEUMONIA IN AN INTERNAL MEDICINE WARD

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Introduction: A proportion of community-acquired pneumonia (CAP) cases is refractory to the initial antibiotic treatment (1), because of a drug-resistant/opportunistic infection or misdiagnosis of a non-infective lung disease. Such cases are commonly referred to as "nonresolving pneumonia" (NRP), but a precise definition of what is considered a failure to improve is lacking. The issue is relevant for Internists, who treat patients with a high prevalence of factors associated with a delayed, though complete resolution of CAP, e.g. age, number of comorbidities and severity of pneumonia. The main objective of this study was to review the impact of NRP cases admitted to an Internal Medicine Ward (IMW) of a town hospital in Friuli Venezia Giulia, Italy.
Methods: Electronic discharge records from the IMW, Hospital of Tolmezzo, Italy, between January 1st and December 31st, 2024, were retrieved and all discharges with a diagnosis of CAP were extracted, defined according to the presence, on admission, of EITHER: A) fever, dyspnea and/or cough AND evidence of consolidation (s) on X-ray / ultrasound (US) or of a focal / diffuse interstitial pattern on US OR B) in the absence of an alternative explanation, CRP > 10 mg/l AND one of the above imaging findings. All patients undergoing chest CT at least 72 hours after the evaluation in the ED were identified among discharges for CAP: those receiving CT because of an insufficient response to the initial treatment, failure to improve or worsening according to clinical judgment were labeled as NRP. In these patients, a final diagnosis of usual lower respiratory tract infection (LRTI) was adjudicated on the basis of a CT pattern not suggestive of an alternative diagnosis, along with microbiology data consistent with CAP or negative; a final diagnosis of an alternative acute lung illness was adjudicated on the basis of the CT pattern, the results of further workup, and a multidisciplinary discussion, were appropriate. Age, sex, number of comorbidities according to the items listed in the Charlson comorbidity index (2) and duration of respiratory prodromes (assumed to be 0 days when not clear from the records) were recorded. Data are shown as median + interquartile range or proportions. Statistical analysis was performed with GraphPad Prysm software, using the Mann-Whitney test for comparisons ($p < 0.0125$ corrected for multiple tests) and including repeated discharges for the same patients as independent events.
Results: In 2024 a total of1481patients were discharged,170with CAP according to the above criteria (11.5%; median age82years, interquartile range75-88; % of patients age >65:91%; male n=85). Overall,7patiens were repeatedly admitted for CAP during2024, none of them more than2times. Fourteen patients underwent a chest CT after at least72hours from ED evaluation. Among the14cases studied with CT, the indication for imaging was NRP according to clinical judgement in7[4.1% of CAP discharges (fig.1)]; the remaining7underwent CT for suspect of malignancy (n=2), X-ray appearance atypical for CAP (n=2), suspect of opportunistic infection (n=2), or ancillary signs of pulmonary hypertension (n=1). CT findings in NRP patients vs those studied for other indications are depicted in fig.2. One patient undergoing chest CT for NRP received a final diagnosis of hypersensitivity pneumonitis, whereas the remaining6were finally diagnosed with a usual LRTI (5cases without isolates,1pneumococcal pneumonia). The median duration of inpatient stay was longer in cases investigated for NRP vs those not investigated (20vs11days, p =0.0062), whereas no difference was found between the former and patients studied with CT for other indications.

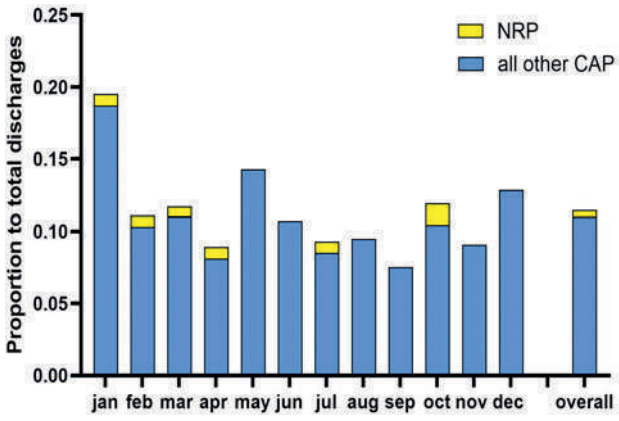

Fig. 1

Discussion: In our study, the proportion of NRP cases to the total of discharges for CAP (4.1%) is lower than the figure of 13% reported by Aliberti et al. (3). This could be due to our different definition of NRP, i.e. the clinical judgment of failure to improve, leading to chest CT rather than a set of objective parameters as a surrogate of clinical failure. Our definition is probably affected by the tendency to refrain from advanced imaging in the older population admitted nowadays to IMWs in Italy, in order to avoid exams whose impact on the overall prognosis of these patients is questionable. Only 1 case out of 7 NRPs received a final diagnosis different from a usual LRTI, a clue that the majority of NRP cases in the IMW represent in fact slowly, but completely resolving pneumonias rather than true NRPs.

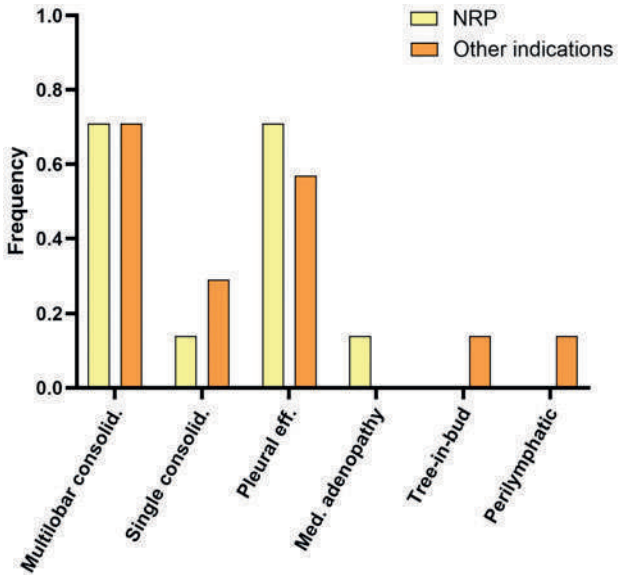

Fig. 2

Conclusions: The prevalence of NRP in an IMW in Italy is lower than expected and does not seem to correlate with a final diagnosis other than a usual LRTI with delayed resolution; systematic referral of NRP to chest CT, whose findings are non specific, is therefore questionable.
References: 1. Finch S et al., EMJ Respir. 2014; 2. Charlson ME et al., J Chron Dis 1987; 3. Aliberti S et al., Chest 2008.

AN OUT-OF-CONTROL IMMUNE SYSTEM: A CASE OF BEHÇET-LIKE SYNDROME INDUCED BY IMMUNOTHERAPY

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A 68-year-old woman presented to the Emergency Department of Fondazione Policlinico A. Gemelli on 28/08/2024 due to persistent watery diarrhea lasting approximately six months. She had previously been hospitalized multiple times at other centers for the same condition.
Her medical history was significant for cervical cancer diagnosed four years earlier, treated with chemotherapy, radiotherapy, and immunotherapy with Pembrolizumab, which she received until April 2024. She had a peripherally inserted central catheter (PICC) placed eight months earlier.
Since the start of immunotherapy, she had experienced severe diarrhea (up to 20 episodes/day), unresponsive to rifaximin and probiotics. She also reported purulent discharge from the left eye.
Home therapy included: atenolol 100 mg/day, aspirin 100 mg/day, esomeprazole 40 mg/day, ramipril/amlodipine 5+5 mg/day, fenofibrate/simvastatin 145+20 mg/day, and levothyroxine 100 µg/day. She had a known allergy to penicillins.
Lab tests in the ED showed neutrophilic leukocytosis (12,000/µL), acute kidney injury (creatinine 4.9 mg/dL), hyperamylasemia, and elevated CRP (71 mg/L). Abdominal X-ray revealed mild gaseous distension of the splenic flexure with sporadic air-fluid levels in the upper quadrants. Abdominal ultrasound was unremarkable. Molecular stool panel for bacterial, viral, and parasitic pathogens was negative.
Blood cultures grew Staphylococcus haemolyticus from both the PICC (positive in 4h) and peripheral blood (positive in 9h54'), indicating catheter-related bloodstream infection.
She was admitted to the Internal Medicine and Aging Unit, where she began

IV antibiotics with meropenem and linezolid. Due to marrow suppression and iatrogenic hypoglycemia, linezolid was replaced with vancomycin.
Orbital CT showed edematous infiltration of the left periorbital and upper eyelid tissues and air collection in the superior conjunctival fornix. Topical therapy was initiated per ophthalmology consult, but ineffective. A corneal ulcer was identified. Tarsorrhaphy and conjunctival graft were performed for corneal melting. Due to worsening, ocular evisceration was performed without immediate complications.
Persistent diarrhea and clinical suspicion of toxic megacolon prompted abdominal CT, which revealed pneumatosis intestinalis and vascular compromise of the transverse colon. Exploratory laparoscopy showed no significant findings.A 14-day course of cholestyramine and rifaximin (400 mg TID) had no effect. However, initiation of corticosteroid therapy with methylprednisolone 0.5 mg/kg led to rapid reduction in stool frequency and progressive normalization of consistency.
Given the chronic diarrhea during checkpoint inhibitor therapy, edematous thickening of the ascending colon, mucositis, and ocular symptoms consistent with uveitis complicated by bacterial superinfection, the clinical picture was interpreted as an immune-related adverse event (irAE) due to Pembrolizumab. The rapid response to corticosteroids supported this diagnosis.
The findings were consistent with a Pembrolizumab-induced Behçet-like syndrome.
Pembrolizumab is a humanized monoclonal antibody against PD-1 that enhances T-cell activity against tumor cells but can also cause off-target immune responses and autoimmune-like inflammation. Such immune-mediated effects can mimic classic autoimmune diseases.
Approximately 10% of oncology patients on checkpoint inhibitors develop musculoskeletal or rheumatologic irAEs. Management depends on severity and includes temporary discontinuation of therapy, high-dose corticosteroids, IV immunoglobulins, and in severe cases, IL-6 receptor or TNF-α inhibitors.

References

1.Alsaab, H.O.; Sau, S.; Alzhrani, R.; Tatiparti, K.; Bhise, K.; Kashaw, S.K.; Iyer, A.K. PD-1and PD-L1Checkpoint Signaling Inhibition for Cancer Immunotherapy: Mechanism, Combinations, and Clinical Outcome. Front Pharmacol2017,8,561, doi:10.3389/fphar.2017.00561.
2. Ni, J.; Zhang, L. [Progress of immuno therapy-related adverse events]. Zhonghua Nei Ke Za Zhi2021,60,84–89, doi:10.3760/cma.j.cn112138-20200308-00204.
3. Shalata, W.; Yakobson, A.; Cohen, A.Y.; Goldstein, I.; Saleh, O.A.; Dudnik, Y.; Rouvinov, K. Unexpected Adverse Events of Immune Checkpoint Inhibitors. Life (Basel)2023,13,1657, doi:10.3390/life13081657.
4.Haanen, J.; Obeid, M.; Spain, L.; Carbonnel, F.; Wang, Y.; Robert, C.; Lyon, A.R.; Wick, W.; Kostine, M.; Peters, S.; et al. Management of Toxicities from Immunotherapy: ESMO Clinical Practice Guideline for Diagnosis, Treatment and Follow-Up. Ann Oncol2022,33,1217–1238, doi:10.1016/j.annonc.2 022.10.001

THE UNUSUAL PRESENTATION OF A SILENT TIETZE'S SYNDROME

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La sindrome di Tietze è una condizione infiammatoria rara e benigna che colpisce le articolazioni costo-sternali, con una presentazione clinica tipica caratterizzata da dolore e tumefazione localizzata al torace, coinvolgente una singola articolazione, tipicamente la seconda o la terza costola. Essa prende il nome dal chirurgo tedesco che nel 1921 per la prima volta ne descrissele caratteristiche. Colpisce prevalentemente giovani adulti e l'eziologia rimane tutt'oggi sconosciuta. Tra i fattori scatenanti principali vi sono lo stress meccanico e gli esiti post-traumatici della parete toracica.Nonostante la presentazione clinica sia generalmente riconoscibile, in presenza di quadri clinici o radiologici atipici, la diagnosi differenziale con patologie neoplastiche può risultare complessa. In tali casi, la biopsia può rappresentare uno strumento indispensabile per una diagnosi definitiva.
Una donna di 82 anni giungeva alla nostra osservazione per febbricola persistente e per riscontro accidentale di una tumefazione duro-elastica, non dolente e a margini mal deIiniti, comparsa da alcune settimane in sede parasternale sinistra, a livello della IV articolazione costostrenale. In anamnesi familiarità per carcinoma della mammella, ipertensione arteriosa e litiasi renale. Agli esami ematochimici riscontro di anemia microcitica e aumento degli indici di flogosi. La TC addome con mezzo di contrasto, descriveva la lesione obiettivata al torace come tumefazione a densità disomogenea dei tessuti molli in assenza di erosione ossea. La stessa veniva ulteriormente valutata con esame ecografico e studio RM.Il quadro radiologico deponeva per un'imbibizione del muscolo gran pettorale e del tessuto adiposo adiacente come da infiammazione cronica, compatibile con la sindrome di Teitze, pur non potendo escludere la natura neoplastica della lesione. Veniva prelevato campione bioptico, che escludeva la presenza di atipiecellulari e descriveva l'aspetto regressivo delle miocellule con infiltrato linfocitario reattivo. S i confermava la diagnosi di Sindrome di Teitze.
La sindrome di Tietze, sebbene benigna, può simulare lesioni toraciche di natura espansiva. Le principali diagnosi da considerare includono il condrosarcoma, i linfomi mediastinici, le metastasi costali e la costocondrite. In presenza di manifestazioni atipiche, e in particolare, come nel nostro caso, l'assenza di sintomatologia dolorosa, la biopsia percutanea rappresenta lo strumento utile perconfermare la diagnosi, evidenziando come condizioni rare e apparentemente semplici possano richiedere un approfondimento diagnostico strutturato.

DEVELOPMENT AND INTERNAL VALIDATION OF A NOVEL PROGNOSTIC SCORE FOR 30-DAY MORTALITY IN PATIENTS WITH ACUTE DECOMPENSATED HEART FAILURE IN INTERNAL MEDICINE WARDS

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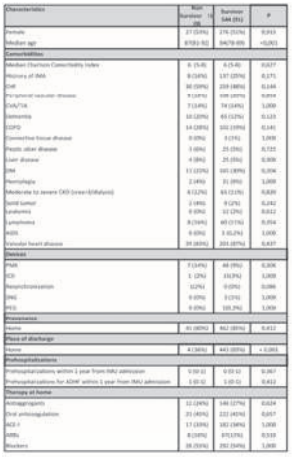
Background: Acute decompensated heart failure (ADHF) is a leading cause of hospitalization and adverse outcomes in older patients, particularly within Internal Medicine settings. Existing prognostic models often lack applicability in this context due to differences in patient demographics and clinical complexity.Objective: This study aimed to develop and internally validate a new prognostic score tailored to predict 30-day mortality in patients admitted with ADHF to Internal Medicine wards.Methods: A retrospective, multicentric cohort study was conducted including 595 patients from two Italian hospitals (Trieste and Venice Mestre) between 2018–2019 and 2022–2023 (Table 1). Variables significantly associated with 30-day mortality were identified through univariate and multivariate logistic regression analyses (Table 2 Table 3).Results: Four independent predictors were identified: hematocrit, blood urea nitrogen, serum albumin, and presence of an infectious trigger. The derived "Trieste Score" showed superior prognostic performance compared to the ADHERE model, with an AUROC of 0.79 versus 0.63. The model also exhibited high sensitivity (86%) and negative predictive value (98%) (Table 4 and Figure 1).Conclusions: The Trieste Score provides a simple and effective tool for early risk stratification of ADHF patients in Internal Medicine. Its performance suggests a strong potential for clinical utility, though external prospective validation is necessary prior to implementation.

Characteristics	N (%)
Female	303 (51)
Median age	84 (78-89)
Comorbidities	
Median Charlson Comorbidity Index	6 (5-8)
History of IMA	145 (24)
CHF	289 (49)
Peripheral vascular disease	117 (20)
CVA/TIA	91 (14)
Dementia	75 (13)
COPD	116 (20)
Connective tissue disease	3 (1)
Peptic ulcer disease	28 (5)
Liver disease	29 (5)
DM	176 (30)
Hemiplegia	33 (6)
Moderate to severe CKD (creat>3/dialysis)	67 (11)
Solid tumor	68 (11)
Leukemia	11 (2)
Lymphoma	12 (2)
AIDS	1 (1)
Valvular heart disease	232 (39)
Devices	
PMK	55 (9)
ICD	16 (3)
Resynchronization	1 (1)
DNS	3 (1)
PEG	1 (1)
Pneumonia	1 (1)
Home	503 (85)
Place of discharge	
Home	447 (75)
Prehospitalisations	
Prehospitalizations at 1 year from IMU admission	301 (51)
Prehospitalizations for ADHF at 1 year from IMU admission	162 (27)
Therapy at home	
Antiaggregants	158 (27)
Oral anticoagulation	245 (41)
ACE-i	199 (33)
ARBs	75 (13)
Blockers	320 (54)

Disease-modifying therapy at IMU admission	
DI	90 (17)
DI in patients with Reduced ejection fraction	74 (12)
Vital Signs at IMU Admission	
Median SBP	130 (120-156)
Median DBP	76 (66-87)
Median MAP	97 (85-108)
Median HR	85 (72-100)
Median sO2	95 (92-97)
Median GCS	15 (13-15)
Median TC	36 (36-37)
Ejection fraction known at IMU admission	**290 (49)**
Preserved	156 (26)
Mildly reduced	41 (7)
Reduced	93 (%)
Ejection fraction known at IMU discharge	**325 (55)**
Preserved	207 (35)
Mildly reduced	57 (10)
Reduced	91 (15)
Complete echocardiography during IMU stay	121 (20)
Laboratory at IMU admission	
Median white blood cell	8,8 (7-11,4)
Median C-reactive protein	5,5 (1,3-25,9)
Median Hemoglobin	11,9 (10,4-13,5)
Median HtC	37,2 (32,5-42)
Median albumin	3,4 (3,1-3,7)
Median sodium	138 (135-140)
Median potassium	4,2 (3,8-4,5)
Median creatinine	1,1 (0,8-2,1)
Median azotemia	58 (40-79)
Triggers	
Infectious disease	324 (55)
Non-infectious disease	271 (46)
Treatments during hospital stay	
NIV	26 (4)
Dyalysis/ultrafiltration	1 (1)
Inotropes/vasoconstrictors	13 (2)
Invasive cardiologist treatment	16 (3)
Mortality from IMU admission	
30-days	51 (9)
1-year	166 (28)

Diuretics	
Furosemide	241 (41)
Furosemide+ MR Antagonist	139 (23)
MR Antagonist	8 (1)
Thiazides	9 (2)
Antiarrhytmics	92 (16)
Statin	170 (29)
Digoxin	50 (8)
SGLT2 inhibitors	18 (3)
ARNI	8 (1)

Table 1. Clinical characteristics at baseline



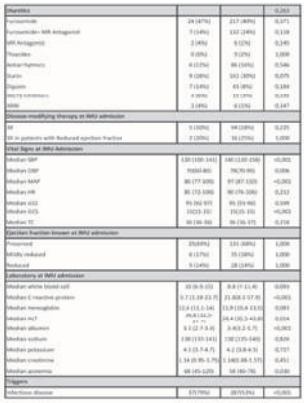


Table 2. Univariate 30-daymortality.

MULTIVARIABLE ANALYSIS					
30-day mortality					
Predictor	B	SE	Wald	P	Odds ratio (95% CI)
Hb*Ht	0,003	0,001	6,736	0,009	1,003 (1,001-1,005)
BUN	0,012	0,005	6,211	0,013	1,012 (1,003-1,021)
Albumin	-1,300	0,426	9,200	0,002	0,274 (0,119-0,632)
Infectious trigger	1,863	0,563	10,652	0,001	6,256 (2,084-18,958)

Table 3. TriesteScore for predicting 30-day mortality.

	GROUP 1 (Trieste+Venice)						
SCORE	AUROC	Sn	Sp	NPV	PPV	NLR	PLR
ADHERE	0,680	0,640	0,660	95,200	14,750	0,550	1,880
TRIESTE	0,790	0,860	0,600	98,200	14,290	0,240	2,160

Table 4. Comparison of 30-day mortalityprediction using the Trieste and ADHERE models

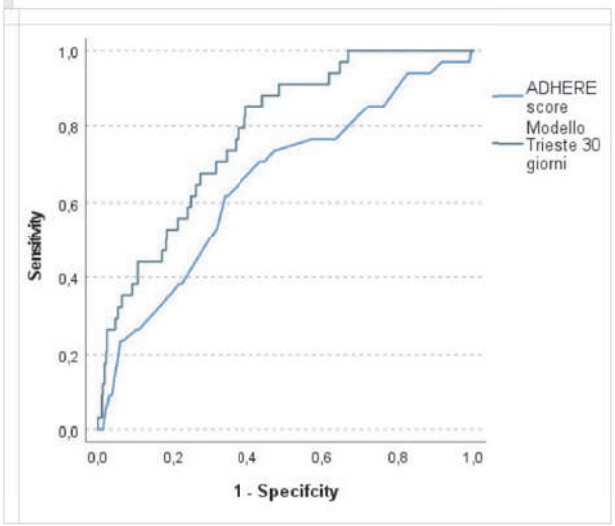


Figure 1. AUROC Triestescore vs ADHERE score

RECURRENT SEROSITIS AND FEVER IN A YOUNG ADULT: A CASE OF ADULT-ONSET STILL'S DISEASE

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Introduction: Autoinflammatory diseases are characterized by recurrent episodes of systemic inflammation in the absence of high-titer autoantibodies or antigen-specific T cells. They are primarily caused by dysregulation of the innate immune system, often due to genetic mutations affecting inflammatory pathways. Among these, Adult-onset Still's disease (AOSD) stands out as a rare but significant systemic autoinflammatory condition, typically marked by high spiking fevers, evanescent salmon-colored rash, arthralgia/arthritis and elevated inflammatory markers. Although its etiology remains unclear, both genetic and environmental factors may contribute to its pathogenesis. Diagnosis is clinical and made by excluding infectious, neoplastic and autoimmune causes, with the Yamaguchi criteria being the most widely used. Early recognition is crucial, as targeted therapies can effectively control disease activity and prevent complications.
Case presentation: We report the case of a 34-year-old man with recurrent fever and pleuropericarditis. He was recently admitted to the Cardiology Unit for fever, dyspnea and chest pain due to pleuropericarditis. Symptoms and pleuropericardial effusions resolved following antibiotic and anti-inflammatory treatment (ibuprofen, colchicine and corticosteroids). He was discharged in January 2025 with a corticosteroid taper. At follow-up, ultrasound showed no pleuropericardial effusion, and inflammatory markers had normalized, despite liver enzymes (ALT 152 U/L) being elevated. Due to corticosteroid-induced ocular hypertension, treatment was fully discontinued. Shortly after, the patient experienced a new onset of fever, peaking at 39 °C for about 14 days, exertional dyspnea, mild retrosternal discomfort, and sore throat. He was admitted to our Internal Medicine Unit in February 2025. On admission, electrocardiography showed diffuse, concave ST-segment elevation, suggestive of pericarditis. Ultrasound confirmed pericardium thickening with mild pericardial effusion and bilateral pleural effusion, more pronounced on the left.The following therapy was started: Ibuprofen 600 mg BID, Colchicine 0.5 mg BID, Pantoprazole 40 mg IV daily. Corticosteroids were withheld pending further diagnostic workup for possible autoimmune or autoinflammatory disease.Blood tests showed elevated inflammatory markers (WBC 14,600/μL, CRP 44.7 mg/dL, Ferritin 2149 ng/mL). ESR was normal (27 mm) as well as Procalcitonin.Infectious workup – including serologies for C. pneumoniae, M. pneumoniae, TORCH panel, HIV, Quantiferon TB, and blood/urine cultures – was negative.Radiological investigations showed no signs of neoplasia.Autoimmune screening (ANA, ENA, RF, anti-CCP, IgG4, fecal calprotectin, HLA-B27) was also negative.Due to strong clinical suspicion of an autoinflammatory condition, additional tests were performed: Serum Amyloid A was markedly elevated (3050 mg/L, normal <0.6), IL-6 was elevated (189.9 pg/mL, normal <6.4), IL-1 was within normal range (8.5 pg/mL), although measured 5 days post-collection, raising concerns of sample degradation.Autoinflammatory diseases may result from polygenic or monogenic mutations. Among the latter, Familial Mediterranean Fever (FMF) is well known for recurrent fever and polyserositis. Israeli criteria can guide diagnosis, but genetic testing remains the gold standard. Therefore, a blood sample was sent to external laboratories for MEFV gene mutation analysis, which yielded a negative result.Based on these findings, high-dose corticosteroids were started (Methylprednisolone 40 mg IV BID) with increased colchicine dosage. The patient showed a good clinical response, with resolution of fever and pleuropericardial effusions. Steroids were tapered to a maintenance dose of Prednisone 25 mg 1+1/2 tablets daily.
Discussion and conclusion: Based on exclusion of infectious, autoimmune, and neoplastic causes, a diagnosis of AOSD was considered. Although FMF was initially suspected due to the recurrent fever and serositis, genetic testing for MEFV mutations returned negative. There is currently no definitive diagnostic test for AOSD, but various diagnostic criteria are available. Yamaguchi criteria are the most widely used and sensitive. In this case, five criteria were met, including two major (fever ≥39 °C lasting ≥1 week; leukocytosis > 10,000/μL with > 80% neutrophils) and three minor (sore throat, elevated liver enzymes, negative ANA and RF).The recurrent, steroid-responsive pleuropericarditis, in the absence of other identifiable causes, further supported the diagnosis. A referral to the Rheumatology Unit was arranged. On March 20, 2025, the diagnosis of AOSD was confirmed, and treatment with Anakinra was started, with scheduled follow-up.This case highlights the importance of a thorough differential diagnosis in patients presenting with recurrent fever and serositis. Even in the absence of full clinical picture (e.g., rash, arthritis, lymphadenopathy), AOSD should be considered, as early treatment can significantly improve outcomes and quality of life.

PROTON PUMP INHIBITORS DIRECTLY BLOCK HERG-POTASSIUM CHANNEL AND INDEPENDENTLY INCREASE THE RISK OF QTC PROLONGATION IN A LARGE COHORT OF US VETERANS

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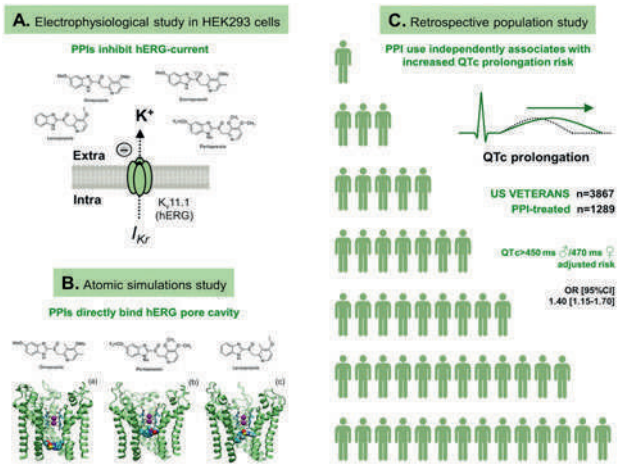
Background: Worldwide, there are millions of chronic proton pump inhibitor (PPI) users, often without a compelling indication. Evidence indicates that PPI treatment can increase mortality, in part, due to a higher risk of heart rate–corrected QT interval-related malignant arrhythmias. Drug-induced hypomagnesemia is currently believed to be the only underlying mechanism, and, therefore, serum magnesium monitoring is recommended to minimize arrhythmic risk. However, recent data suggest that PPIs might also directly interfere with cardiac electrophysiology. To test this hypothesis, a translational study was performed using a combination of electrophysiology, molecular dynamics simulations, and population data.
Methods: First, the effect of different PPIs on the human ether-a-go-go-related gene potassium channel (hERG) current was evaluated in human embryonic kidney 293 cells expressing hERG. Then, free-energy calculations were performed to investigate the binding of these drugs to hERG. Finally, the impact of PPIs on the risk of heart rate–corrected QT interval prolongation was assessed in a retrospective observational cohort of 3867 US veterans, including 1289 PPI-treated subjects.
Results: Clinically relevant concentrations of different PPIs induced a significant inhibition of the hERG current in vitro, pantoprazole and lansoprazole being the most potent compounds. Atomic simulations demonstrated that such a blocking class effect is likely due to direct PPIs binding to hERG channel pore cavity. Accordingly, in a US veterans cohort, PPI treatment was independently associated with an ≈20% to 40% increased risk of heart rate–corrected QT interval prolongation, also regardless of hypomagnesemia. Moreover, a synergistic interaction between PPIs and most of the traditional QT-prolonging risk factors was demonstrated.
Conclusions: Altogether, this study provides, for the first time, strong evidence that PPIs can per se promote heart rate–corrected QT interval prolongation, by directly inhibiting hERG function. A careful evaluation of the benefit/risk ratio is recommended whenever PPIs are administered in subjects with other QT-prolonging risk factors, even in the absence of hypomagnesemia.
References:
1. Malfertheiner P, Kandulski A, Venerito M. Proton-pump inhibitors: understanding the complications and risks. Nat Rev Gastroenterol Hepatol.2017;14:697–710. doi:10.1038/nrgastro.2017.117
2. Manolis AA, Manolis TA, Melita H, Katsiki N, Manolis AS. Proton pump inhibitors and cardiovascular adverse effects: real or surreal worries? Eur J Intern Med.2020;72:15–26. doi:10.1016/j.ejim.2019.11.017
3. Xie Y, Bowe B, Li T, Xian H, Yan Y, Al-Aly Z. Risk of death among users of Proton Pump Inhibitors: a longitudinal observational cohort study of United States veterans. BMJ Open.2017;7:e015735. doi:10.1136/bmjopen-2016-015735
4. Xie Y, Bowe B, Yan Y, Xian H, Li T, Al-Aly Z. Estimates of all cause mortality and cause specific mortality associated with proton pump inhibitors among US veterans: cohort study. BMJ.2019;365:l1580. doi:10.1136/bmj.l1580



PATIENTS WITH SUDDEN SENSORINEURAL HEARING LOSS HAVE A HIGH PREVALENCE OF RIGHT-TO-LEFT SHUNT AND HIGHER PREVALENCE OF PATENT FORAMEN OVALE WHEN COMPARED TO GENERAL HEALTHY POPULATION

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Background and Aims: Sudden sensorineural hearing loss (SSHL) is a 30 dB hearing loss over at least 3 contiguous frequencies occurring within 3 days. It is mostly classified as idiopathic, though inflammatory and vascular compromise of the inner ear have been reported. A possible cause of SSHL is represented by paradoxical micro-embolization due to right-to-left shunt (RLS), most frequently in case of patent foramen ovale (PFO). It has been postulated that patients with SSHL have a higher prevalence of PFO compared to the healthy adult population (i.e., 15-25%).
We investigated the prevalence of RLS, PFO and co-existing major cardiovascular and thrombophilic risk factors in patients suffering from SSHL.
Methods: We conducted a retrospective study on a cohort of patients with a diagnosis of idiopathic SSHL following ear-nose-throat (ENT) examination. Clinical data and blood samples were collected to investigate cardiovascular and thrombophilic risk factors, while RLS/PFO was detected either through contrast-enhanced transcranial Doppler ultrasound (C-TCD), contrast-enhanced transthoracic echocardiography (C-TTE) or transesophageal echocardiography (TEE). Data from brain MRI were also included whenever available.
Results: We included 237 patients, of whom 147/237 (62%) were screened for RLS; in particular, C-TCD was performed in 31/147 (21%), C-TTE in 66/147 (44.9%), and TEE in 50/147 (34%). C-TCD was positive in 14/31 patients (45%), C-TTE in 29/66 (43.9%), TEE in 23/50 (46%), allowing us to detect RLS in 66/147 patients (44.8%). Thus, the prevalence of PFO in our cohort of patients with SSHL was 52/116 (44.8%), which is significantly higher than what is known in the general healthy population ($p < 0.001$).
We investigated additional potential risk factors, according to the presence of RLS (as seen in table). No difference was seen in terms of age and sex. Prevalence of thrombophilic risk factors investigated were similar, except for a higher prevalence of heterozygosity for FV Leiden in the group with RLS [6/43 (13.9%)] compared to the counterpart [1/45 (2.2%)]. Cardiovascular risk factors were also equally distributed among the two groups, but with a lower prevalence of systemic arterial hypertension in patients with RLS [9/66 (13.6%)] compared to those without RLS [20/78 (25.6%)].
Furthermore, our analysis shown a slightly higher prevalence of ischemic signs in patient with RLS than in those without RLS.
Conclusions: We report a prevalence of RLS exceeding 40% in patients with SSHL. We also demonstrate that PFO is more represented in this patient subset compared to the general population, in which it has been reported in up to 25% subjects. Thus, RLS assessment should be considered as part of the evaluation in patients with SSHL.
This association may suggest that either paradoxical embolism, such as a venous embolism through of PFO, or "in situ" clot could be the cause of SSHL in a proportion of patients previously labelled as "idiopathic".
Moreover, we report that the prevalence of heterozygosity for FV Leiden is slightly higher in patients having RLS, while such trend is not observed for major cardiovascular risk factors. Our hypothesis warrants confirmation in larger cohorts because of the potential to early identify and properly treat patients at risk for further and more severe ischemic complications.

Table. Thrombophilic and cardiovascular risk factor according to presence pf RLS in SSHL population

	Investigated	Positive	%
PFO	116	52	45%
RLS	147	66	45%

SEX-DIFFERENCE IN THE ASSOCIATION BETWEEN TRIGLYCERIDE-GLUCOSE (TYG) INDEX AND DEMENTIA

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Introduzione: la Malattia di Alzheimer (MA) rappresenta il 60-70% dei casi di demenza, seguita dalla demenza vascolare (VD), che ne costituisce circa il 20-30%. Le femmine mostrano una maggiore incidenza e mortalità associate alla

demenza rispetto ai maschi. Tale differenza è in parte correlata alla maggiore aspettativa di vita; tuttavia, questa non spiega da sola le differenze sesso-specifiche osservate. Un crescente interesse si è focalizzato sul ruolo dell'insulino-resistenza (IR) come fattore di rischio per demenza, essendo questa implicata nella patogenesi della MA attraverso l'accumulo di β amiloide, iperfosforilazione della proteina tau e alterazioni neurovascolari. Inoltre, essa può influire sulla patologia cerebrovascolare tipica della VD. L'indice Trigliceridi-Glucosio (TyG Index) è correntemente utilizzato come biomarcatore semplice ed economico di IR in ambito clinico. Il nostro studio si propone di valutare la possibile associazione tra TyG index e disturbi neurocognitivi e se questa sia influenzata dal sesso.
Pazienti e Metodi: sono stati inclusi nello studio 1.350 soggetti di età ≥65 anni (858 femmine e 492 maschi) valutati presso il Centro Disturbi Cognitivi e Demenze della UOC di Medicina Interna Universitaria e Geriatria dell'Azienda Ospedaliero-Universitaria S. Anna di Ferrara. I soggetti sono stati classificati in cinque gruppi in base allo stato cognitivo: MA (n=335), demenza mista (MA e VD, n=301), VD (n=99), Mild Cognitive Impairment - MCI (n=442) e funzioni cognitive integre (Controlli, n=173). Sono stati esclusi soggetti con patologie acute, neoplasie, gravi comorbidità, uso di farmaci come steroidi o antibiotici ed affetti da disturbi psichiatrici. I pazienti sono stati sottoposti a prelievo ematico. Il TyG index è stato calcolato mediante la formula: TyG = Ln [trigliceridi (mg/dl) × glucosio (mg/dl)/2]. I pazienti sono stati sottoposti a valutazione neuropsicologica e diagnostiche strumentali (RM encefalo e/o PET cerebrale con 18F-FDG) per formulare la diagnosi neurocognitiva.
Risultati: il campione era rappresentato prevalentemente da femmine (63.5%); il 16.4% era diabetico e la comorbilità più frequente era l'ipertensione (66.4%). Il 32.7% risultava affetto da MCI, il 24.8% MA, il 22.3% demenza mista e il 7.3% VD. Il TyG index è risultato più alto nei soggetti con MCI, VD e demenza mista rispetto al gruppo con MA. Analizzando i sottogruppi in base al sesso, solo nelle femmine il TyG index era significativamente più elevato nei soggetti affetti da MCI, VD e demenza mista rispetto ai Controlli ed al gruppo MA. All' analisi multivariata, solo nelle femmine un TyG index più elevato era associato ad una maggiore probabilità di ricevere diagnosi di MCI (O.R.: 1.91, 95% C.I.: 1.08–3.34), VD (O.R.: 2.23; 95% C.I.: 1.10–4.51) e demenza mista (O.R.: 1.92, 95% C.I.: 1.10–3.33), ma non MA (O.R.: 1.07, 95% C.I.: 0.63–1.85) rispetto ai Controlli.
Discussion: e: lo studio ha evidenziato come livelli elevati di TyG index siano correlati ad alcune forme di demenza, in particolare quella vascolare e che tale associazione sia significativa nel sesso femminile. La letteratura supporta il ruolo dell'IR nella patogenesi delle malattie cerebrovascolari e la sua correlazione con eventi ischemici cerebrali, infiammazione sistemica, disfunzione endoteliale ed ipoperfusione cerebrale, fattori che contribuiscono al danno neuronale. La maggiore incidenza in soggetti di sesso femminile potrebbe derivare da una diminuzione degli estrogeni durante la menopausa, influenzando negativamente il metabolismo glucidico e la sensibilità insulinica. Un limite del presente studio può essere dato dal fatto che non sono stati valutati fattori come la dieta, l'attività fisica e il genotipo APOE che potrebbero aver influenzato i risultati.
Conclusion: i: questo è uno dei primi studi che dimostra la correlazione tra sesso e TyG index nel determinare il rischio di insorgenza di diverse forme di demenza. I risultati suggeriscono che l'IR, misurata attraverso il TyG index, possa rappresentare un importante fattore di rischio per lo sviluppo di declino cognitivo e demenza vascolare nei soggetti di sesso femminile. Saranno necessari ulteriori studi per consolidare l'utilizzo del TyG index nella pratica clinica, per confermare queste associazioni e per valutare se il trattamento dell'IR possa effettivamente ridurre il rischio di demenza nelle femmine.

FROM TRIALS TO CLINICAL PRACTICE: A CASE OF SAFE AND EFFECTIVE USE OF ACETAZOLAMIDE AS ADD-ON DIURETIC IN AN OLDEST-OLD PATIENT

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Acute decompensated heart failure (ADHF) represents one of the most common causes of admission in internal medicine ward, especially in elder patients. Loop diuretics represent the cornerstone of management of ADHF, reducing the symptoms of congestion. The 2022 ADVOR trial enhanced the role of acetazolamide as an additional diuretic in ADHF; despite an relatively old age of those study population (78.2±8.9 years-old), data about the safety of acetazolamide in oldest-old patients lack.
We report the case of a 95-years-old female admitted to the internal medicine unit due to the development of ADHF and respiratory failure. Her history included type 2 diabetes mellitus, arterial hypertension complicated by stage IV chronic kidney disease, a previous transient ischemic attack, and chronic anaemia due to iron-deficiency and renal disease.
The patient was initially treated with high dose furosemide (250 mg over 24 hours) associated with potassium canreonate 100 mg, leading to the improvement of respiratory dynamic, up to the necessity of only minimal oxygen support; both inferior vena cava ultrasound (IVC-US) and chest X-ray demonstrated improvement of congestion on day-2 after admission, allowing to decrease the dose of loop diuretic.
On day-4 after admission the patient's parameters deteriorated with the development of respiratory acidosis (pH 7.26, pCO2 65 mmHg, pO2 60 mmHg, HCO3- 25 mmol/L), thus, after the failure of a trial with c-PAP due to failure of the patient to adapt, respiratory support with high-flow nasal cannula (HFNC) was started. Laboratory test showed a remarkable increase of BNP up to 1900 ng/mL, while an increased congestion was observed both by chest X-ray and by IVC-US (VExUS score 3). High dose furosemide where promptly re-prescribed, however a suboptimal response was observed after 24 hours, with persistent need of HFNC support and VExUS score unchanged.
On day-5 additional diuretic treatment with acetazolamide (500 mg daily) was started. A progressive improvement of respiratory dynamic was observed, allowing oxygen support discontinuation of day-7, and a consensual decrease of furosemide dose and acetazolamide discontinuation. VExUS score decreased to 2.
On day-9 the patient was discharged with a daily dose of 100 mg of oral furosemide; chest X-ray showed only mild congestion, and consistently IVC-US showed VExUS score of 1.
Our case supports the safety and effectiveness of acetazolamide as add-on diuretic for the management of congestion in ADHF in oldest old patients. Future research will have to further investigate the opportunity of use of acetazolamide as an additional treatment for congestive symptoms in ADHF in this population, often excluded from clinical trials.

THE ASSOCIATION BETWEEN INTRAVENTRICULAR HAEMODYNAMIC FORCES, TRADITIONAL ECHOCARDIOGRAPHIC PARAMETERS AND VENTRICULAR-ARTERIAL COUPLING IN PATIENTS AT HIGH RISK FOR HEART FAILURE

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Aim: Softwares that enable assessment of hemodynamic forces (HDF) of the left ventricle on pre-acquired echocardiographic images offer a new opportunity for advanced cardiac imaging, identifying early markers associated with the progression of cardiac damage toward heart failure (HF) in patients at high risk for the disease. HDF analysis can quantify intraventricular pressure gradients, recovering information on early wall dyssynchrony and left ventricular energetic expenditure. Our objective was to assess the relationship between the apex-to-base intraventricular forces (ABF, a measure of left ventricular contractile efficiency obtained from HDF analysis) and other measures of left ventricular systolic function and ventricular-arterial coupling in patients at high risk of developing HF.
Methods: A cohort of 57 patients at high risk for HF (stages A and B according to the AHA/ACC HF classification) underwent standard trans-thoracic echocardiography at rest. The ABF was recovered from the intraventricular haemodynamic forces analysis performed using the QStrain Echo v.4.4.30 (Medis Medical Imaging, Leiden, NL) software. The left ventricular wasted pressure effort ratio (LV-WPE), a measure of ventricular-arterial uncoupling previously validated was estimated from central blood pressure values obtained with ap-

planation tonometry, central pressure wave decomposition and doppler flow sampled at the left ventricular outflow tract level.
Results: The patient's average age was 67.3±1.9 years, 63% males, while the BMI was 27.13±0.52, and the systolic and diastolic blood pressure values were 146±21/86±11 mmHg. The LV-WPE was 0.78±0.49, the ABF 9.5±0.65%, the left ventricular ejection fraction (LVEF) 58.6±1.7%, the global longitudinal strain (GLS) 14.3±4.4%. ABF was associated with both LVEF ($R = 0.67$, $p < 0.001$) and GLS ($R = 0.58$, $p = 0.003$). Furthermore, a higher ABF was correlated with a lower LV-WPE ($R = -0.28$, $p = 0.04$) and age ($R = -0.43$, $p < 0.001$).
Conclusions: Results suggest that the analysis of intraventricular forces, mainly the ABF, might provide important information on the left ventricular systolic function and inform the left ventricular-arterial coupling. While requiring further validation, the current data support using advanced echocardiographic analyses for the early identification of patients at higher risk of HF.

IRINOTECAN-INDUCED INTERSTITIAL LUNG DISEASE IN A PATIENT WITH METASTATIC COLORECTAL CANCER: A CASE REPORT

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Pulmonary toxicity associated with chemotherapeutic agents such as irinotecan is an uncommon but potentially life-threatening complication, particularly in patients with advanced-stage malignancies and prior exposure to multiple lines of chemotherapy. Early identification and timely corticosteroid initiation are essential to prevent severe outcomes.
We describe the case of a 67-year-old woman with stage IV metastatic colorectal cancer who presented with progressive dyspnea over the past month, intermittent fever, and diarrhea, attributed to oral magnesium supplementation for chemotherapy-induced hypomagnesemia. She was undergoing treatment with panitumumab and FOLFIRI (5-fluorouracil and irinotecan), with the most recent cycle administered two weeks prior to admission.
On admission, the patient exhibited mild hypoxemia (SpO_2 89% on room air), bilateral basal crackles on auscultation, and inflammatory infiltrates on chest radiography. Laboratory investigations revealed mild leukopenia, elevated C-reactive protein levels, and anemia. Given the patient's immunocompromised status due to chemotherapy, an empiric antibiotic regimen with piperacillin/tazobactam was initiated, along with low-flow oxygen supplementation and supportive care.
Due to persistent fever and worsening respiratory function despite escalation to vancomycin and azithromycin, a contrast-enhanced chest and abdominal computed tomography (CT) scan was performed. It revealed bilateral pulmonary consolidations, with surrounding ground-glass opacities and interstitial thickening—findings suggestive of interstitial pneumonitis ().
Repeated blood cultures, as well as bronchoalveolar lavage (BAL) analysis, were negative for bacterial, mycobacterial, fungal, and viral pathogens. Candida dubliniensis was isolated at low titer and considered colonization. Autoimmune panels including ANA, ENA, ANCA, anti-MPO, PR3, Jo-1, and Scl-70 were negative. Interferon-gamma release assay (IGRA) was positive but not consistent with active tuberculosis.
Given the absence of clinical and radiologic response to antimicrobial therapy, the exclusion of infectious and autoimmune etiologies, and the temporal relationship with recent irinotecan exposure, a presumptive diagnosis of irinotecan-induced interstitial pneumonitis was made. High-dose corticosteroid therapy with methylprednisolone (1 mg/kg/day) was initiated and antibiotics were withdrawn.
Within 72 hours, the patient showed marked clinical improvement, with defervescence, reduced oxygen requirement, and improved respiratory parameters. Follow-up high-resolution CT imaging demonstrated substantial regression of pulmonary consolidations and near-complete resolution of ground-glass opacities—supporting the diagnosis of chemotherapy-induced pneumonitis ().
This case highlights the diagnostic challenges of differentiating drug-induced interstitial lung disease from infectious pneumonia in immunocompromised oncology patients. An exhaustive exclusion of infectious and autoimmune etiologies, in conjunction with the patient's temporal exposure to irinotecan and rapid response to corticosteroid therapy, confirmed the diagnosis of irinotecan-associated interstitial pneumonitis. Early identification and initiation of immunosuppressive therapy are critical to preventing progression to respiratory failure and ensuring favorable clinical outcomes.

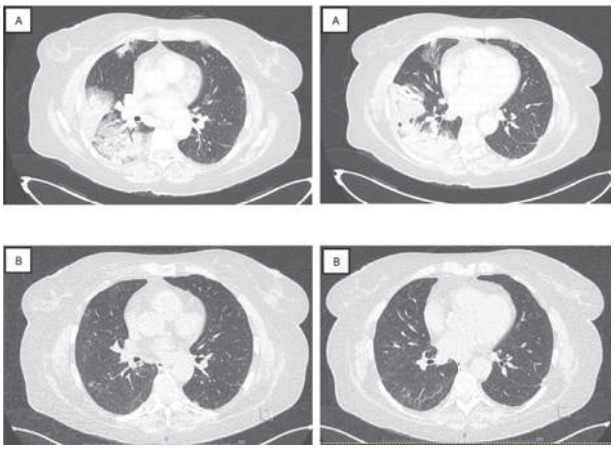

Figure1. Chest computed tomography (CT) of the patient. (Figure 1, A) On admission showing consolidations and ground-glass opacities on both lungs, mainly on the right lungs. (Figure 1, B) After steroid therapy showing an essentially complete radiological remission.

INVESTIGATING THE SAFETY OF SECOND-LINE TREATMENTS IN HIGH-RISK PRIMARY AND SECONDARY IMMUNE THROMBOCYTOPENIA (ITP): A SYSTEMATIC REVIEW OF PUBLISHED STUDIES

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Background and Aims: Immune thrombocytopenia (ITP) is an acquired autoimmune disease characterized by a transient or persistent reduction in the platelet count, resulting in an increased risk of bleeding. Paradoxically, ITP patients also face a higher risk of both arterial and venous thrombosis compared to general population. Patients with primary ITP (pITP) with antiphospholipid antibodies (aPL) positivity and ITP secondary to systemic lupus erythematosus (SLE), antiphospholipid antibody syndrome (APS), Evans' syndrome, inflammatory bowel diseases (IBD) or rheumatoid arthritis (RA) are at even higher risk. ITP-specific therapies can contribute to the thrombotic risk, as well. Available second-line treatments for ITP [thrombopoietin receptor agonists (TPO-RAs), fostamatinib, rituximab, immune suppressants, and splenectomy] have been associated to side effects, with thrombosis being a significant safety concern. However, there is a lack of studies that have investigated the safety of second-line treatments in ITP patients at high thrombotic risk. To clarify these concerns, we conducted a systematic review.
Methods: On March 8th, 2025, two independent reviewers (E.T. and G.M.) systematically searched Medline and Embase from 2010 onwards with a predefined research string. We included peer-reviewed studies in English reporting on the primary outcome, which was the frequency of thrombotic events in patients with high-risk pITP and secondary ITP (sITP) with available data on second-line treatment(s). Eligible second-line treatments included TPO-RAs, fostamatinib, rituximab, other immune suppressants (cyclosporine, cyclophosphamide, azathioprine and mycophenolate), and splenectomy. Studies including fewer than 5 patients and congress abstracts were excluded. Patients with no ongoing second-line treatment were excluded from the final analysis. We defined high-risk pITP as pITP with positive aPL without an associated APS and high-risk sITP as ITP secondary to an autoimmune disease associated with an increased thrombotic risk (SLE, APS, Evans' syndrome, IBD, and RA). We further analysed data by stratifying high-risk sITP patients based on their underlying disease. Data are presented as proportions with 95% confidence intervals (CI) calculated with the exact method. Risk of bias was independently assessed by E.T. and B.C. using the ROBINS-I V2 tool.
Results: We retrieved 5478 citations through our literature search. After the exclusion of duplicates (n=437) and ineligible studies (n=5029), 12 studies were included, for a total of 228 high-risk ITP patients (14 pITP and 214 sITP) on at least one eligible second-line treatment. SLE was the most frequent cause of sITP (n=168), followed by Evans' syndrome (n= 34), APS (n=7) and RA (n=2). Six patients had both SLE and APS. None of the eligible studies described ITP secondary to IBD. Among eligible high-risk ITP patients with known outcome by treatment, 108 received TPO-RAs, 22 rituximab, 28 immune suppressants and 51 underwent splenectomy. None of them received fostamatinib. Some patients (8 treated with rituximab and 27 patients on immune suppressants)

received combination therapy with another eligible second-line treatment during follow-up. A thrombotic event was reported in 24 high-risk ITP patients (11%, 95% CI 7-15). Stratifying patients by second-line treatment, thrombosis occurred in 14 patients on TPO-RAs (13%, 95% CI 7-21), in 3 patients treated with rituximab (14%, 95% CI 3-35), in 3 patients on immune suppressants (11%, 95% CI 2-28) and in 6 of those who underwent splenectomy (12%, 95% CI 4-24) over a median follow-up ranging from 6 to 42 months. Among SLE patients, the thrombosis rate was 7% (11/168, 95% CI 3-11) in the whole cohort, 5% (3/57, 95% CI 1-15) in patients on TPO-RAs, 17% (2/12, 95% CI 2-48) in patients treated with rituximab, 5% (1/19, 95% CI 0-26) in patients on immune suppressants, and 12% in splenectomised patients (6/50, 95% CI 4-24). All eligible patients with APS, APS secondary to SLE and Evans' syndrome were on treatment with TPO-RAs, with thrombosis rates of 29% (2/7, 95% CI 4-71), 50% (3/6, 95% CI 11-88) and 18% (6/34, 95% CI 7-34), respectively. All studies were deemed at critical risk of bias due to uncontrolled confounding of treatment selection.
Conclusions: The results of this systematic review, although limited by the low quality of eligible studies and considerable heterogeneity in follow-up period, show a clinically relevant rate of thrombosis in high-risk ITP patients on second-line treatment, which was evident across all available treatment options. It is possible that such propensity to thrombosis does not represent harm of administered second-line treatments but rather reflects the underlying prothrombotic environment of these autoimmune diseases.

SYSTEMIC CONGESTION IN HFPEF AND HFMREF: PREVALENCE OF UNDERLYING DISEASE AND SEVEREMITRAL REGURGITATION REGRESSION

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Background: Heart failure with preserved (HFpEF) and mildly reduced ejection fraction (HFmrEF) account for a growing proportion of acute heart failure (AHF) hospitalizations. In clinical practice, systemic congestion in these patients is often attributed to isolated diastolic dysfunction. However, whether true isolated HFpEF can account for marked congestion remains unclear.
Objectives: To assess the prevalence of significant cardiac or extracardiac causes underlying systemic congestion in HFpEF/HFmrEF patients and to evaluate the reversibility of severe mitral regurgitation (MR) after decongestive therapy.
Methods: We retrospectively analyzed 773 AHF patients, focusing on those with left ventricular ejection fraction (LVEF) >40% and inferior vena cava (IVC) congestion. Significant cardiac abnormalities and predictors of MR regression were assessed.
Results: Among 323 HFpEF/HFmrEF patients, 252 (78%) showed systemic congestion. Severe valvular disease was present in 81.7% (more frequent in congested patients, p=0.0038), and 10.3% had other major cardiac conditions or end-stage renal disease. Only 8% of congested patients presented true isolated HFpEF. Lack of significant cardiac or extracardiac pathology was independently associated with absence of IVC congestion (OR 0.037, 95% CI 0.017–0.078, p<0.001). In severe MR cases, functional aetiology predicted regression after decongestive therapy (OR 19.1, 95% CI 5.003–72.610, p<0.001), while organic and ischemic MR persisted.
Conclusions: In HFpEF/HFmrEF, systemic congestion almost always reflects significant underlying cardiac pathology. Severe MR was common among congested patients and frequently regressed when functional, suggesting a reversible contribution to acute decompensation.

THE ROLE OF NUTRITIONAL COUNSELING IN A MULTIDISCIPLINARY CLINIC FOR METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD): A CASE-CONTROL STUDY

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Background: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is a prevalent condition characterized by excessive liver fat accumulation, often progressing to fibrosis and cirrhosis. Lifestyle modifications, including dietary changes, are essential for MASLD management. This study aimed to evaluate the effectiveness of nutritional counseling in a multidisciplinary clinic setting on reducing liver stiffness, as measured by FibroScan, in patients with MASLD.
Methods: This comparative study included 100 patients divided in two groups of patients with MASLD: Group A (58 patients) received nutritional counseling as part of a multidisciplinary clinic approach, while Group B (42 patients) received standard ambulatory care without specific dietary guidance. Liver stiffness was assessed using FibroScan at baseline and after 1 year, such as biochemical parameters. A subgroup analysis of patients with a baseline Fibroscan more than 7.2Kpa (fibrosis grade 2) was conducted.
Results: After 1 year, a significance reduction of 2.2 Kpa (-2.8-0.0) was documented in both group A and B only in the subgroup analysis. Group A recorded a major decrease in weight (mean -4 kg (-9.5-0.0, p<0.05) compared with Group B.
At univariate e multivariate analysis confirmed that liver stiffness reduction was related with weigh loss.
Conclusion: This study highlights the importance of nutritional counseling in a multidisciplinary clinic setting for MASLD management in particular in patients with high fibrosis. Patients receiving tailored dietary advice demonstrated a more significant reduction in body weight that result link with a better liver stiffness measured by FibroScan; however, the herpetological approach (informations and support, drugs, etc) is important to decrease liver stiffness.
These findings support the integration of nutritional counseling into MASLD treatment plans to improve patient outcomes and slow disease progression.

SERUM BAG3 AS A PROMISING BIOMARKER FOR NON-INVASIVE ASSESSMENT OF FIBROSIS SEVERITY IN METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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Background: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is defined as steatotic liver disease accompanied by at least one cardiometabolic risk factor, such as obesity, insulin resistance, or dyslipidemia. MASLD has emerged as the leading cause of chronic liver disease and may progress to more severe stages, including cirrhosis and hepatocellular carcinoma. Its pathogenesis involves both environmental and genetic factors, including PNPLA3(I148M) and TM6SF2(E167K) variants, which promote hepatic steatosis and fibrosis. Fibrosis results from hepatocyte injury and immune activation, leading to hepatic stellate cells (HSCs) transdifferentiation into collagen-producing myofibroblasts. Heat shock proteins (HSPs), induced by cellular stress, modulate protein homeostasis and fibrotic signaling. BAG3(Bcl-2-associated athanogene3), a co-chaperone of the Hsp70, acts regulating autophagy, apoptosis, and cell survival. Emerging evidence suggests that BAG3may influence HSCs activation and fibrogenesis, potentially serving as both a biomarker and therapeutic target in MASLD
Aims: The aim of this study was to examine the association between serum BAG3levels and hepatic fibrosis in patients with MASLD. Additionally, we investigated the relationship between BAG3levels and the PNPLA3and TM6SF2genetic variants to better understand their contribution to MASLD pathophysiology.
Methods: We enrolled a cohort of 146 patients diagnosed with MASLD (Tab.1). Liver fibrosis was assessed using the non-invasive Fibrosis-4 (FIB-4) index, which incorporates age, AST, ALT, and platelet count. The population was stratified into three groups based on FIB-4 values: low-risk (1.3), intermediate risk (1.3-2.67), high risk (>2.67). Notably, in individuals older than 65 years, a different lower FIB-4 cut-off of 2.0 has been applied. Serum BAG3 levels were measured using enzyme-linked immunosorbent assay (ELISA). Genetic analysis for PNPLA3(I148M) and TM6SF2 (E167K) variants was performed using TaqMan SNP genotyping assays
Results: We observed a significant positive correlation between serum BAG3 levels and FIB-4 index (Spearman's correlation, p=0.012, R^2=0.025; Figure 1A), suggesting that elevated BAG3 levels are associated with more advanced hepatic fibrosis. FIB-4 scores were significantly higher in individuals with BAG3 levels exceeding 23.13 pg/mL (mean in healthy controls, p=0.023) and 30.35 pg/mL (95th percentile in healthy controls, p=0.008). Notably, subjects with BAG3 levels above 100 pg/mL also exhibited significantly higher FIB-4 scores (p=0.004; Fig. 1B). Furthermore, FIB-4 values progressively increased across five BAG3 level categories based on healthy control distribution (Kruskal-Wallis p=0.027, ANOVA p=0.006; Fig. 1C). Although BAG3 levels did not significantly vary with the number of PNPLA3 risk alleles (ANOVA p=0.361), a significant association was found with the number of TM6SF2 risk alleles (ANOVA p=0.028). Moreover, BAG3 levels increased with the combined number of PNPLA3 and TM6SF2 risk alleles (ANOVA p=0.003).
Discussion: and future perspectives: Our findings demonstrate a positive association between serum BAG3levels and hepatic fibrosis severity in MASLD patients, suggesting that BAG3may serve as a non-invasive biomarker for

fibrosis assessment. Moreover, BAG3expression appears to be influenced by genetic variants, particularly in TM6SF2, and to a lesser extent by PNPLA3. This highlights the complex interplay between genetic predisposition and molecular mechanisms underlying disease progression in MASLD. Although the exact mechanistic role of BAG3in hepatic fibrogenesis remains to be fully elucidated, its known involvement in autophagy, apoptosis, and cellular stress responses suggests a potential regulatory function in hepatic stellate cell activation and extracellular matrix deposition. These data open new avenues for future research, including the exploration of BAG3as a therapeutic target **Conclusion:** Non-invasive tools for fibrosis assessment are crucial for early diagnosis and management in the adult population with MASLD or at-risk individuals. Early detection and appropriate management of fibrosis are essential to prevent its progression to cirrhosis and related complications. BAG3 is upregulated in fibrotic conditions and may serve as both a biomarker and a potential therapeutic target. Further studies are needed to elucidate its role in hepatic fibrogenesis and MASLD-related pathways.

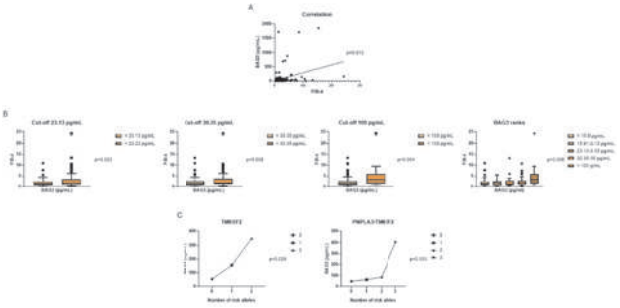

Figure 1 – Statistical analysis

Study Cohort N = 146	
Sex M/F (%)	83/63 (57/43)
Median age, years (range)	64 (93-20)
Age > 65 years (%)	64 (44)
Dysglycemia (%)	71 (48)
Dyslipidemia (%)	106 (72)
Hypertension (%)	107 (73)
Obesity (%)	113 (77)
Median FIB-4	1,59

Table 1 – Characteristics and cardiometabolic risk factors in MASLD cohort

INHIBITION OF H2S PRODUCTION REDUCES PORTAL PRESSURE BY DECREASING INTRAHEPATIC RESISTANCE IN RATS WITH CIRRHOSIS

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Hydrogen sulfide (H2S) is a gasotransmitter known for its vasodilatatory properties, and is also involved in regulating oxidative stress, inflammation and fibrosis in the liver. However, it is not clear its role in the developement of portal hypertension and complications of cirrhosis. We evaluated the hemodynamic effects of in vivo inhibition of H2S production in a rat model of experimental cirrhosis. Eight control rats and sixteen rats with bile duct ligation-induced cirrhosis were studied. Eight cirrhotic rats were treated with propargylglycine (PAG;30mg/kg), a specific inhibitor of cystathionine γ-lyase (CSE), the main source of H2S in the cardiovascular system and liver. Portal and systemic pressures were measured via polyethylene-50catheters. Small resistance mesenteric arteries were mounted on a wire myograph system, and dose-response curves to acetylcholine (ACh) and sodium hydrosulphide (NaHS), an H2S donor, were evaluated. Serum levels of ALT, creatinine and bilirubine were assessed. Hepatic mRNA expression of inducible nitric oxide synthase (iNOS), endotelial nitric oxide synthase (eNOS), IL-6, TGF-β, collagen I, CSE, cystathionine-β-synthase (CBS), and glutathione synthetase (GSS) was measured. In cirrhotic rats, PAG treatment significantly reduced portal pressure (10.4±2.7mmHg versus16.0±3.9mmHg, P=<0.05) without affecting systemic pressure. No differences were observed in mesenteric artery responses to ACh or NaHS between treated and untreated cirrhotic rats. Treated cirrhotic rats had significantly lower creatinine (24.2±6.5μmol/L versus34.2±7.9μmol/L; P=0.003) and ALT levels (23.3±20.1U/L vs103.5±21.9U/L; P=<0.001), with no significant difference in bilirubin. In the liver, PAG reduced the expression of CBS (P=0.032) and eNOS (P=0.016), and increased the expression of iNOS (P=0.03), with no effect on CSE. In the liver, PAG also reduced IL-6(P=0.008), TGFβ (P=0.008), and collagen I (P=0.008), while increasing GSS (P=0.016). Conclusion: In vivo inhibition of H2S synthesis in cirrhotic rats reduces portal pressure and markers of hepatic inflammation and fibrosis, without affecting mesenteric vasodilation. These findings suggest that targeting H2S may benefit portal hypertension by acting on intrahepatic resistance.

A CHALLENGING BACKACHE: WORK-UP OF FEVER IN INTERNAL MEDICINE… AND MORE

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In June 2024, a 70-years patient- who had a history of arterial hypertension and atrial fibrillation treated with Apixaban -presented to the Emergency Department due to persistent high-grade fever. In the preceding days, he had experienced dysuria, stranguria and a syncopal episode. During anamnesis, he also reported lower back pain that had started a few weeks before.
Laboratory tests revealed elevated inflammatory markers, impaired renal function and hypokalemia. A chest X-ray showed signs of pulmonary congestion, while an abdominal contrast-enhanced CT scan reported: "Hypodense areas in the left renal parenchyma compatible with pyelonephritis. Perirenal fat stranding on the left side".
Due to persistent fever, blood and urine samples were collected and empirical treatment with Meropenem was started, yielding clinical improvement. The patient was then admitted to the Nephrology Unit. During hospitalization, blood cultures returned positive for E. Coli (pan-sensitive), so the antibiotic regimen was continued and enhanced with Clarithromycin, with further improvement in inflammatory markers and renal function.
The patient was discharged after 20 days with diagnosis of: "Acute pyelonephritis, acute kidney injury, sepsis, atrial fibrillation, benign hypertensive cardionephropathy."
In the following days, due to the recurrence of fever poorly responsive to outpatient therapy, the patient accessed the Emergency Department of another hospital. After a new positive blood culture for E. coli, Meropenem therapy was restarted, and a follow-up CT scan showed improvement of the pyelonephritis. However, the patient discontinued the diagnostic and therapeutic process, leaving the hospital against medical advice.
At the end of July, he presented again to the Emergency Department of our University Hospital with high-grade fever. Screening tests were performed: rectal swab for carbapenem-resistant organisms, rapid antigen test for SARS-CoV-2, urine and blood cultures. Empirical therapy with Piperacillin-Tazobactam was started. All tests returned negative, except for the SARS-CoV-2 test. Thus the patient was treated with short-course Remdesivir and continued on antibiotics. Chest X-ray was normal and he was admitted to our Internal Medicine ward "C.Frugoni".
Upon admission, the patient was alert, breathing spontaneously in room air and afebrile, but he presented with asthenia and loss of appetite. The antibiotic therapy was completed with clinical benefit. However, due to the reappearance and persistence of fever in the following days, multiple blood cultures were performed (all negative) while urine cultures returned positive for multi-drug-resistant Klebsiella pneumoniae. A new rectal swab confirmed carbapenem resistance. Antibiotic therapy with Ceftazidime-Avibactam was initiated, later combined with Daptomycin given the lack of clinical improvement.
An echocardiogram excluded endocarditic vegetations. During the hospital stay, the patient developed abdominal pain with a positive Murphy's sign and negative Blumberg's sign. Abdominal ultrasound re-evaluation revealed thickening of the gallbladder walls and pericholecystic fluid that where not present at the admission scan. Meropenem was reintroduced.
A thoraco-abdominal CT scan, performed to rule out abscesses, confirmed a diagnosis of acalculous cholecystitis and revealed morphostructural alterations of the opposing vertebral endplates of L2–L3. General surgery was consulted; no indication for surgery was given and conservative management was advised with fasting and continuation of antibiotic therapy.
Given the CT findings and the patient's history of back pain, an MRI of the lumbosacral spine was performed, showing spondylodiscitis with bilateral inflammation, extending to the paravertebral and iliopsoas muscles. The ongoing therapy with Meropenem and Daptomycin was confirmed, resulting in improvement of inflammatory markers and persistent apyrexia. Antibiotic therapy was planned to continue until mid-September (with the option of transitioning to long-acting Dalbavancin in a day-hospital setting).
Spinal surgery consultation recommended the use of an MZ orthopedic brace when sitting or standing and a follow-up by physiatrists to adapt the rehabilitation program, which had been initiated early in the hospitalization to promote mobilization.
Following completion of antibiotic therapy, the patient was discharged in stable

condition, apyretic and breathing spontaneously in room air.
This case illustrates how, in patients with recurrent fever, it is essential to rule out all possible underlying causes (infections, autoimmune diseases, neoplasms, drug-induced fever, endocrine, thromboembolic or factitious fever) before confirming a diagnosis. Moreover, as shown in our patient with spondylodiscitis, urinary tract infection and cholecystitis, different causes of fever may coexist. A thorough diagnostic workup must be guided by the patient's clinical history (congenital conditions, previous infections, recent travel or procedures), always keeping in mind the possibility of hidden infectious foci.

PASTRY-INDUCED ANGINA: WHEN DESSERT TURNS DANGEROUS

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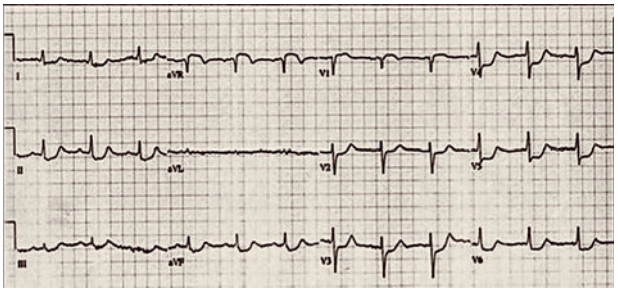
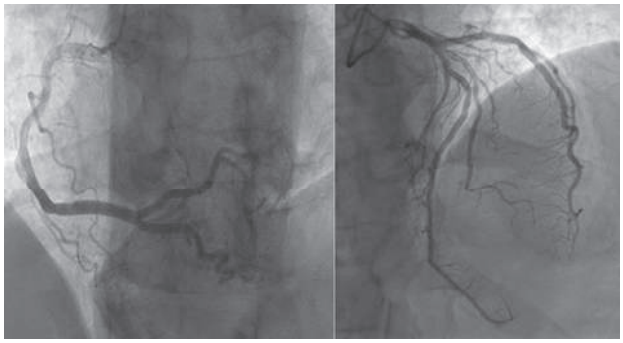
Background: Kounis Syndrome (KS) is an uncommon form of acute coronary syndrome (ACS) that encompasses coronary artery spasm, myocardial infarction and stent thrombosis, all triggered by allergic, hypersensitivity, or anaphylactic reactions.
Clinical Presentation: A 68-year-old man presented to the Emergency Department following a syncopal episode accompanied by a diffuse urticarial rash. His past medical history included dyslipidemia, active smoking, and a family history of coronary artery disease. Upon arrival, he was hypotensive (90/60 mmHg), tachypneic, with an oxygen saturation of 95% on room air and a Glasgow Coma Scale of 15. Physical examination revealed widespread itchy maculopapular skin rash, without signs of bronchospasm or gastrointestinal involvement.
According to his wife, the patient experienced transient loss of consciousness—without incontinence and followed by complete recovery—shortly after ingesting a traditional pastry approximately 30 minutes prior to admission. An initial diagnosis of food-induced anaphylaxis was considered, and intravenous methylprednisolone (60 mg) and chlorphenamine (10 mg) were administered. Within minutes, the patient reported severe retrosternal chest pain with a positive Levine's sign. Given the new onset of chest pain, intramuscular epinephrine was withheld due to concerns of potential myocardial ischemia. An electrocardiogram (EKG) and bedside transthoracic echocardiogram (TTE) were performed.
Results: EKG findings included ST-segment elevation in aVR and diffuse ST depression (Figure 1). Bedside TTE revealed regional wall motion abnormalities involving the apex, without apical ballooning. Serial troponin assays demonstrate a typical rise-and-fall pattern (49–3187–815 ng/L). The patient was referred for emergent coronary angiography, which revealed angiographically normal coronary arteries without any evidence of atherosclerotic lesions (Figure 2).
Subsequent laboratory tests demonstrated a mild elevation in serum IgE (200 IU/ml) and tryptase levels (20 ug/L). During follow-up, allergologic evaluation, including skin testing, confirmed sensitization to hazelnuts, peanuts and specific ingredients of the ingested pastry.
Pathophysiology: KS is a form of ACS precipitated by allergic or hypersensitivity reactions. It typically presents with acute chest pain, often accompanied by systemic allergic manifestations such as flushing, urticaria, bronchospasm, or hypotension. Common triggers include drugs, foods, and insect stings. The syndrome may mimic classical myocardial infarction due to EKG changes and mild elevations in cardiac biomarkers.
KS comes in four variants: type I in patients with normal coronary arteries; type II in patients with inactive pre-existing atheromatous disease; type III in patients with pre-existing coronary artery stenting; type IV in patients with a pre-existing coronary artery bypass. A central role is played by IgE, especially in Type I KS. Upon exposure to a sensitizing allergen, cross-linking of IgE bound to mast cells triggers the release of histamine, leukotrienes, and other mediators, which can induce coronary vasospasm or myocardial injury. Identifying elevated IgE levels or a history of hypersensitivity may aid diagnosis and inform management.
Differential Diagnosis: The differential diagnosis of KS includes other causes of chest pain and/or anaphylaxis. Type I KS must be differentiated from:
Recognition of a clear allergen trigger, allergic symptoms, and response to antihistamines supports KS diagnosis.
Discussion: This case illustrates the clinical complexity of Type I KS, in which coronary vasospasm is triggered by food-induced anaphylaxis. Management poses a dilemma: while epinephrine is the first-line treatment for anaphylaxis, its administration in the context of suspected myocardial ischemia must be approached with caution due to the risk of aggravating cardiac injury.
In such scenarios, individualized management is essential. Anti-allergic therapy with glucorticoids and H1 and H2 blockers should be promptly initiated, while cardiac work-up—including EKG, biomarkers, echocardiography, and coronary angiography—must proceed in parallel. Furthermore, it highlights the importance of structured follow-up with allergy testing to identify specific triggers and prevent future episodes. Current guidelines lack standardized protocols for KS, and further studies are warranted to define optimal management strategies.
Conclusion: We report a case of Type I KS triggered by food allergens in a patient with no prior history of coronary artery disease. Greater awareness of this syndrome is critical to avoid misdiagnosis and ensure appropriate and timely treatment.





IMPACT OF HEART FAILURE ON EARLY P OST-DISCHARGE MORTALITY IN PATIENTS ADMITTED TO AN INTERNAL MEDICINE WARD

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Background: patients discharged from Internal Medicine wards are at high risk of early rehospitalization and mortality. Heart failure (HF) is frequently diagnosed in these patients, either as the primary reason for admission (primary HF) or as a concomitant condition (secondary HF). We aimed to evaluate the prognostic impact of primary and secondary HF on early post-discharge mortality in patients admitted to an Internal Medicine ward.
Methods: All consecutive patients discharged from the Unit of Internal and Translational Medicine Ward at Terni Hospital between April and July 2024 were prospectively followed for 6 months. The primary outcomes were all-cause mortality and first rehospitalization.
Results: 236 patients (median age 78±2 years, 50% men) were analyzed. HF was diagnosed in 81 patients (34%), including 12% with primary HF and 22% secondary HF. Over a median follow-up of 4.7 months [IQR 3.7 – 5.6], 70 patients (30%) were rehospitalized, and 48 patients (20%) died. In age- and sex-adjusted Cox proportional hazard models, HF was independently associated with an increased risk of all-cause mortality (aHR 1.79, 95%CI 1.01-3.29), with no significant difference between primary and secondary HF (p for interaction: 0.21). In contrast, primary HF significantly enhanced the risk of rehospitalization among HF patients (p for interaction: 0.03), as well as early rehospitalization further mediated an increased risk of mortality among HF patients (p for interaction 0.02).
Conclusions: HF, whether primary or secondary, showed an age-independent association with early post-discharge mortality. A diagnosis of primary HF also confers an increased risk of rehospitalization. The occurrence of rehospitalization in HF patients does not alter the natural history of the disease.

EXPLORING THE IMPACT OF GLP-1 RECEPTOR AGONIST TREATMENT ON BODY MASS COMPOSITION IN OBESITY WITHOUT DIABETES: AN OBSERVATIONAL STUDY.

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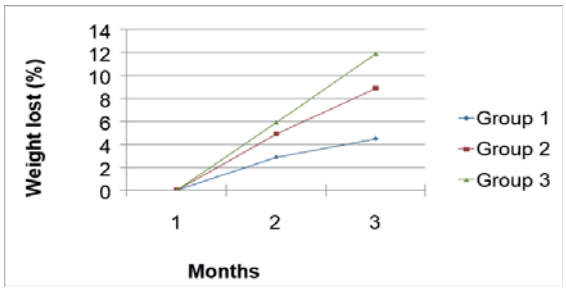
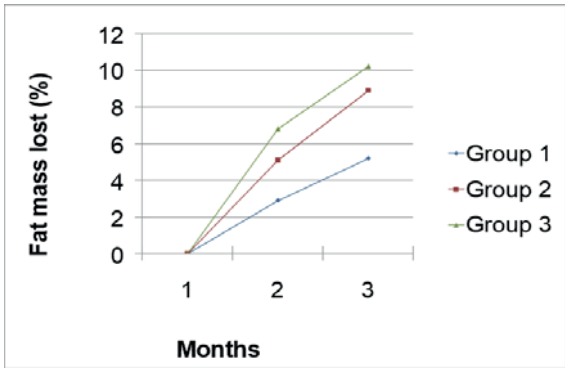
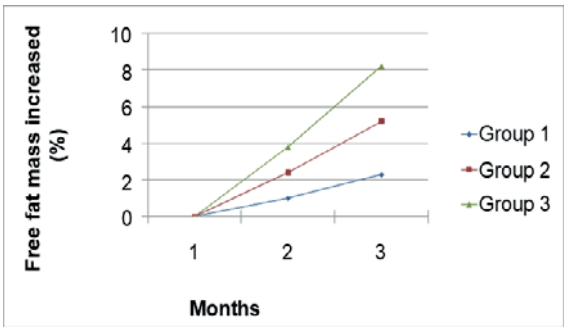
Background: Glucagon-like peptide-1 (GLP-1) is an incretin hormone produced in the gut that plays a key role in regulating blood glycaemia and satiety. Its importance in obesity treatment stems from its effects on appetite suppression, gastric emptying, and insulin secretion. GLP-1 receptor agonists (GLP-1 RAs) as liraglutide and semaglutide have been developed and approved for treating obesity and type 2 diabetes. Clinical trials have shown significant weight loss in patients treated with these medications, even in those without diabetes. Beyond weight loss, GLP-1 RAs may also contribute to improvements in body composition by decreasing fat mass while preserving fat-free mass, thus decreasing cardiovascular risk and fat accumulation in the liver. The aim of the present study is to analyze the changes in body weight and composition induced by these drugs in non-diabetic subjects affected by obesity.
Methods: Over a period of 7 months, 90 patients (equally divided by gender) were analyzed; out of them 30 (group 1) followed only low-calorie diets, 30 (group 2) were treated with Liraglutide at dose escalation, while the remaining 30 (group 3) with Semaglutide at dose escalation (along with low-calorie diet treatments). Visits were scheduled monthly and included a clinical examination adn a multifrequence bioimpedance analysis along with anthropometric measurements.
Results: After 7 months of treatment, group 1 had a weight loss of 4.5% (± 0.2%) of its initial weight, group 2 lost 8.9% (± 0.4%), and group 3 lost 11.9% (± 0.3%, P< 0.001 vs group 1 and P<0.05 vs group 2) (Fig.1). As far as body composition was concerned, fat mass reduction was 5.2% (±0.4%) in group 1, 8.9% (± 0.3%) in group 2 and 10.2% (± 0.5%) in group 3 (P< 0.001 vs group 1 and P<0.05 vs group 2) (Fig.2). Fat-free mass increased by 2.3% (± 0.2%) in group 1, 5.2% (± 0.3%) in group 2, 8.2% (± 0.4%) in group 3 (P< 0.01 vs group 1 and P<0.05 vs group 2) (Fig.3).
Discussion: Conclusion: GLP-1 receptor analogs play a crucial role in the reduction of visceral fat through their multifaceted mechanisms. Given their promising benefits, GLP-1 receptor analogs represent an effective therapeutic approach for managing obesity and improving overall metabolic health.







ASSOCIATION BETWEEN AUGMENTED LEVELS OF PRONEUROTENSIN AND CARDIOVASCULAR DISEASE

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Neurotensin (NT) is a peptide hormone released by intestinal N cells in response to a fat-rich meal, capable of regulating gastrointestinal motility and secretion, thereby promoting intestinal fatty acid absorption and, consequently, weight gain. Additionally, NT has been shown to exert pro-inflammatory effects and contribute to adipose tissue dysfunction, insulin resistance, and vascular damage.
Recently, growing evidence has demonstrated a longitudinal association between elevated circulating levels of proneurotensin (proNT)—a stable NT precursor produced in equimolar amounts with NT—and the development of cardiovascular diseases (CVDs). However, whether increased proNT levels identify individuals at higher risk of CVDs independently of cardiometabolic risk factors remains to be determined.
In this cross-sectional study, the presence of CVDs (including coronary artery disease, cerebrovascular disease, peripheral arterial disease, and carotid artery disease) was assessed in 151 non-diabetic individuals stratified into tertiles based on fasting serum proNT concentrations, measured using a specific ELISA assay. All participants underwent a detailed medical history and physical examination, including collection of anthropometric parameters such as BMI and waist circumference. They also underwent biochemical profiling, including a 75 g oral glucose tolerance test with blood sampling at 0, 30, 60, 90, and 120 minutes for plasma glucose and insulin measurements.
No significant differences in age or sex distribution were observed across the three tertiles. However, individuals in the intermediate and highest proNT tertiles exhibited a progressively worse cardiometabolic risk profile, with higher BMI, triglycerides, and 2-hour post-load insulin levels, as well as lower HDL cholesterol and insulin sensitivity (estimated by the Matsuda index), compared to those in the lowest tertile. In contrast, no significant differences were observed in fasting or post-load glucose levels, or HbA1c.
The prevalence of CVDs was significantly higher in the second and third proNT tertiles (40% and 45%, respectively) compared to the lowest tertile (15%, P=0.01). In a logistic regression analysis adjusted for multiple cardiometabolic risk factors—including age, sex, BMI, systolic and diastolic blood pressure, total and HDL cholesterol, triglycerides, and the Matsuda index—individuals in the highest proNT tertile had a 3.3-fold increased risk of CVDs (OR: 3.34; 95% CI: 1.0–11.18; P=0.04) compared to those in the lowest tertile. A non-significant 2.7-fold increased risk was also observed in the intermediate tertile (OR: 2.66; 95% CI: 0.87–8.09; P=0.084).
In conclusion, our data provide evidence that elevated circulating proNT levels are associated with an increased risk of CVDs in non-diabetic individuals, independently of traditional cardiometabolic risk factors. These findings, in conjunction with previous experimental and clinical studies, suggest that increased proNT/NT levels may represent not only a biomarker of CVDs but also a potential pathogenic factor involved in cardiovascular organ damage and a novel therapeutic target.

FROM CAGLIARI'S UNIVERSITY HOSPITAL TO THE CITY SQUARES: AN INTEGRATED MODEL OF HCV SCREENING IN THE GENERAL POPULATION IN SARDINIA.

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Background: In 2016 the World Health Organization proposed eliminating hepatitis C as a public health goal by 2030 [1]. Only a small number of countries are on track to meet the WHO's target due to many barriers in healthcare systems and COVID - 19 pandemic [2-4]. Several programs of case-finding and linkage-to-care have been performed in different subpopulations at high prevalence and/or at high risk for HCV infection, such as injection drug users, people living with HIV, prisoners, or migrants from high endemic countries [5-6]. To control HCV infection in the general population, the elimination strategy must necessarily involve the implementation of structured and coordinated interventions in different health programs and services, aimed at case-finding and linkage-to-care [7]. In 2021, free screening for HCV infection began in Italy for SerD users, prisoners and citizens born between 1969 and 1989. [4]. Sardinia has been excluded from the Italian National screening planning, and regional government has started to plain a screening in the same key population. With the aim of achieving micro-elimination, in 2023 we designed and conducted a hospital-wide project focusing on inpatients born between 1933 and 1958. On the other side we also carried out a screening campaign for HCV named "PensaCi, fai il test, scegli di guarire!" in the city of Cagliari to increase disease awareness in the general population.
Patients and Methods: From 1 November 2023 to 31 March 2025 all patients aged between 65 and 90 years admitted to the University Hospital of Cagliari for any medical reason has been tested for anti HCV antibody (HCVAb) by third-generation ELISA. In case of positive result, reflex HCV - RNA testing and genotyping have been performed. The screening was voluntary based. From December 2023 to April 2024, we performed rapid diagnostic test (RDT) for HCV antibodies in different hot spots in the city of Cagliari chosen for their ''popularity" (shopping district) or social and economic criticality (municipal market and farmer's market). The screening was voluntary based. Pre and post test counseling has been offered. Subjects who tested positive were referred to our Liver Unit for HCV RNA testing.
Results: In the hospital setting, 2096 participants were enrolled, 50.02% male, median age 77 years old, 82 (3.91%) subjects were HCVAb positive and of them 9 (0.43%) were HCVRNA positive. Despite co-morbidities, all 9 patients were treated with direct acting antivirals (DAAs) with sustained virological response (SVR).During the campaign "PensaCi, fai il test, scegli di guarire!", we enrolled 1018 subjects; 545 (53,53%) were male. The median age was 57 years (range 10- 90 years). 3 subjects (0.29%) were positive on RDT and were admitted to the hospital to perform HCV RNA and genotype test. 2 of them were negative to HCV RNA, while one (0.09%) had HCV RNA positive and started DAA treatment, achieving SVR. One of the patients with anti HCV antibodies positivity and negative HCV RNA underwent an abdominal ultrasound with evidence of liver cirrhosis and suspected of hepatocellular carcinoma(HCC). Liver lesion was confirmed to be an HCC in CT scan and the patient underwent evaluation for liver transplantation according to international guidelines.
Conclusions: Our data have highlighted how the rate of active HCV infections in the general population is much lower than in the past, when it was very high in the elderly. Moreover, the use of DAAs since 2014 has contributed to reducing the circulation of the virus. Unfortunately, the incidence of new HCV infections in Italy is increasing. Consequently, to achieve the objectives of WHO, it is essential to extend screening to other age groups and launch information campaigns on risk factors, partly unknown to the population, and on the therapeutic revolution of DAAs.

A RARE CASE OF MORPHEA (LOCALIZED SCLERODERMA)

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Background: Morphea, or localized scleroderma, is an uncommon chronic inflammatory condition that affects the derma and the connective tissue. Characterized by sclerosis of the skin and in some cases of the fascia, muscle or bone, morphea, unlike systemic sclerosis (scleroderma), lacks visceral involvement. The pathogenesis is still unclear related to genetic susceptibility, vascular dysfunction, autoimmune dysregulation and environmental factors, including trauma and infection. Several clinical forms of Morphea are recognized: Circumscribed, Linear, "en coup de sabre", and generalized morphea. Other forms exist but are very rare. The nature of the skin involvement may change over time typically progressing through three phases: oedema, induration and atrophy.
Here we report a 67 years old male patient who presented sclerotic plaque with progressive itching and hardening of the skin and subcutaneous connective tissue localized the neck and the upper trunk.
Case presentation: In February 2025 a 67y.o. Caucasian man was referred to our Internal Medicine Unit at Policliclinico Riuniti Foggia. Over the previous 3 months he had reported the appearance of an unspecified erythematosus eczema with thickening of the skin around the neck neck, gradually extending to the upper back and starts to cause itching of mild entity. No other symptoms were reported.
Firstly, in December he was evaluated by a dermatologist who suspected Mycosis Fungoides/Sezary syndrome or diabetic skin lesions. In January he was reviewed by an endocrinologist during a diabetes follow-up, who denied the diabetes involvement of the skin lesions, and requested blood sample (VES, PCR, B2-microglobulin and thyroid profile) which were all within normal limits, confirming well-controlled diabetes mellitus, hypovitaminosis D and dyslipidaemia. He also performed an US of the abdomen that showed a mild splenomegaly with no further signs. There were no signs of systemic sclerosis (e.g., Raynaud's phenomenon, sclerodactyly, calcinosis cutis, and telangiectasia).
On February 18th, he was re-evaluated by his dermatologist, who recommended admission to Internal Medicine department to get a biopsy of the lesions. At the first examination the lesions seem to be a thickening of the skin around the neck of the patient like a necklace, flat, hyperpigmented with mild itching (figure 1). Autoimmune screening (ANA) and neoplastic markers test (CEA, CA 19.9, CA125, Beta2microglobulina, PSA, LDH) were requested – all within normal range. Cervical lymph nodes were evaluated for possible infectious or autoimmune causes, with no significant findings. A plastic surgery's consultation was obtained and a biopsy and a Total Body CT scan were performed. **Histopathological examination revealed dermal collagen fiber alterations characterized by thickening and parallel orientation to the epidermis, with eosinophilia. Dermal fibrosis extended to the hypodermis, causing thickening of fibrous septa and encasing adnexal structures. A mild to moderate lymphoplasmacytic inflammatory infiltrate was observed, primarily distributed perivascularly and peri-adnexally in the dermis and hypodermis, with lymphoid aggregates lacking germinal centers. These findings were consistent with a late inflammatory/sclerotic phase of morphea.** The CT scan concluded for "COPD, thickening of the pleura, small and diffuse nodule in the parenchyma of both lungs, slight thickening of the subcutaneous adipose planes in the right anterosuperior pectoralis region, pericentimetric lymph nodes of the abdomen.
Discussion: management of morphea depends on subtype, depth of involvement, and activity of disease. The treatment is based on topical corticosteroidal treatment or topical tacrolimus 0.1%. They seem to offer very good results for the circumscribedform of mild entity. Phototherapy is also excellent for the widespread form. In rapidly progressive or deep involvement forms, systemic therapy such as metrotrexate in combination with corticosteroids or Mycophenolate mofetil are preferred.
Conclusion: this case highlights the importance of considering Morphea in the differential diagnosis of chronic, localized skin thickening, even in the absence of systemic features. Early diagnosis and treatment are necessary to minimize damage such as cosmetic sequelae and joint contractures or limb deformities in patients with severe forms of morphea (especially in childhood). Patches of morphea that are superficial, as the one in our patient, may be relatively benign, and the prognosis is good. In our case report, histopathology remains crucial for diagnosis. The patient was diagnosed with a localized late-stage morphea and was successfully referred for dermatologic and rheumatologic management with topical corticosteroids and tacrolimus. At follow-up, the condition remained stable without progression to deeper structures or systemic involvement.
Key-Words: localized scleroderma, morphea, thickening skin

REFRACTORY BLEEDING AND ACUTE RENAL FAILURE WITH MASSIVE PROTEINURIA AS PRESENTING SYMPTOMS OF MYELODISPLASTIC SYNDROME: A DIAGNOSTIC AND THERAPEUTIC CHALLENGE.

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Introduction: The bleeding phenotype associated with fibrinolytic disorders is characterized by delayed bleeding following trauma, surgery or tooth procedures. Hyperfibrinolytic conditions are likely underdiagnosed due to limited awareness and the lack of accurate diagnostic tools. Fibrinolysis -the process of fibrin clot degradation- is regulated by a balance between activators, inhibitors and cofactors. Hyperfibrinolytic bleeding may result from deficiencies in fibrinolysis inhibitors or from an excess of fibrinolytic activators. In the absence of these abnormalities, differential diagnoses include paraneoplastic consumptive coagulopathy and fibrinolytic activity associated with myelodysplastic syndrome (MDS) or hyperfibrinolysis and coagulopathy caused by disseminated intravascular coagulation (DIC).
Case report: In July2024, a78-year-old male patient was admitted following the development of mucocutaneous bleeding. His recent medical history revealed: episodic macroscopic hematuria at the first detection of chronic kidney disease (creatinine1.28mg/dL), a post-intramuscular injection hematoma and bleeding after tooth extraction. An initial diagnosis of chronic DIC was made based on the following results: fibrinogen77mg/dL, D-dimer86,967µg/L, hemoglobin8.4g/dL, platelets57x10^9/L, PT ratio1.28, and aPTT ratio1.11. The patient was treated with fresh frozen plasma (15ml/kg in2daily doses) and red blood cell units. Standard coagulation assays could not differentiate between DIC with secondary hyperfibrinolysis and primary fibrinolytic activation due to unidentified trigger. Factor XIII was40%, α2-antiplasmin was reduced to38%, and plasminogen activator inhibitor and tissue fibrinogen activator, tested using the mixture test, were normal. Further workup to identify the cause of this coagulopathy included a negative FDG-PET Total Body, exclusion of infectious causes, and detection of only a homogeneous ANA pattern (1:320). The patient developed macroscopic hematuria, acute kidney injury and massive mixed proteinuria (8g/dL) without nephrotic syndrome; but given the bleeding risk, renal biopsy was deferred. During hospitalization, anemia and thrombocytopenia worsened, prompting bone marrow biopsy on July30th after fibrinogen (2g IV every12hours), tranexamic acid, fresh frozen plasma, and platelet transfusions. Despite prophylaxis, the patient developed a psoas hematoma requiring embolization and continuous plasma infusion (15mg/kg die), due to persistent hypofibrinogenemia unresponsive to intravenous fibrinogen therapy. In the following days renal function deteriorated (creatinine peaking at5mg/dL), the patient developed fluid overload (respiratory failure and weight gain >10kg) and a thrice-weekly dialysis has been started. While waiting for the outcome of the bone marrow biopsy, we interpreted the clinical case as autoimmune phenomena associated with a possible myelodysplasia. High-dose intravenous steroids (1mg/kg/day up to2mg/kg/day) was introduced on July31st. The coagulopathy improved and hematuria resolved allowing discontinuation of fibrinogen and fresh frozen plasma support. Therapy was continued with steroids, tranexamic acid and a course of intravenous immunoglobulins, leading to stable fibrinogen levels >100mg/dL and D-dimer reduction (to2000µg/L). Dialysis was discontinued after one month (creatinine stabilized at1.6mg/dL), and steroids were tapered to0.75mg/kg/day, allowing discharge after three months of treatment. Bone marrow evaluation revealed multilineage myelodysplastic syndrome with chromosome8trisomy (+8). Due to the autoimmune-like features UBA1mutation was searched and resulted negative. Genetic testing identified a previously undescribed heterozygous nonsense mutation in exon3of the fibrinogen gene: c.174T>A; p.Y58X. Subsequently NGS revealed an NPM1mutation, establishing a diagnosis of NPM1-positive acute myeloid leukemia, with an indication for treatment with azacitidine and venetoclax, which was never initiated due to its high toxicity. The patient is currently in disease stability with low-dose steroid therapy and azacytidine monotherapy, administered according to the patient's tolerance and fitness.
Conclusions: We report a complex hematologic case requiring three-month of hospitalization in which establishing a final diagnosis was particularly challenging. The diagnosis of MDS/LMA in this patient pinpoints the importance of keeping high surveillance on myeloid malignancies in fibrinolytic disorders on unexplained origin, in addition in this case associated with AKI and significant proteinuria. These latest findings have likely been interpreted as autoimmune manifestations, also supported by the favorable response to steroid therapy. In the future, diagnostic accuracy may be enhanced by integrating thrombin and plasmin generation assays and next-generation sequencing.

CMV-INDUCED AUTOIMMUNE HEMOLYTIC ANEMIA DUE TO COLD AGGLUTININS: WHEN THE COOMBS TEST IS MISLEADING

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Introduzione: il test di Coombs costituisce il cardine diagnostico delle anemie emolitiche autoimmuni. Si distinguono varianti da autoanticorpi caldi (idiopatiche o secondarie a lupus eritematoso sistemico, linfomi, leucemia linfatica cronica o indotte da farmaci) e da autoanticorpi freddi (idiopatiche o secondarie a infezioni come polmoniti da mycoplasmapneumoniae, mononucleosi o a disturbi linfoproliferativi).
Case report: Un uomo di 44 anni si è recato presso il Pronto Soccorso (PS) del nostro ospedale per marcata astenia e ittero comparso da circa 4 giorni. Assenza di rilievi significativi all'anamnesi patologica remota. Dagli esami di laboratorio eseguiti in PS si evidenziava un quadro di anemia emolitica: Hb 8 g/dl, bilirubina totale 6,4 mg/dl, con prevalenza della forma indiretta, aptoglobina<5,4 mg/dl, aumento di LDH , lieve leucopenia e piastrinopenia, reticolocitosi. Allo striscio di sangue periferico assenza di schistociti e alterazioni morfologiche eritrocitarie. I test di Coombs diretto e indiretto negativi.
Il paziente veniva ricoverato presso la nostra UOC di Medicina Generale. Gli esami di laboratorio confermavano il quadro riscontrato in PS: Hb 6,4 g/dl, bilirubina totale 8,7 mg/dl, aptoglobina<5,4 mg/dl, LDH aumentato, lieve leucopenia e piastrinopenia, reticolocitosi.All'esame obiettivo ittero,lieve epatosplenomegalia. Assenti emoglobine patologiche e negativo il test in citofluorimetria per emoglobinuria parossistica notturna (EPN). Coombs diretto e indiretto si confermavano negativi. L' aspirato midollare evidenziava la presenza di numerosi precursori eritroidi e la biopsia osteomidollare escludeva localizzazione di processo linfoproliferativo. Negativa l' autoimmunità (ANA, Anti-DNA e ANCA) e i test per i principali patogeni responsabili di anemia emolitica (HAV, HBV, HCV, HEV, HIV, Mycoplasma Pneumoniae, Epstein Barr, CMV, Salmonella typhi e paratyphi) con risultati tutti negativi per infezioni acute.La TC torace-addome con mdc escludeva la presenza di tumori solidi o linfomi. Alla polymerase chain reaction (PCR) alto titolo di replicazione di CMV (9200 UI/ml); crioagglutinine positive per auto-IgM a specificità anti-I a 37°C, che spiega la negatività dei test di Coombs effettuati a temperature inferiori.
Conclusion: i: Questo raro caso di anemia emolitica autoimmune, da crioagglutinine, secondaria a infezione da CMV, con test di Coombs negativo, sottolinea la necessità di considerare eziologie inusuali nella diagnosi differenziale dell'anemia emolitica negli adulti immunocompetenti. La ricerca di crioagglutinine e l'indagine su potenziali trigger virali, come il CMV, possono rivelarsi cruciali per una diagnosi accurata e un trattamento steroideo tempestivo, come dimostrato nel nostro paziente, responder alla terapia cortisonica.

ROLE OF NODULAR LYMPHOID HYPERPLASIA AS IMMUNOLOGIC PRECURSOR OF IBD DEVELOPMENT IN PATIENTS WITH IBS-LIKE SYMPTOMS: AN OBSERVATIONAL, AMBISPECTIC, MULITICENTER STUDY "THE NILE STUDY"

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Background: Irritable bowel syndrome (IBS) and chronic inflammatory bowel diseases (IBD) share overlapping pathophysiological mechanisms, including dysbiosis, impaired intestinal barrier function, and immune dysregulation, while maintaining distinct clinical and diagnostic profiles. Lymphoid follicular hyperplasia (LFH), detectable through ileocolonoscopy and histopathology in IBS-like patients, represents an immunological alteration potentially indicative of a preclinical phase of IBD. However, the prognostic value of LFH remains poorly characterized, warranting further investigation into its utility as a biomarker for IBD progression.
Objectives: The primary objective is to evaluate the incidence and risk factors of IBD development in IBS-like patients with LFH by characterizing their immunophenotypic profiles. Secondary aims include the identification of molecular, serological, and fecal biomarkers associated with LFH and the assessment of gut microbiota composition and intestinal epithelial barrier integrity.Study Design:This multicenter, ambispective, observational cohort study includes a retrospective phase (2011–2023) and a prospective phase with a 10-year fol-

low-up. The study population comprises adults aged 18–70 years, categorized into three cohorts: (1) IBS-like patients with diffuse ileal and/or colonic LFH; (2) IBS-like patients with LFH associated with IBD; and (3) IBS-like patients without LFH (control group).Methods:The study integrates clinical, endoscopic, histopathological, and biomarker data. Serological (e.g., C-reactive protein, serum zonulin), fecal (e.g., calprotectin), and molecular biomarkers will be analyzed. Gut microbiota composition will be characterized using high-throughput sequencing technologies. Immunophenotypic profiling of peripheral blood and intestinal biopsy samples will identify immune cell subsets and activation markers associated with LFH. Statistical analyses, including multivariate regression and survival models, will evaluate predictors of IBD progression.The study aims to establish LFH as an early immunological marker of IBD progression, identifying specific biomarkers and immune profiles (e.g., IgG subclasses, eosinophil cationic protein, C-reactive protein, IgA, IgG, IgM, total IgE, and specific IgE for staphylococcal enterotoxins, Alt a 1, Aspergillus fumigatus, and Alternaria alternata) that may predict the transition from IBS-like symptoms to chronic intestinal inflammation.Conclusions:This study aims to elucidate the pathophysiological role of LFH in IBS-like conditions and its progression to IBD. Early identification of high-risk individuals could enable precision medicine approaches, fostering targeted preventive and therapeutic strategies in chronic intestinal disorders.

COMPLEX MANAGEMENT OF A PLURICOMORBID PATIENT WITH PLATYPNEA-ORTHODEOXIA SYNDROME

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Background: Platypnea-orthodeoxia syndrome is a rare disorder characterized by dyspnea and oxygen desaturation in upright position, with improvement of symptoms and blood oxygenation in supine position. A right-to-left shunt (intracardiac or pulmonary) or a ventilation/perfusion mismatch are necessary to develop the syndrome: atrial septal defects, including patent foramen ovale (PFO), are known to be frequent causes. High level of suspicion, especially with hypoxemia without significant pulmonary disease, that does not easily correct with supplemental oxygen, should lead the clinician to obtain echocardiographic imaging, documenting right to left shunting. Transcatheter closure of the congenital interatrial communication is highly successful in relieving symptoms of dyspnea and resolving hypoxemia in the majority of patients.
Case report: A 71-year-old man presented to the emergency department for dyspnea and desaturation up to values of 88%; cardiac and pulmonary objectivity were normal. His medical history included arterial hypertension, previous lacunar ischaemic stroke, cerebral microhaemorrhages with mixed genesis (hypertensive and probable cerebral amyloid angiopathy), traumatic bilateral frontal intraparenchymal and subarachnoid cerebral haemorrhage. Blood gas analysis performed during oxygen therapy (40% inspired O2 fraction) showed a pO2 value of 54 mmHg and a pCO2 value of 20 mmHg. A contrast-enhanced thoracic CT scan was performed for suspected pulmonary thromboembolism, which was excluded; furthermore, there were no pulmonary phlogistic thickening or pleural effusion. Blood tests did not show an increase in inflammatory indices. Nasopharyngeal swabs for SARS-CoV-2, influenza A/B and respiratory syncytial virus were negative. The patient was admitted to High Care Internal Medicine Unit and during his stay he developed multiple episodes of desaturation and hypoxaemia, only partially corrected with high-flow oxygen therapy: most of them occurred in orthostatism, with partial regression by assuming the supine position. A cardiological origin of the disease was considered most probable, therefore the patient underwent a transthoracic echocardiography and, upon its limited usefulness because of very poor acoustic window, a transcranial Doppler ultrasound with microbubble, which evidenced high intensity transient signals (HITS) with massive passage in a "shower curtain" pattern. A transesophageal echocardiogram was subsequently performed, which confirmed the presence of severe right-to-left shunt from a probable PFO. In view of the high complexity of the case (PFO likely conditioning platypnea-orthodeoxia syndrome, cerebral ischaemic outcomes, recent cerebral subarachnoid haemorrhage and cerebral microhaemorrhages in the context of amyloid angiopathy) a multidisciplinary assessment was performed with cardiologist and neurologist. From a cardiology point of view, there would be indication for interventional closure of PFO, with the subsequent need for double antiplatelet therapy (DAPT) for at least 6 months; however, after assessing the risk/benefit ratio and the patient's clinical history, it was noted that the procedure would have entailed an excessive cerebral haemorrhagic risk following the introduction of DAPT, and was therefore not performed.
The patient was then discharged once weaned from oxygen therapy at rest stance with a remaining need for support with low-flow oxygen therapy during mobilisation.
Conclusions: This report shows a clinical case of platypnea-orthodeoxia syndrome due to the most common cause, a patent foramen ovale. However, the complexity of the clinical scenario did not allow a definitive treatment, but forced to find a compromise by making a risk/benefit balance on the individual patient.

ULTRASOUND DIAGNOSIS OF PNEUMONIA: A CASE REPORT

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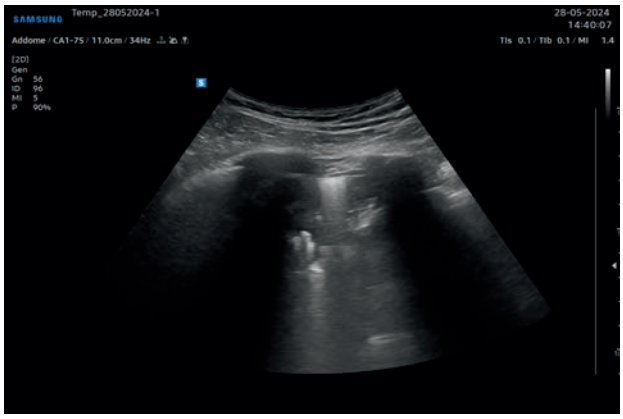
Background: A 54-year-old man presented himself in the emergency room with worsening dyspnea for a few hours and persistent fever for approximately three days. He appeared tachypnoeic, with a respiratory rate of 28 breaths/minute, pyretic (TC 38.5°C), with normal vital signs. It was performed an arterial blood gas analysis which showed pO2 equal to 64 and subsequent placement of oxygen therapy. Blood tests revealed leukocytosis with predominance of neutrophils, PCR 18 mg/dl, negative troponin.
Case history: In view of the clinical picture, a bedside thoracic ultrasound (TUS) was performed. The ultrasound examination highlighted a consolidated hypoechoic area with a dynamic air bronchogram in the right upper lobe, compatible with a focus of pneumonia.
For diagnostic confirmation and better characterization of the extension of the pathology, a chest CT was performed which confirmed the presence of a large consolidative area with air bronchogram in the upper lobe of the right lung, without significant pleural effusion.
Discussion: Although CT is the gold standard in the diagnosis of pneumonia, TUS offers a good radiation-free alternative, is portable and can be used at the bedside, but is operator-dependent and less detailed than CT [1].



2A CHALLENGING DIFFERENTIAL DIAGNOSIS OF SEVERE HYPERTRIGLYCERIDEMIA

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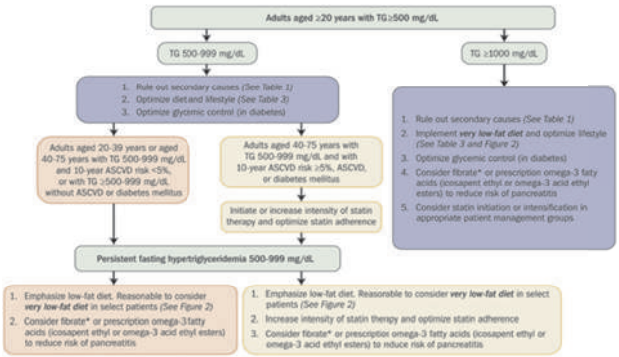
The patient is a 24-year-old Caucasian woman referred to our clinic in July 2022 by the Emergency Department due to the following abnormal laboratory findings while on lipid-lowering therapy with omega-3 (1000 mg three times daily), fenofibrate (200 mg), and ezetimibe/simvastatin (10/10 mg): total cholesterol 517 mg/dL, HDL 21 mg/dL, triglycerides 3200 mg/dL, LDL cholesterol 144 mg/dL, and HbA1c 7.2%. The patient reported elevated triglyceride levels since at least 2015 and was diagnosed with type 1 diabetes mellitus in 2016. At that time, she began basal-bolus insulin therapy as well as fibrate treatment. In 2017, she experienced her first episode of pancreatitis and was discharged on fibrates and omega-3. Her therapy was gradually optimized over the years to the regimen in place at the time of the Emergency Department

visit. She also reported hepatic steatosis and a family history of hypertriglyceridemia (father affected).
Given the triglyceride levels, the patient underwent a diagnostic scoring assessment for familial chylomicronemia syndrome (FCS), obtaining a score of 10, suggestive of a very likely diagnosis. A genetic test was subsequently performed at our university hospital to further clarify the differential diagnosis between FCS and multifactorial chylomicronemia syndrome (MCS). To better stratify cardiovascular risk, a carotid ultrasound with Doppler was performed, showing increased intima-media thickness (IMT 1.2 mm) on the right side without stenosis.
Follow-up visits revealed a wide fluctuation in triglyceride levels, ranging from 200 to 2000 mg/dL, which showed some correlation with HbA1c values (6.8%–8.6%). Her weight also varied over time, with an initial reduction followed by regain, remaining within the overweight BMI range. The genetic test did not reveal mutations in genes associated with FCS (LPL, APOA5, APOC2), nor did it show macrodeletions or macroduplications in the LPL gene. However, the possibility of other variants or major rearrangements in regions not analyzed by the current protocols, or in other potentially related genes, could not be excluded.
In January 2023, the patient was hospitalized for a second episode of pancreatitis, with a triglyceride level of 1811 mg/dL at admission. At the subsequent follow-up in July 2023, fenofibrate (145 mg) was replaced with gemfibrozil (600 mg), and omega-3 was increased to four capsules per day (1000 mg each). A new genetic test was performed using a broader panel including: **LPL, APOC2, APOA5, GPIHBP1, LMF1, GPD1, APOE, ANGPTL3, CREB3L3, APOC1, APOC3, APOC4, APOA1, APOA4, GCKR, LRP1**, all of which returned negative results.
Discussion: The collective findings in this clinical case point more strongly toward a diagnosis of **Multifactorial Chylomicronemia Syndrome (MCS)**. When analyzing the components of the diagnostic score (Fig. 2), the repeated fasting triglyceride values >1000 mg/dL, history of pancreatitis, poor response to lipid-lowering therapy, and the patient's age are suggestive of FCS. Conversely, the presence of a family history of hypertriglyceridemia and concomitant diabetes (a known secondary cause of hypertriglyceridemia) argue in favor of MCS. In this case, diabetes, in the presence of a predisposing genetic alteration, may have unmasked and exacerbated hypertriglyceridemia. Although an even broader gene panel could theoretically be useful, the available genetic testing – in line with current knowledge – does not support a diagnosis of FCS and instead favors MCS. Regardless of the specific diagnosis, **severe hypertriglyceridemia** is a condition that must be identified and treated due to the high risk of acute pancreatitis, and finding the optimal therapeutic approach remains a challenge. Moreover, the coexistence of diabetes and hypertriglyceridemia likely increases cardiovascular risk, making the achievement of therapeutic goals even more urgent. The presence of hepatic steatosis and mild intima-media thickening are concerning signs, especially considering the young age of the patient.
Volanesorsen, an antisense oligonucleotide that inhibits apoC-III production, has been shown to reduce triglyceride levels by 77% in FCS and is reimbursable in genetically confirmed FCS patients with a history of acute pancreatitis despite dietary and pharmacological therapy with fibrates and omega-3. Recently, this drug has also shown a 71.2% reduction in triglyceride levels in patients with MCS, and an extension of its indication to this patient population is currently awaited.



A LIFE ON THE EDGE: THE CRUCIAL ROLE OF EARLY DIAGNOSIS IN SURVIVING WELLENS' SYNDROME

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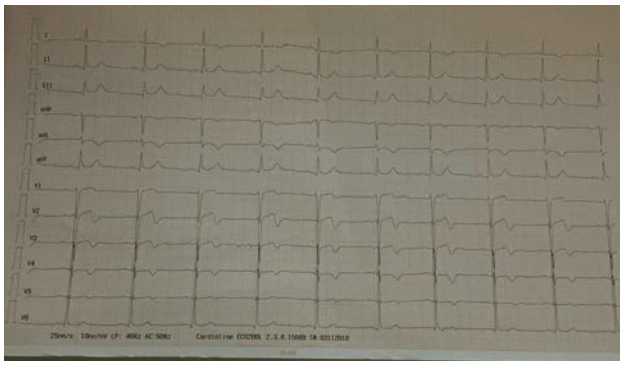
A 40-year-old physically active, normal-weight man presented to the emergency department with retrosternal chest pain at rest, which had started approximately two hours earlier. The pain was not affected by movement or breathing, radiated to the left upper limb, and was associated with diaphoresis. On presentation, there were no signs of dyspnea or congestive heart failure. Blood pressure was slightly elevated (140/90 mmHg), while other vital parameters were within normal limits. The patient was a heavy smoker and had a family history of cardiovascular disease. His past medical history included surgery for a herniated disc and carpal tunnel syndrome. Cardiac, thoracic, and abdominal examinations were unremarkable.
The ECG revealed biphasic T waves in leads V2–V3 and inverted T waves in leads I and aVL. Laboratory tests showed elevated cardiac enzymes, while routine blood tests were within normal limits. Given the suspicion of Wellens' syndrome, the patient was transferred to the coronary care unit (CCU) for urgent coronary angiography, which revealed acute atherothrombotic occlusion of the mid left anterior descending (LAD) artery, treated with PCI and drug-eluting stent (DES), and moderate stenosis of the distal right coronary artery (RCA). Post-procedure, the patient was monitored in the CCU, where approximately four hours after the angiography, a short episode of non-sustained ventricular tachycardia (4 beats) was recorded on telemetry.
The following day, he was transferred to the intensive cardiology unit, where a 24-hour Holter ECG was performed and showed no significant arrhythmic events, with a mean heart rate of approximately 60 bpm. During hospitalization, clinical, laboratory, and echocardiographic evaluations demonstrated preserved left ventricular function (LVEF estimated at 55%). Thrombophilia screening was negative; familial hypercholesterolemia screening is ongoing.
He was discharged in stable clinical condition with the diagnosis of "NSTEMI with angiographic evidence of mid-LAD occlusion treated with PCI and DES." He was strongly advised to quit smoking and was prescribed the following home therapy: esomeprazole 20 mg once daily, aspirin 100 mg once daily, prasugrel 10 mg once daily, and ezetimibe/atorvastatin 10/80 mg once daily.
At the one-month outpatient follow-up, laboratory tests and Holter ECG were within normal limits, with a mean heart rate of 58 bpm.
Discussion: Wellens' syndrome, also known as the "left anterior descending coronary syndrome," is characterized by specific electrocardiographic changes due to a critical stenosis of the proximal LAD artery. Two ECG patterns are described: Type A (25% of cases) with biphasic T waves (positive-negative) in V2 and V3; and Type B (75% of cases) with deeply and symmetrically inverted T waves in V2 and V3, sometimes extending to V1, V4–V6. Both patterns are associated with an isoelectric or slightly elevated ST segment. Cardiac biomarkers are usually normal or mildly elevated.
Risk factors for Wellens' syndrome are similar to those for coronary artery disease and include hypertension, diabetes, dyslipidemia, obesity, and smoking. The syndrome is caused by transient occlusion of the LAD artery, usually due to plaque rupture with subsequent clot lysis or spontaneous resolution of the occlusion before the onset of myocardial infarction. However, due to unstable coronary perfusion, these patients are at high risk of developing a large anterior wall myocardial infarction and potentially sudden death.
Symptomatically, patients typically present with signs consistent with acute coronary syndrome, including oppressive chest pain radiating to the neck, jaw, or shoulder, often triggered by exertion and relieved by rest. Nevertheless, patients may be pain-free at the time of presentation, making prompt recognition of the ECG pattern vital. Immediate management is crucial and includes transfer to a coronary care unit for continuous monitoring and urgent coronary angiography to assess the severity of stenosis and guide the appropriate intervention (either percutaneous coronary intervention or coronary artery bypass grafting). Until definitive treatment is provided, Wellens' syndrome should be managed similarly to acute myocardial infarction, including antiplatelet therapy with aspirin, anticoagulation with heparin, nitrates, and beta-blockers (if the patient is not hypotensive).



WOLFRAM SYNDROME: A RARE BUT CRITICAL DIAGNOSIS BEHIND HYPERGLYCEMIA

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A 35-year-old male presented to the out-of-hours care service with hyperglycemia. His past medical history revealed a diagnosis of type 1 diabetes mellitus at the age of 14. Over recent years, he experienced progressive visual acuity loss and worsening sensorineural hearing loss. There was no family history of diabetes or neurological disorders.
Since childhood, the patient had reported polyuria and polydipsia, requiring insulin therapy early on. Glycemic control had been suboptimal, with persistent difficulty in achieving therapeutic targets. In the past few years, he developed blurred vision and reading difficulties, along with bilateral sensorineural hearing loss, predominantly at low frequencies. He denied central neurological symptoms such as headache or vertigo.
Following treatment for hyperglycemia, the patient was referred for diabetic follow-up and further diagnostic evaluation.
Clinical Examination: Ophthalmological examination revealed proliferative diabetic retinopathy with retinal neovascularization, reduced visual acuity, and peripheral visual field loss. Audiometric testing confirmed bilateral sensorineural hearing loss, more severe at low frequencies. The general neurological examination was within normal limits, with no focal deficits.
Laboratory and Imaging Studies: Persistent hyperglycemia was noted (fasting glucose 280 mg/dL, HbA1c 9.8%) along with ketonuria. Brain CT and MRI did not show any significant structural abnormalities.
Diagnosis and Discussion: The clinical picture raised suspicion for Wolfram syndrome, a rare genetic disorder characterized by the combination of type 1 diabetes mellitus, optic atrophy, and sensorineural hearing loss, due to mutations in the **WFS1** gene. The diagnosis was confirmed by genetic testing. The differential diagnosis includes other forms of diabetes associated with neurological or sensory disorders, such as DIDMOAD syndrome (Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy, and Deafness), which shares overlapping features.
Treatment and Management: Management is symptomatic and multidisciplinary. Optimization of insulin therapy is essential to minimize the risk of microvascular complications. Regular ophthalmologic monitoring is crucial to assess indications for laser photocoagulation or anti-VEGF therapy. Hearing loss management includes audiologic follow-up and potential use of hearing aids. Genetic counseling is recommended for the patient and family to assess transmission risk and provide psychological support.
Conclusion: Wolfram syndrome represents a diagnostic and management challenge, requiring a multidisciplinary approach to ensure personalized and integrated care. Awareness of such rare conditions is critical for early diagnosis and optimal management, aiming to improve the patient's quality of life.

IDIOPATHIC DEEP VEIN THROMBOSIS REVEALING SILENT CROHN'S DISEASE: A DIAGNOSTIC PITFALL AND THERAPEUTIC CHALLENGE

Bracco C.[1], Komguem Simo V.[2], Melchio R.[1], Fenoglio L.[1], Dupuis A.[2], Galliano R.[2], Biagini F.[2], Sasia G.[2], Posilico F.[2], Mao F[2], Ferrua A.[2], Morgillo T.[1], Ruoco I.[1], Polla V.[1], Testa E.[2]
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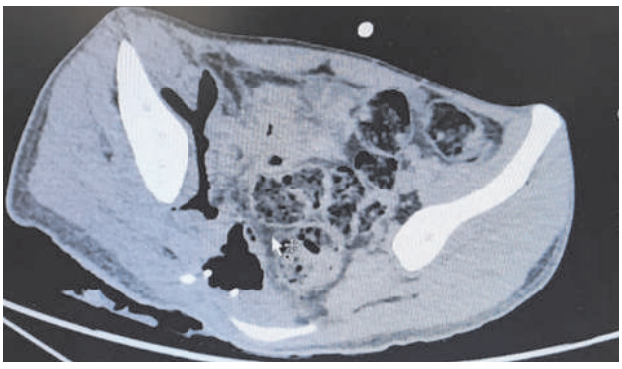
Introduction: Crohn's disease can present extraintestinal manifestations even in the absence of overt gastrointestinal symptoms. Deep vein thrombosis (DVT), although rare as an initial presentation, may represent an early and underrecognized sign of the disease. We present a paradigmatic clinical case of complicated Crohn's disease diagnosed in the subacute phase in a young patient with idiopathic DVT.
Case report: A 25-year-old male factory worker, active smoker, with a Western diet, normal weight, and regular physical activity, had a past medical history notable only for asthma and persistent idiopathic DVT diagnosed in December 2024, treated with rivaroxaban 20 mg. He presented it to the Emergency Department three months later with a weight loss of 10 kg and right-sided Lumb sciatica unresponsive to analgesics. He denied fever, diarrhea, melena, or other symptoms. Physical examination revealed only a limitation in right leg extension. Blood tests showed normocytic anemia, thrombocytosis, elevated inflammatory markers, and increased ALP and GGT. Initial imaging (chest, pelvis, sacroiliac joints, right femur X-rays, and abdominal ultrasound) was negative. During observation, due to worsening clinical picture and suspicion of septic picture, the patient was admitted to Internal Medicine, where thrombophilic screening (fibrinogen 668, ATIII 79, FVL absent, normal C and S proteins, normal Factor II, prothrombin 20210 mutation, Apl, coagulative C and S proteins, homocysteinemia in the normal range), Autoimmune screening (anti-cardiolipin antibodies, anti-beta2GPI negative, anti-MOG negative), Blood culture/uroculture, CT abdomen with mdc and CT pelvis/sacroiliac joints which showed a voluminous abscess at the right iliopsoas muscle associated with ileal thickening and enterovesical fistula. CT scan and pancolonscopy oriented toward complicated Crohn's type IBD. Initiated antibiotic therapy and EBPM. After multidisciplinary discussion (interventional radiologist, general surgeon, infectiology's, gastroenterologist, orthopedic surgeon, anesthesiologist-algologist, urologist, dietician, internist), percutaneous abdominal drainage, placement of caval filter, and right hemicolectomy were performed, with subsequent histologic diagnosis confirmed. During the hospital stay, further investigations such as procalcitonin 1412, resting color Doppler echocardiogram (to exclude PFO), CT abdomen (to exclude entero-vesical fistulae), lower extremity venous Echo-ColorDoppler (for indication of preoperative caval filter placement) were performed.
Discussion: The case highlights the importance of broad clinical suspicion and a multidisciplinary approach in the management of idiopathic DVT in young adults. Chronic inflammatory bowel disease (IBD) is a systemic condition that manifests not only at the gastrointestinal level, but also with extraintestinal symptoms (EIM), which can significantly impair quality of life and appear before or after diagnosis: 26% of patients report their onset up to 25 months earlier (median of 5 months) (1). In patients with IBD thromboembolic events, both arterial and venous. Venous thromboembolism (VTE) is up to 3-4 times more frequent than in the general population and is considered a major cause of morbidity and mortality in these patients. Among the most common locations of DVT in individuals with IBD are the lower limbs; disease activity, the presence of fistulas and abscesses are significant risk factors for the occurrence of VTE (2). Specifically, in our clinical case, DVT was found to be the initial manifestation of complicated and hitherto silent Crohn's disease, with subsequent identification of abscess, fistula, and ileal thickening. The therapeutic management of VTE in patients with IBD therefore requires careful evaluation of the risk-benefit balance, supported by the latest scientific evidence. Long-term follow-up is also essential to assess thrombotic risk and decide on the appropriateness of prolonged or permanent anticoagulation therapy.
Conclusion: Early recognition of thromboembolic manifestations as a possible telltale sign of IBD can radically alter the diagnostic-therapeutic course. More clinical awareness is needed to avoid delays in diagnosis and optimize thrombotic risk management in young patients with idiopathic DVT.
Bibliography:
(1) Rogler, G. et al. Extraintestinal Manifestations of Inflammatory Bowel Disease. Gastroenterology. 2021; 161(4): 1118-1132.
(2) Gala D. et al. Thromboembolic events in patients with inflammatory bowel disease: a comprehensive overview. Diseases. 2022; 10(4): 73.
(3) ECCO guidelines on extraintestinal manifestations in inflammatory bowel disease, Journal of Crohn's and Colitis , Volume 18, Number 1, January 2024,
(4) American Society of Hematology. Guidelines for Management of Venous Thromboembolism. Blood Adv. 2020; 4(19): 4693-4738.



Abscess at the right iliopsoas muscle associated with ileal thickening and enterovesical fistula

SPONTANEOUS RENAL HEMATOMA, ATYPICAL COMPLICATION OF MICROSCOPIC POLYANGIITIS: A CASE REPORT.

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Background: Microscopic polyangiitis (MPA) represents a systemic disorder characterized by multi-organ involvement, typically including rapidly progressive glomerulonephritis, interstitial lung involvement and peripheral neuropathy, often associated with anti-Myeloperoxidase (p-ANCA) antibodies. Spontaneous renal hematoma is a rare complication of ANCA-associated vasculitis, more commonly associated with polyarteritis nodosa (1). We report a case of MPA presenting with this unusual complication.
Case presentation: An 82-year-old female with a medical history of asthma, arterial hypertension, and previous Hepatitis B Virus (HBV) infection presented at the Emergency Department (ED) of Cisanello Hospital (Pisa) because of persistent myalgias and worsening general condition.
She had a recent prior ED visit to the Versilia Hospital (Viareggio) for palpitations and lower limb edema, reporting the onset, approximately one month earlier, of proximal arthro-myalgias with functional limitation, associated with mild weight loss and marked asthenia. On that occasion findings included preserved renal function (creatinine 0.72 mg/dL), elevated C-reactive protein (CRP 18 mg/dL), and neutrophilic leukocytosis. In light of those findings, along with low-grade fever and a chest X-ray suggestive of faint middle lobe consolidation, she was discharged on empiric antibiotic therapy following a normal echocardiogram and a brief observation period in the Observation Unit.
On the current admission via the ED, findings included acute kidney injury (Creatinine 2.06 mg/dL) with normal renal ultrasound, moderate normocytic anemia, neutrophilic leukocytosis, mild thrombocytosis, and persistently elevated inflammatory markers (CRP 20.8 mg/dL, Procalcitonin 1.2 ng/mL). The patient was admitted to the Internal Medicine ward, where further deterioration of the renal function was observed, including non-nephrotic range 24-hour proteinuria (310 mg/day) and microhematuria with an active urinary sediment. Renal artery Doppler ultrasound showed no evidence of significant stenosis or venous thrombosis. Urine output was maintained with mild diuretic stimulation.
Empiric antibiotic therapy with piperacillin/tazobactam, initiated in the ED, was subsequently discontinued due to no evidence of infection (negative microbiological workup).
Considering the arthro-myalgic presentation, steroid therapy with methylprednisolone 20 mg/day was initiated, resulting in a marked and rapid clinical improvement. High-resolution computed tomography (HRCT) of the chest revealed diffuse ground-glass opacities bilaterally involving the upper and lower lobes. Subsequent serial chest X-rays showed progression of interstitial thickening with the development of a reticulo-micronodular pattern. Due to the onset of lower limb dysesthesias, nerve conduction studies (NCS) were performed, revealing evidence of bilateral sensory-motor neuropathy.
Serological workup revealed positive Antinuclear Antibodies (ANA) (titer 1:160, fine dense speckled pattern) and positive p-ANCA (38 IU/mL); Extractable Nuclear Antigens (ENA) and c-ANCA were negative.
In light of the multi-organ involvement consistent with ANCA-positive vasculitis, specifically microscopic polyangiitis (MPA), high-dose steroid therapy was initiated. Due to the detection of elevated HBV-DNA and CMV-DNA levels, antiviral therapy with entecavir and ganciclovir was initiated, and planned Rituximab therapy was deferred during the admission.
The clinical course was complicated by the onset of left iliac fossa pain, accompanied by acute worsening of anemia (Hemoglobin 7.1 g/dL) and further deterioration of renal function (creatinine 4.72 mg/dL). A contrast-enhanced thoraco-abdominal CT scan revealed active arterial bleeding at the left lower renal pole, a large subcapsular renal hematoma, and a large retroperitoneal hematoma. Consequently, the patient underwent angiography with successful embolization of two branches of the left renal artery.
Clinical stabilization ensued, with renal function plateauing at a creatinine level of approximately 2.8 mg/dL and stabilization of hemoglobin levels. The patient was subsequently discharged with instructions to continue a tapering course of steroid therapy.
The patient was followed up in the Rheumatology outpatient clinic, with documented stability of her clinical condition, creatinine levels, and complete blood count (CBC).
Conclusion: Spontaneous renal hematoma represents a rare but potentially life-threatening complication of MPA, likely due to to vasculitic involvement of renal vessels. This case underscores the diagnostic challenges posed by persistent non-specific constitutional symptoms, particularly in elderly patients, when initial symptoms are vague and mimic common conditions like infection. The case also highlights the importance of considering systemic vasculitis in the differential diagnosis of unexplained multi-organ dysfunction.

SUSPECTED CARDIAC SARCOIDOSIS PRESENTING AS RESUSCITATED SUDDEN CARDIAC ARREST AND HIGH-GRADE ATRIOVENTRICULAR BLOCK.

Bracco C.[1], Benso P.[2], Melchio R.[1], Galliano R.[1], Ferrua A.[3], Komguem Simo V.[3], Ruocco I.[1], De Caterina R.[4], Fenoglio L.[1]
[1]Division of Internal Medicine, Department of Medicine, "Santa Croce e Carle" Hospital, Cuneo, Italy; [2]School of Internal Medicine, University of Pisa, Italy; [3]School of Internal Medicine, University of Turin, Italy; [4]Cardiology Division, Pisa University Hospital, University of Pisa, Italy

Background: Cardiac sarcoidosis (CS) is an infiltrative granulomatous disease that can lead to conduction abnormalities, ventricular arrhythmias, heart failure, and sudden cardiac death (SCD) [1]. Diagnosing CS can be challenging, especially when it occurs in the absence of typical findings of pulmonary involvement.
Case presentation: We report the case of a 48-year-old male who experienced an out-of-hospital cardiac arrest due to ventricular fibrillation at his workplace. He was successfully resuscitated with cardiopulmonary resuscitation, two DC shocks and amiodarone, achieving return of spontaneous circulation before being intubated and transferred to the Emergency Department (ED). Initial electrocardiogram showed sinus rhythm with first-degree AV block (AVB) and right bundle branch block. While hemodynamically stable, an initial cardiac workup did not reveal a definitive cause. Total-body CT imaging excluded acute aortic syndromes and pulmonary embolism but revealed extensive pulmonary consolidations (likely due to aspiration), mediastinal and retroperitoneal lymphadenopathy, hepatosplenomegaly, and multiple hypodense lesions in the liver and kidneys. During ED observation, the patient developed third-degree AVB requiring temporary pacemaker insertion. Subsequent coronary angiography showed no significant coronary artery disease. Following the transfer to the ICU and then to the Cardiology Unit, he experienced multiple episodes of non-sustained ventricular tachycardia. Echocardiography revealed biventricular dilation with moderately reduced left ventricular ejection fraction (LVEF 43%). After the temporary pacemaker's removal, high-degree AVB recurred. Cardiac MRI (CMR) demonstrated multiple focal areas of late gadolinium enhancement in both ventricles, suggestive of granulomatous lesions consistent with CS. A PET-CT scan supported this tentative diagnosis, showing patchy myocardial hypermetabolism and widespread hypermetabolic lymphadenopathy. Nevertheless, the biopsy of an inguinal lymph node was non-diagnostic and serum ACE levels were normal. Infectious and hematologic workup was negative.
Management and Outcome: Due to recurrent high-degree AVB and previous cardiac arrest due to ventricular fibrillation in the context of suspected CS, a cardiac resynchronization therapy defibrillator was implanted. The patient was discharged with a diagnosis of suspected multisystem sarcoidosis with cardiac involvement. Given the high clinical and imaging suspicion despite the non-diagnostic biopsy, empiric high-dose tapering steroid therapy was initiated ad juvantibus.
Conclusion: This case highlights cardiac sarcoidosis as a critical differential diagnosis in a patient presenting with resuscitated SCD, particularly when associated with conduction system disease in an individual <60 years of age and systemic findings. Advanced cardiac imaging (CMR, PET-CT) plays a crucial role in making a diagnosis when histological confirmation is challenging, by guiding management decisions including device implantation and immunosuppressive therapy. Given the high risk of malignant ventricular arrhythmias, in patients with cardiac sarcoidosis who have AVB requiring permanent pacing, an implantable cardioverter-defibrillator is preferred over a conventional pacemaker.
References: 1.Cheng RK, Kittleson MM, Beavers CJ,et al. Diagnosis and Management of Cardiac Sarcoidosis: A Scientific Statement From the American Heart Association. Circulation 2024; 149(21):e1197-e1216

IDIOPATHIC DEEP VEIN THROMBOSIS REVEALING SILENT CROHN'S DISEASE: A DIAGNOSTIC PITFALL AND THERAPEUTIC CHALLENGE

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Introduction: Crohn's disease can present extraintestinal manifestations even in the absence of overt gastrointestinal symptoms. Deep vein thrombosis (DVT), although rare as an initial presentation, may represent an early and underrecognized sign of the disease. We present a paradigmatic clinical case of complicated Crohn's disease diagnosed in the subacute phase in a young patient with idiopathic DVT.
Case report: A 25-year-old male factory worker, active smoker, with a mediterranean diet, normal weight, and regular physical activity, had a past medical history notable only for asthma and persistent idiopathic DVT diagnosed in

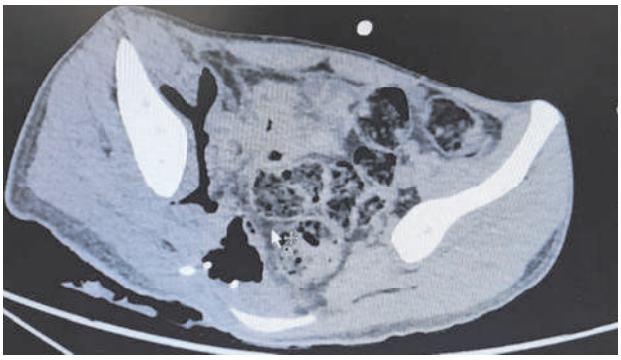
December 2024, treated with rivaroxaban 20 mg. He presented it to the Emergency Department three months later with a weight loss of 10 kg and right-sided Lumb sciatica unresponsive to analgesics. He denied fever, diarrhea, melena, or other symptoms. Physical examination revealed only a limitation in right leg extension. Blood tests showed normocytic anemia, thrombocytosis, elevated inflammatory markers, and increased ALP and GGT. Initial imaging (chest, pelvis, sacroiliac joints, right femur X-rays, and abdominal ultrasound) was negative. During observation, due to worsening clinical and suspicion of septic, the patient was admitted to Internal Medicine, where thrombophilic screening (fibrinogen 668, ATIII 79, FVL absent, normal C and S proteins, normal Factor II, prothrombin 20210 mutation, Apl, coagulative C and S proteins, homocysteinemia in the normal range), Autoimmune screening (anti-cardiolipin antibodies, anti-beta2GPI negative, Blood culture/ uroculture, CT abdomen with mdc and CT pelvis/sacroiliac joints which showed a voluminous abscess at the right iliopsoas muscle associated with ileal thickening and enterovesical fistula. CT scan and pancolonscopy oriented toward complicated Crohn's type IBD. Antibiotic therapy and EBPM were administered. After multidisciplinary discussion (interventional radiologist, general surgeon, infectiology's, gastroenterologist, orthopedic surgeon, anesthesiologist-algologist, urologist, dietician, internist), percutaneous abdominal drainage, placement of caval filter, and right hemicolectomy were performed, with subsequent histologic diagnosis confirmed. During the hospital stay, further investigations such as procalcitonin 1412, resting color Doppler echocardiogram (to exclude PFO), CT abdomen (to exclude entero-vesical fistulae), lower extremity venous Echo-ColorDoppler (for indication of preoperative caval filter placement) were performed.

Discussion: The case highlights the importance of broad clinical suspicion and a multidisciplinary approach in the management of idiopathic DVT in young adults. Chronic inflammatory bowel disease (IBD) is a systemic condition that manifests not only at the gastrointestinal level, but also with extraintestinal symptoms (EIM), which can significantly impair quality of life and appear before or after diagnosis: 26% of patients report their onset up to 25 months earlier (median of 5 months) (1). In patients with IBD thromboembolic events, both arterial and venous. Venous thromboembolism (VTE) is up to 3-4 times more frequent than in the general population and is considered a major cause of morbidity and mortality in these patients. Among the most common locations of DVT in individuals with IBD are the lower limbs; disease activity, the presence of fistulas and abscesses are significant risk factors for the occurrence of VTE (2). Specifically, in our clinical case, DVT was found to be the initial manifestation of complicated and hitherto silent Crohn's disease, with subsequent identification of abscess, fistula, and ileal thickening. The therapeutic management of VTE in patients with IBD therefore requires careful evaluation of the risk-benefit balance, supported by the latest scientific evidence. Long-term follow-up is also essential to assess thrombotic risk and decide on the appropriateness of prolonged or permanent anticoagulation therapy.

Conclusion: Early recognition of thromboembolic manifestations as a possible telltale sign of IBD can radically alter the diagnostic-therapeutic course. More clinical awareness is needed to avoid delays in diagnosis and optimize thrombotic risk management in young patients with idiopathic DVT.

Bibliography:

(1) Rogler, G. et al. Extraintestinal Manifestations of Inflammatory Bowel Disease. Gastroenterology. 2021; 161(4): 1118-1132.
(2) Gala D. et al. Thromboembolic events in patients with inflammatory bowel disease: a comprehensive overview. Diseases. 2022; 10(4): 73.
(3) ECCO guidelines on extraintestinal manifestations in inflammatory bowel disease, Journal of Crohn's and Colitis , Volume 18, Number 1, January 2024.
(4) American Society of Hematology. Guidelines for Management of Venous Thromboembolism. Blood Adv. 2020; 4(19): 4693-4738.



LONG-TERM OUTCOMES OF ANTITHROMBOTIC TREATMENTS IN RETINAL VEIN OCCLUSION

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Background: Retinal vein occlusion (RVO) is a leading cause of visual impairment and its occurrence has been associated with a broad spectrum of thrombotic risk factors. Antithrombotic agents are commonly prescribed, but their impact on long-term outcomes remains uncertain.
Aim of the study: To evaluate the impact of antithrombotic treatment on long-term clinical outcomes in RVO patients.
Methods: This is a multicenter, retrospective, observational study of patients with RVO from three academic hospitals. Incidence rates per 100 person-years (PY) were calculated for recurrent RVO, cardiovascular events, venous thromboembolic events, bleeding complications, and death.
Results: Between 2004 and 2023, 198 patients were included (median age 65 years, IQR: 54-75; 105 females, 53.0%) and followed for a median of 2.6 (IQR: 0.9-4.5) years. 41.4% received antiplatelet therapy, 15.7% anticoagulant therapy, and 58.6% received no antithrombotic treatment. The incidence rate of cardiovascular events and mortality rate were higher in the untreated (vs treated) group (3.8 events per 100 PY, 95% CI 1.6-9.3 and 5.8 deaths per 100 PY, 95% CI 3.0-11.1 in the untreated group versus 0.6 events per 100 PY, 95% CI 0.2-2.0 and 1.5 deaths per 100 PY, 95% CI 0.7-3.0 in the treated group, respectively). Thirteen (6.6%) patients experienced recurrent RVO, with similar rates across treatment subgroups. Bleeding complications occurred in 27 (13.6%) patients with no differences across treatment groups. Table 1 shows the incidence rates of all relevant outcomes comparing untreated patients, those who received antiplatelet treatment and those who received anticoagulant treatment.
Conclusions: Our study shows that patients with RVO who did not receive any antithrombotic therapy had a higher incidence rate of cardiovascular events as well as higher mortality rate as compared with treated patients, while no difference was found with respect to recurrent RVO and bleeding complications.

Events	Number	PY	IR * 100PY	95% CI	IRR (95% CI) I: No treatment vs Antiplatelet II: No treatment vs Anticoagulant III: Antiplatelet vs Anticoagulant
RVO Recurrences					
No treatment	3	134.6	2.2	0.7-6.9	I: 0.9 (0.2-3.5)
Antiplatelet treatment	9	356.3	2.5	1.3-4.8	II: 2.3 (0.28-119.5)
Anticoagulant treatment	1	102.1	1.0	0.1-6.5	III: 2.6 (0.4-113.4)
Cardiovascular Arterial Events (AMI, Stroke)					
No treatment	5	129.6	3.8	1.6-9.3	I: 7.0 (1.1-73.1)
Antiplatelet treatment	2	360.6	0.5	0.1-2.2	II: 4.2 (0.5-199.3)
Anticoagulant treatment	1	109.2	0.9	0.1-6.5	III: 0.6 (0.0-35.7)
Venous Thromboembolic Events					
Antiplatelet treatment	8	355,28	2.2	1.1-4.5	/
Hemorrhagic Events (excluding retinal bleedings)					
No treatment	7	136.2	5.1	2.4-10.8	I: 1.2 (0.4-3.1)
Antiplatelet treatment	15	344.8	4.3	2.6-7.2	II: 1.0 (0.3-3.8)
Anticoagulant treatment	5	92.2	5.4	2.2-13.0	III: 0.8 (0.3-2.8)
Deaths					
No treatment	9	156.0	5.8	3.0-11.1	I: 5.2 (1.5-23.3)
Antiplatelet treatment	4	363.1	1.1	0.4-2.9	II: 2.1 (0.5-12.1)
Anticoagulant treatment	3	109.8	2.7	0.9-8.3	III: 0.4 (0.1-2.8)

238. ABILITY OF THE FIBROSIS-4 (FIB-4) INDEX TO PREDICT ALL-CAUSE MORTALITY IN A COHORT OF PATIENTS AT HIGH CARDIOVASCULAR RISK AND THE ROLE OF KIDNEY DYSFUNCTION

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Background: Coronary artery disease (CAD) and, more in general cardiovascular disease (CVD), still represents the main cause of mortality in Western Countries, with a major impact on healthcare costs. The prevalence of cardiometabolic risk factors (i.e. obesity, type 2 diabetes mellitus (T2DM), dyslipidemia, sedentary behavior and unhealthy dietary patterns) is constantly increasing in these Regions, and metabolic dysfunction-associated steatotic liver disease (MASLD) is a common manifestation. Similarly, chronic kidney disease represents a CV risk equivalent.
The fibrosis-4 (FIB-4) index is a non-invasive tool to predict the presence of advanced liver fibrosis in MASLD patients: indeterminate (≥1.3) and high (≥2.67) values of the FIB-4 index are significantly associated with an increased all-cause mortality risk, mainly due to CVD. In addition, a high FIB-4 score is also a risk factor for chronic kidney disease (CKD).
The aim of the present study was to investigate the association between FIB-4 index and risk of all-cause mortality in patients at high cardiovascular (CV) risk and to determine whether coexisting renal dysfunction mediates this association.
Materials and methods: Monocentric prospective study evaluating 994 patients with established or suspected coronary artery disease undergoing coronary angiography, followed for a median of 44 months. Mortality data were obtained through the Italian Health Card Database.
The FIB-4 score was calculated for each patient according to the following formula: (age [years] * AST [U/L])/(platelet [109/L] * √ALT [U/L]). The FIB-4 index was evaluated both as a continuous measure or categorized as low, indeterminate or high risk of advanced liver fibrosis using cut-offs previously shown to be associated with advanced fibrosis and in alignment with clinical guidelines (i.e., FIB-4 low risk: <1.3; indeterminate risk: ≥1.3 and <2.67; high risk: ≥2.67).
Results: At baseline, the median FIB-4 index was greater in deceased vs. alive patients (1.71 vs. 1.38, $p < 0.001$) and in those with reduced eGFR than in those with normal eGFR (1.65 vs. 1.37, $p < 0.001$). For each unit increase in the baseline log-FIB-4 index, the risk of all-cause mortality sharply increased during the follow-up (hazard ratio [HR] 2.31, 95%CI 1.31–4.08, $p = 0.004$). Similarly, assuming the lowest baseline FIB-4 risk category as the reference, the risk of all-cause mortality progressively increased across the indeterminate (HR 1.82, 95%CI 1.18–2.82, $p = 0.007$) and the highest baseline FIB-4 risk categories (HR 2.33, 95%CI 1.37–3.97; $p = 0.002$). A causal mediation analysis showed that about one-third of the effect of FIB-4 index on mortality risk was mediated by reduced eGFR (32.8 %, $p = 0.01$).
Conclusions: An increase in FIB-4 index represents a predictor of the long-term risk of all-cause mortality in a high-cardiovascular-risk population, independently from the underlying liver disease. Moreover, a reduction of eGFR can, at least in part, mediate this increased mortality risk.

IMPROVING PERFORMANCE OF CEUS LI-RADS WITH A MULTIPARAMETRIC ULTRASOUND-BASED RISK PREDICTION MODEL FOR HEPATOCELLULAR CARCINOMA: THE PERSON4 MODEL.

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Background: Hepatocellular carcinoma (HCC) accounts for 70–75% of primary liver tumors and remains a major global health burden. In patients with liver cirrhosis, HCC typically exhibits a characteristic dynamic vascular pattern on contrast-enhanced imaging with an arterial hyperenhancement followed by late and mild wash-out in the portal-venous phase. However, a substantial proportion of HCCs display atypical features, complicating non-invasive diagnosis and often necessitating liver biopsy, especially in cases classified as indeterminate (LR-3, LR-4, or LR-M) by CEUS LI-RADS. While CEUS is widely used for focal liver lesion (FLL) assessment due to its safety and real-time perfusion evaluation, its sensitivity remains suboptimal. Recent studies have proposed modifications to CEUS LI-RADS criteria, but challenges in differentiating HCC from non-HCC malignancies, such as metastases and intrahepatic cholangiocarcinoma, persist, particularly in patients with coexisting extrahepatic cancers. Dynamic Contrast-Enhanced Ultrasound (D-CEUS), which allows quantitative assessment of microvascular perfusion using standardized software, has shown promise in improving diagnostic accuracy for FLLs.
Aim: This study aims to evaluate the role of integrating D-CEUS into the diagnostic algorithm for HCC in cirrhotic patients undergoing liver biopsy.
Methods: Between January 2021 and November 2023, consecutive patients with chronic liver disease and liver nodules candidate for liver biopsy were enrolled in this prospective cohort study. CEUS was perfomed in all patients before biopsy and assessed by CEUS Liver Imaging Reporting and Data System (LI-RADS). Clips were examined by VueBox® software. Clinical and ultrasound parameters were compared among the different histological entities, analyzed with univariable analysis, and incorporated into a logistic regression model for HCC diagnosis. The diagnostic accuracy of the identified model was evaluated by Receiver Operating Characteristic (ROC) curve and relative Area Under the Curve (AUC). The model was then tested on a validation cohort made of consecutive patients from two centers.
Results: A total of 88 patients (57 HCC, 17 intrahepatic cholangiocarcinoma, 11 liver metastases and 3 benign lesions) were enrolled. Statistically significant differences between HCC and non-HCC patients in the training cohort were incorporated in an optimal logistic regression model that included the following predictive variables: sex, number of nodules ≥4, peripheral rim-like hyperenhancement and Peak Enhancement percent change. The model displayed high accuracy (AUC 0.91) for diagnosis of HCC. In the validation cohort, the model showed a sensitivity of 48.8% and a specificity of 100.0%, with a PPV of 100.0%, maintaining a fair diagnostic accuracy (AUC of 0.74).
Conclusions: This model could improve the performance of CEUS LI-RADS criteria for non- invasive diagnosis of HCC, possibly leading to non-invasive diagnosis of HCC in nearly 50% of patients currently candidate for liver biopsy.
Keywords: dynamic contrast enhanced ultrasound, HCC, CEUS- LI RADS.

MULTIPARAMETRIC ULTRASOUND FOR THE PREDICTION OF THE OUTCOMES OF ENDOSCOPIC VARICEAL BAND LIGATION

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Background: Endoscopic Variceal Band Ligation (EVBL) is the primary treatment for high-risk varices in cirrhotic patients who cannot tolerate non-selective beta-blockers (NSBBs), and is also employed in secondary prophylaxis alongside NSBBs. Despite its effectiveness, up to 90% of patients show residual varices after a single EVBL session, requiring follow-up endoscopy within 2–4 weeks to assess treatment response and determine the need for further sessions. At present, there are no noninvasive methods available to accurately predict the outcome of EVBL. Currently, no noninvasive methods exist to reliably predict the outcome of EVBL.
Aim: The aim of this study was to identify noninvasive predictors of variceal eradication following EVBL using a multiparametric ultrasound approach, including B-mode imaging, 2D-Shear Wave Elastography, and Dynamic Contrast-Enhanced Ultrasound (DCE-US).
Materials and methods: Consecutive cirrhotic patients undergoing EVBL for bleeding prophylaxis, who were either intolerant to or had contraindications for beta-blockers, were prospectively enrolled. Prior to the first EVBL session (T0), all patients underwent abdominal ultrasound, including liver and spleen 2D-Shear Wave Elastography and Dynamic Contrast-Enhanced Ultrasound (DCE-US). Time–intensity curves were analyzed using VueBox® software in two regions of interest: the liver parenchyma and portal vein. One month later (T1), the same ultrasound assessments were repeated prior to follow-up endoscopy, which was used to evaluate variceal eradication, defined as either complete absence of varices or residual varices not requiring further ligation.
Results: A total of 41 patients were enrolled (mean age 63 ± 7.5 years; 75.6% male). Following the initial EVBL session at T0, 28 patients (68.3%) achieved variceal eradication, while 13 patients (31.7%) required a second EVBL at T1. Patients with successful eradication showed a significant reduction in spleen stiffness (SS) at T1 compared to baseline (39 kPa vs 52.5 kPa; $p = 0.014$). Logistic regression analysis confirmed that the percentage decrease in SS was a significant predictor of eradication (OR = 1.156, $p = 0.033$). Furthermore, changes in DCE-US parameters between T0 and T1 were also predictive. Spe-

cifically, increases in peak enhancement (PE; OR = 0.905, p = 0.003) and area under the curve (AUC; OR = 0.957, p = 0.009) in the liver parenchyma, along with percentage increase in PE (OR = 0.947, p = 0.003), AUC (OR = 0.947, p = 0.006), and wash-in rate (OR = 0.973, p = 0.029) in the portal vein, were significantly associated with variceal eradication.
Conclusions: Our study showed the sSpleen stiffness and DCE-US are reliable predictors of varices eradication after performing EVBL.

HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS SECONDARY TO VIRAL INFECTIOUS TRIGGER, IN PATIENTS WITH COMMON VARIABLE IMMUNODEFICIENCY AND SPLENOMEGALY

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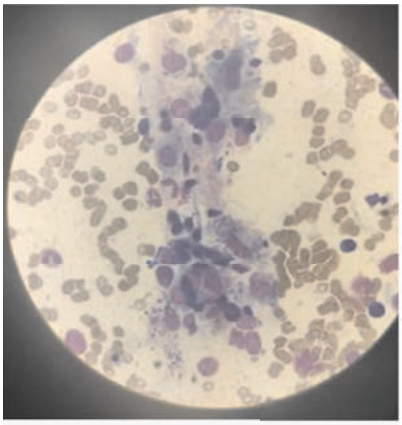
Background: Hemophagocytic lymphohistiocytosis (HLH) is a rare, severe hyperinflammatory syndrome. The main trigger in secondary forms are viral infections, especially EBV. Various alterations can be found on blood tests such as: hyperferritinemia, hypertriglyceridemia, hypofibrinogenemia and liver dysfunction, but none is pathognomonic.
Case report: A 73-year-old woman came to the ED for cough, dyspnea and fever; she had a history of hypogammaglobulinemia, recurrent bronchitis and splenomegaly, already investigated. In the ED were highlightened normocytic anemia, increased CRP and ground-glass pulmonary thickenings. She was admitted to Internal Medicine department with oxygen therapy and empirical antibiotic therapy. Fever persisted and she worsened with the onset of pancytopenia, hypoalbuminemia with anasarca, increase of hepatic enzymes, spleno and hepatomegaly. Infectious disease laboratory tests were performed and highlighted EBV viremia and the presence of Haemophilus Influenzae, Adenovirus and Rhinovirus/Enterovirus at bronchoalveolar lavage. Elevated level of triglycerides and ferritin were also found. In the strong suspicion of hemophagocytosis secondary to a probable infectious trigger, high-dose steroids and intravenous immunoglobulins were started. The patient continued to worsen therefore a therapy with Etoposide, Rituximab and Dexamethasone was started and a bone marrow aspirate (Fig.1) was performed, which confirmed HLH. EBV DNA copies rapidly decreased, however the patient died due to other infection occurred during hospitalization.
Conclusions: In patients with viral infection and worsening of general conditions, with characteristic laboratory alterations, is fundamental to consider HLH among differential diagnoses.
Ponnatt TS, Lilley CM, Mirza KM. Hemophagocytic Lymphohistiocytosis. Arch Pathol Lab Med. 2022 Apr 1;146(4):507-519. doi: 10.5858/arpa.2020-0802-RA. PMID: 34347856.



The marrow aspirate demonstrates clusters of activeted large macrophagic cells which contain various particles, cellular debris and multiple vacuoli. The blue dots consist mainly of iron-loaded ferritin. Charatteristically, erythroblasts and mieloid cells are found in the macrophagic cytoplasma after the phagocytic process

THE UNLIKELY PROTAGONIST OF A FEVER OF UNKNOWN ORIGIN

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Case presentation: We report the case of a 76 years old woman, admitted to our department for recurrent febrile episodes every 10-15 days, not accompanied by chills, started five months before, for which corticosteroids and non-specified antibiotics were prescribed. The patient presented a history of valvular heart disease, paroxysmal atrial fibrillation, arterial hypertension, dyslipidemia, pulmonary emphysema. She had recently undergone a mitral valvuloplasty for a severe mitral insufficiency. To rule out infectious causes of the fever, hemocultures, urine cultures, serologic tests (Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila, Coxiella Burnetii, HSV, VZV, EBV, CMV, HIV, HBV, HCV, Coxsackie virus, Leishmania, Leptospira, Histoplasma and Bartonella), Wright reaction, Quantiferon, B-D-Glucan, were performed, resulting negative. After 4 days of hospitalization, the patient presented fever (37.2°C) associated with chills, hence hemocultures and urine culture were performed again and tested negative. Complete blood count showed a normocytic normochromic anemia. C reactive protein levels increased up to 60 mg/L and procalcitonin was negative. A chest X-ray didn't show any inflammatory alterations, in presence of a left pleural effusion. The fever then resolved spontaneously. In the subsequent days, several hemocultures were performed in apyrexia, resulting negative. In consideration of the recent cardiac surgery, the patient underwent transthoracic and transesophageal echocardiogram, which ruled out infectious endocarditis.The patient presented a new-onset chest pain located to the left hemithorax, associated with a slight ST superelevation, for which high-sensitivity troponin was dosed, resulting within the normal limits. A high-resolution CT scan of the chest didn't show inflammation of the lungs and confirmed the presence of left pleural effusion. Autoantibodies were dosed to exclude autoimmune causes: p-ANCA, c-ANCA, ANA, anti- ENA SSA/Ro,anti- ENA SSB/La, anti-ENA Sm, anti-ENA RNP, anti-SCL 70, anti-ds DNA tested negative. C3, C4 and Immunoglobulins were within normal limits. Urinalysis was positive for dysmorphic erythrocytes. Due to the new-onset of pain in the left hemiface and left temporal region, the patient underwent a temporal artery ultrasound, which was negative for the "halo sign". A chest and abdomen CT scan with contrast didn't reveal enlarged lymph nodes or inflammatory foci. In consideration of the clinical history, the normochromic normocytic anemia, the presence of left pleural effusion, the urinalysis positive for dysmorphic erythrocytes, and to exclude autoinflammatory diseases or vasculitis a PET-CT scan was performed. The PET-CT scan showed a diffuse increased FDG uptake in relation to the wall of ascending and thoracic aorta. Given the clinical presentation and test results, our findings were consistent with a diagnosis of Clinically Isolated Aortitis. Hence, the patient was evaluated by a rheumatologist and corticosteroid therapy was prescribed.
Conclusions: Aortitis is an inflammatory disorder of the aorta that can result from infectious and non-infectious causes. It is most commonly associated with large vessel vasculitis, such as Giant Cell Arteritis and Takayasu's Arteritis. In rare cases, it can present as an isolated condition, referred to as Clinically Isolated Aortitis (CIA). This idiopathic form is hypothesized to be a variant of large vessel vasculitis. CIA primarily affects females in the seventh decade, most frequently involves the ascending aortic arch and thoracic aorta, and typically spares the aortic branches. Common symptoms are non-specific, comprising pain in the area involved by the inflammation, fever, chills and weight loss. Large vessel imaging is important for the diagnosis, in fact CT angiography can reveal thickening and enhancement of the vessel wall, aneurysms, findings suggestive of vasculitis; a functional study with FDG PET-CT can show active inflammation of the aorta as an elevated FDG uptake [1-3]. Early recognition is crucial, as aortitis carries a significant risk of vascular complications, including aortic aneurysm and dissection. Notably, in some cases these complications may represent the initial clinical presentation. Clinicians should maintain a high index of suspicion for isolated aortitis in patients presenting with unexplained systemic symptoms or imaging findings suggestive of vascular pathology, as early diagnosis is key to preventing life-threatening complications.

HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS COMPLICATING S.HOMINIS SEPSIS IN A PATIENT WITH ESOPHAGEAL CANCER: A CHALLENGING, LIFE-THREATENING DIAGNOSIS

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Background: Hemophagocytic lymphohistiocytosis (HLH) is a rare but life-threatening condition resulting from hyperinflammation caused by uncontrolled proliferation of activated immune cells. The prognosis is very poor if the cause is not promptly treated. It can be primary/genetic or secondary: the latter can be associated with autoimmunity, immunodeficiency disorders, infections, malignancies or rheumatic diseases. Treatment options are immunosuppressive therapy and, if possible, HSC transplantation.
Case Description: A 74-year-old woman was admitted to our ward with hypoglycemia and fever. She was in treatment with chemotherapy and radiotherapy for esophageal cancer. During the hospitalization, her general conditions rapidly worsened with severe hypotension and blood cultures were positive for Staphylococcus hominis.
Clinical Hypothesis: Because of the rapid course of the illness despite the early introduction of broad spectrum antibiotic therapy, associated with the findings of pancytopenia, very high levels of ferritin (42518 ng/ml) and increased LDH (1254 U/L), the hypothesis of a secondary HLH was raised.
Diagnostic Pathway: H-Score was performed. It is a diagnostic score which includes clinical, laboratory, radiological and histological parameters. Despite the impossibility of performing invasive diagnostic procedures useful for the diagnosis (i.e. osteomedullar biopsy), the result was a H-Score of 241, with >99% prior probability of HLH. An attempt with high-dose steroids was performed, but unfortunately the patient died in few days.
Discussion And Learning Points: In our case, HLH was probably due to the combination of sepsis and advanced cancer. Even if rare, clinicians should consider this disease when symptoms are suggestive, in order to start the appropriate therapy as soon as possible.

H-SCORE for Hemophagocytic Lymphohistiocytosis

Parameters	Values of our patient	Options	Score of our patient
1.Known underlying immunosuppression (HIV positive or receiving long-term immunosuppressive therapy)	Yes	No: 0 Yes: +18	+18
2.Highest body temperature (°C)	38.6°C	<38.4°C: 0 38.4-39.4°C: +33 >39.4°C: +49	+33
3.Organomegaly	Splenomegaly	None: 0 Hepatomegaly or splenomegaly: +23 Hepatomegaly and splenomegaly: +38	+23
4.Number of cytopenias	3 lineages	1 lineage: 0 2 lineages: +24 3 lineages: +34	+34
5. Ferritin (ng/ml)	42518	<2000: 0 2000-6000: +35 >6000: +50	+50
6.Triglycerides (mg/dL)	524	<132.7: 0 132.7 - 354: +44 > 354: +64	+64
7.Fibrinogen (mg/dL)	290	>250: 0 ≤250: +30	0
8. AST (U/L)	377	<30: 0 ≥30: +19	+19
9.Hemophagocytosis features on bone marrow aspirate	No	No: 0 Yes: +35	0

Total: 241 points → >99% probability of hemophagocytic syndrome

THE IMPORTANCE OF LIPID MONITORING IN THE GENERAL POPULATION DESPITE ANTHROPOMETRIC MEASURES

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Background: Elevated low-density lipoprotein cholesterol (LDL-C) represents a primary causal risk factor for atherosclerotic cardiovascular disease, with robust evidence supporting lipid-lowering interventions. Traditional cardiovascular risk assessment often focuses on metabolic syndrome features, potentially creating a bias toward screening individuals with elevated body mass index (BMI). We investigated whether LDL-C target achievement shows any association with anthropometric measures or metabolic parameters in patients attending a specialized lipid clinic.
Methods: We analyzed data from all consecutive patients (aged 18-75 years) evaluated at San Raffaele Hospital's Metabolic Health Clinic from January 2023 to October 2024. Patients were stratified according to current guideline-based LDL-C targets as "at target" or "not at target." Comprehensive evaluation included anthropometrics, fasting lipid profiles, liver enzymes, and metabolic parameters. Statistical analysis employed non-parametric comparisons (Wilcoxon rank-sum test), categorical analysis (Chi-squared test), correlation coefficients (Spearman's rho), and multivariate techniques to explore relationships between variables.
Results: Our study population comprised 496 consecutive patients, of whom 114 (23%) had LDL-C at target and 382 (77%) had LDL-C not at target. Patients with LDL-C not at target exhibited distinctive clinical characteristics that were surprisingly disconnected from typical metabolic risk factors. No significant differences were observed in BMI (27.1 vs 27.2 kg/m², p=0.531), waist circumference (96.0 vs 97.5 cm, p=0.248), or waist-to-height ratio between groups.
The absence of correlation between LDL-C and body composition markers was particularly striking (LDL-C vs BMI: rho=-0.061, p=0.176; LDL-C vs waist circumference: rho=0.007, p=0.875). Similarly, no associations were observed between LDL-C status and liver steatosis prevalence (25% vs 26%, p=0.895) or transaminase levels. Network analysis confirmed this independence, with LDL-C loading separately from metabolic syndrome components.
Notably, patients with above-target LDL-C were predominantly female (67% vs 51%, p=0.002), less frequently treated with statins (39% vs 63%, p<0.001), and paradoxically reported less family history of dyslipidemia (67% vs 79%, p=0.013). These patients also demonstrated slightly higher HDL-C levels (56.0 vs 50.0 mg/dL, p=0.009), further differentiating them from typical metabolic syndrome profiles.
Conclusion: Our findings challenge conventional assumptions about the relationship between body weight and LDL-C, demonstrating that LDL-C elevations occur across the entire BMI spectrum. This metabolic independence supports universal lipid screening regardless of anthropometric parameters, as risk-based screening focusing exclusively on individuals with elevated BMI may systematically miss significant LDL-C elevations in normal-weight individuals.

EVALUATION OF ATHEROSCLEROSIS AND ATHEROSCLEROSIS RISK FACTORS IN AN AGING COHORT OF BETA EVALUATION OF ATHEROSCLEROSIS AND ATHEROSCLEROSIS RISK FACTORS IN AN AGING COHORT OF BETA THALASSEMIA PATIENTS. THALASSEMIA PATIENTS

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Background: In the last decades, the improvement in thalassemia management led to a dramatic increase in life expectancy, with non-transfusion dependent (NTDT) and transfusion dependent (TDT) beta-thalassemia patients reaching their sixth decade of life. Thus, age-related complications are emerging. In general population the most common age-related disease is atherosclerosis. Data on the prevalence of atherosclerosis in thalassemia patients are scarce, referring only to small cohorts or pediatric/young adult subjects. Moreover, the impact of iron and other disease-related factors still needs to be elucidated. Some data support the hypothesis that hemoglobin, heme and iron interact with plaque lipids, promoting endothelial dysfunction, the first step of atherosclerosis. However no data have been published from cohorts that reflect the current ageing thalassemia population.
Aims: Our study aims to evaluate the prevalence of atherosclerotic plaques, according to the European Society of Cardiology (ESC) definition, in a cohort of adult TDT and NTDT patients and to explore potential risk factors for atherosclerosis in this population.

Methods: This is a cross-sectional study. We collected clinical and laboratory parameters and performed Doppler ultrasound of the carotid artery to detect atherosclerotic plaques and measure the intima media thickness (IMT)
Results: 196 patients were enrolled, with 131 TDT and 65 NTDT, 58% were females. Hematological parameters are presented in Fig.1.Atherosclerotic plaques prevalence was 3.81%(5/131, IC 0.6-7%) in TDT and 17% (11/65; IC 8-26% in NTDT), the latter higher compared to the age and sex-matched general population. Conversely, the median IMT was 0.55 mm(range 0.4-1 mm), significantly lower than the age and sex-matched general population. IMT increases with age, with males showing a slightly higher IMT than females. No difference in IMT was observed between TDT and NTDT. Regarding known risk factors for atherosclerosis, preliminary data suggest that our patients don't exhibit an atherogenic lipid profile, as indicated by low total cholesterol and LDL, hampering us to use the 10-year risk of cardiovascular disease score proposed by ESC. As for general population, a history of smoking, alcohol and diabetes raises the risk for plaques. Physical activity was measured using the IPAQ score: our cohort was overall sedentary, with most of the patients in the minimally active category. Regarding disease-specific risk factors that have been hypothesised to contribute to the development of atherosclerosis, when comparing patients with and without plaques, no differences in iron, inflammation, and haemolysis parameters were observed. Of note, as shown by ferritin levels and NTBI (fig1) our cohort is overall well chelated.
Summary/Conclusion: To our knowledge, this is the largest and oldest cohort of thalassemia patients in which atherosclerosis and its risk factors were investigated. Our data showed an increased prevalence of atherosclerotic plaques in the NTDT cohort than general population and highlight the risk associated with aging, smoking history, and alcohol consumption. Current guidelines do not consider carotid doppler ultrasound in the routine follow up of thalassemia patients;however our data suggest the importance of performing this test in the at-risk population Further studies are necessary to explore the peculiar lipid profile in these patients and establish a specific cardiovascular risk score considering disease peculiarities

PHASE ANGLE AS A FUNCTIONAL MARKER OF NUTRITIONAL AND METABOLIC STATUS IN OVERWEIGHT AND OBESE INDIVIDUALS: PRELIMINARY DATA FROM AN OUTPATIENT COHORT

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Background: Obesity is a complex and multifactorial condition associated with significant alterations in body composition that are not fully captured by conventional metrics such as body weight or BMI. In this context, bioelectrical impedance analysis (BIA), particularly the phase angle (PhA), a parameter derived from resistance (Rz) and reactance (Xc), has emerged as a potential tool for assessing cellular integrity, hydration status and metabolically active lean mass. Although promising, the routine clinical use of PhA remains limited due to physiological variability related to hydration and fat-free mass distribution. This study aimed to explore the association between PhA, anthropometric characteristics, muscle function and metabolic risk indicators in a real-world outpatient population with overweight or obesity.
Methods: A total of 315 consecutive patients attending the Metabolic Health Clinic at San Raffaele Hospital, Milan, between July 2024 and February 2025 were enrolled. Each subject underwent a comprehensive clinical evaluation, including anthropometric measurements (weight, height, BMI, waist circumference, waist-to-height ratio), multifrequency BIA (BIA 101 BIVA®) and assessment of muscle strength through handgrip dynamometry. BIA-derived parameters included fat mass percentage, lean body mass, total body water and PhA. Statistical analysis involved Student's t-test, ANOVA with post hoc comparisons, and Spearman correlation to explore associations between PhA and clinical variables.
Results: The cohort had a mean BMI of 35.6 ± 5.7 kg/m² and a waist-to-height ratio of 0.66 ± 0.08. The average fat mass percentage was 40.1% ± 8.3% and the mean PhA was 5.8° ± 0.7 (range: 3.0° to 7.8°). Male participants showed significantly higher PhA values than females (6.2° ± 0.7 vs. 5.6° ± 0.6, $p < 0.001$).PhA exhibited significant positive correlations with systolic and diastolic blood pressure and handgrip strength, while inverse associations were observed with age, female sex and waist-to-height ratio. Notably, PhA did not correlate significantly with BMI, highlighting the limited utility of BMI in capturing functional and cellular health.
Conclusions: Our findings underscore the potential clinical relevance of PhA as a functional biomarker in individuals with overweight and obesity. The significant association between PhA and waist-to-height ratio supports the integration of structural and functional markers in obesity assessment. Higher PhA values in males further suggest sex-specific differences in cellular integrity and muscle mass distribution, reinforcing the importance of individualized reference ranges. PhA may represent a valuable complementary tool to traditional anthropometric indices, providing insights into muscle quality and metabolic health that are otherwise overlooked by BMI alone. Its incorporation into multidisciplinary obesity care pathways may enhance diagnostic precision and patient stratification in both research and clinical practice.

ATHEROSCLEROTIC RENAL ARTERY STENOSIS: ROLE OF URIC ACID/CREATININE RATIO ON AUTONOMIC DYSFUNCTION AND LEFT VENTRICULAR MASS

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Introduction: Atherosclerotic Renal artery stenosis (ARAS) is an increasingly common cause of secondary hypertension and progressive chronic kidney disease. It frequently occurs in patients with other atherosclerotic conditions like coronary artery disease or peripheral vascular disease, leading to high morbidity and mortality. Hypertension significantly contributes to the development of cardiovascular and kidney diseases, increasing these risks. Furthermore, autonomic dysfunction is a well-known risk factor for cardiovascular disease, and inflammation may play a crucial role in the link between the autonomic nervous system and atherosclerosis, including in ARAS patients. In addition to hypertension, high levels of serum uric acid (SUA) have been found to negatively impact cardiovascular outcomes. Large studies have identified an optimal SUA cut-off of 5.6 mg/dL for CV mortality. Patients with ARAS and elevated SUA levels, are associated with higher blood pressure and left ventricular hypertrophy (LVH), as indicated by an increased left ventricular mass index (LVMI). Studies have shown that the SUA/ serum Creatinine ratio (SUA/SCr) can be a better predictor of cardiovascular risk and mortality than SUA alone. Given the high cardiovascular risk in ARAS patients, the aim of this study was to investigate whether SUA levels and SUA/SCr could represent markers of autonomic dysfunction and increased LVMI in patients with ARAS.
Methods: Patients diagnosed with ARAS were enrolled in the study. All patients underwent clinical evaluation, biochemical analysis, 24-hour electrocardiogram (ECG) and renal Doppler ultrasound with hemodinamic parameters including renal resistive index. Heart rate variability for global autonomic dysfunction was assessed through the analysis of 24-hour ECG to detect standard deviation of normal-to-normal RR intervals (SDNN). Echocardiographic measurement of LVMI was performed at the time of diagnosis. Patients with heart disease, arrhythmia, diabetes mellitus and fibromuscular dysplasia were excluded. Patients did not take anti-arrhythmic and QTc prolonging drugs.
Results: Twenty-seven patients [F=16 (59%), median age 67 years (IQR 60-77)] diagnosed with ARAS were enrolled in the study. We found a statistically significant negative linear correlation between SUA/sCr and SDNN ($r = -0.519$, $p < 0.01$). We found a statistically significant positive linear correlation between SUA/sCr and LVMI ($r = 0.413$, $p < 0.05$). Median SDNN was significantly lower in patients with SUA ≥ 5.6 mg/dl than patients with SUA < 5.6 mg/dl [94.2 (IQR 86.8-108.1) vs 112.8 (IQR 108.9-114.7), $p < 0.01$]. Median LVMI was significantly higher in patients with SUA ≥ 5.6 mg/dl compared to patients with SUA < 5.6 mg/dl [133 g/m2 (IQR 120-149) vs 111 g/m2 (IQR 99-129), $p < 0.05$].
Conclusion: In patients with ARAS, SUA/sCr is associated with autonomic dysfunction and LVMI. The ratio and related cut-off value of SUA/sCr could represent a useful biomarker to evaluate cardiovascular risk in ARAS patients.

SPIROMETRY IN GENERAL PRATICTIONER'S OFFICE AND OPTIMIZATION OF COPD PATIENT MANAGEMENT: ANALYSIS OF DATA FROM AN OBSERVATIONAL STUDY

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The management of the COPD patient is complex and must aim to improve the quality and life expectancy, reduce the impact of symptoms on daily activities and contain the risk of exacerbations. The introduction in 2021 of the Aifa note 99 regarding the prescribability of drugs for COPD has focused interest on the management of these subjects and the importance of the role of the general practitioner both in the first diagnosis and in the control of the known COPD patient, especially with the possibility of performing spirometry

in the GP's office. For this reason, it seems interesting to know the real-life data on how the GP uses the spirometric test in his/her practice. In light of this, we wanted to conduct an observational study, which involved the SIMG research group of Messina, to outline this new approach to the COPD patient. The aim of the research is to: a) know the use of spirometry with pharmacological bronchodilation tests in the management of COPD, b) know how many patients were recognized as new COPD patients and how many known COPD patients were managed in the follow-up by the GP, c) evaluate some parameters (smoking data, BMI, mMRC and CAT, spirometry and bronchodilation tests, appropriate pharmacological therapy.
Materials and methods: The study involved the population attending the general medicine practices of the SIMG research group in Messina (so far 10 doctors have contributed for a population of approximately 13,000 subjects). This study planned to examine the data from the period October 2023 - October 2024 of spirometric tests with bronchodilation tests performed on smokers with pack years>20, aged over 40 years and of the clinical evaluation through the mMRC and CAT questionnaires. Data collection was performed through a computerized form structured to know the following characteristics: age, BMI, smoking status, spirometric data with bronchodilation test, mMRC and CAT questionnaire results, number of patients with new COPD diagnosis and known COPD patients, FEV1 data by severity staging, prescribed pharmacological therapy...
Results: and conclusions: Preliminary data revealed that 370 spirometric tests with pharmacological bronchodilation test were performed in smokers with py>20 and with age>40 years (2.83% of the general population - F 21%, U 79%). The subjects had an average age of 66 years, an average pack year of 42, and an average BMI of 27.46. 121 subjects with a first diagnosis of COPD (32.5%) and 180 subjects with a known diagnosis of COPD (48.7%) were identified. The subjects COPD had a mean CAT of 12.36 and a mean mMRC of 1.2. 7.5% had a FEV1<50%, 37% a FEV1 between 50-80% and 55.5% a FEV1 >80%. The subjects with new diagnosis had the following data: mean CAT values of 10.7 and mMRC of 0.8, FEV1: <50%: 5% - 50-80%: 30% - >80%: 65%. In 40% of the subjects, therapy with LAMA-LABA was prescribed, in 60% therapy with LAMA. While in patients already known to have COPD, in 30% of cases the therapy was changed from LAMA to LAMA-LABA and 15% of the subjects were referred to a Specialist Center for the prescription of triple association. The study has shown how the use of proactive medicine and the use of spirometry in GP allows the identification of new COPD patients who, as the data show, are not always in an early stage. It has also been found that spirometry in the clinic can allow the optimization of therapy in known COPD patients with an excellent cost-benefit ratio for the National Health System.

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS AND THE VASCULITIC DOMINO: SKIN, GUT, AND CLOT

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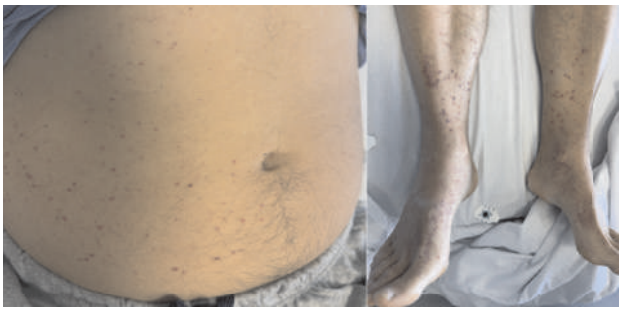
Background: Drug-induced vasculitis is a rare but important clinical entity that may mimic systemic autoimmune diseases. Nonsteroidal anti-inflammatory drugs (NSAIDs) are well-known triggers, occasionally associated with gastrointestinal involvement such as collagenous colitis.
Clinical Presentation: A 51-year-old man presented with abdominal pain and a purpuric rash. Two weeks before admission, he had experienced a self-limiting febrile pharyngitis treated with morniflumate and ibuprofen. One week later, he developed polyarthralgia and a palpable purpuric rash on the lower limbs. His past medical history was unremarkable, although his family history included breast and lung cancer.
On examination, the patient was hypotensive (BP 85/60 mmHg), tachycardic, and eupneic, with normal heart and lung sounds. His abdomen was soft but diffusely tender, especially in the right iliac fossa. He had symmetrical, palpable purpura on the lower limbs, with milder lesions on the abdomen and upper limbs (Figure 1). Joint tenderness was noted without swelling. Pulse oximetry showed 95% saturation on room air.
Laboratory tests revealed elevated D-dimer (3200 ng/mL). Given the clinical suspicion of mesenteric ischemia, a contrast-enhanced abdominal CT scan was performed, which demonstrated free pelvic fluid, thickening of the terminal ileum wall, and adjacent fat stranding. Incidentally, a pulmonary embolism (PE) was detected, with filling defects in the right lower lobar artery and segmental branches, despite the absence of respiratory symptoms.
Diagnostic Workup: Extensive workup included negative results for ANA, anti-dsDNA, ANCAs, cryoglobulins, viral serologies (CMV, EBV, HSV-1/2), and blood and throat cultures. Complement levels were normal. Thrombophilia screening revealed heterozygosity for the Factor V Leiden mutation (G1691A). Colonoscopy revealed terminal ileitis, sigmoid colitis, and left-sided diverticulosis. Histopathology showed collagenous colitis with subepithelial eosinophilic bands, suggestive of hypersensitivity etiology. Given the purpura, gastrointestinal symptoms, and recent NSAID use, systemic vasculitis was suspected. A skin biopsy from a purpuric lesion revealed leukocytoclastic vasculitis. Paracetamol was administered for pain control but was followed by rapid worsening of the rash with pruritus, suggesting hypersensitivity. Discontinuation led to partial improvement. A corticosteroid taper (starting at prednisone 80 mg) was initiated, with significant resolution of symptoms and cutaneous findings. For PE and sintomatic arterial hypotension patient was treated with fluids and low molecular weight heparin, later transitioned to oral anticoagulants.
Discussion: The differential diagnosis included Henoch–Schönlein Purpura (IgA vasculitis), although rare in adults and not supported by serologic markers. Behçet's disease and Crohn's disease were considered but deemed unlikely based on clinical and histologic findings. VEXAS syndrome was excluded due to the absence of cytopenias or myelodysplastic features. The temporal association with NSAID exposure, together with histologic findings of collagenous colitis and leukocytoclastic vasculitis, strongly supported a diagnosis of drug-induced vasculitis with gastrointestinal involvement. The mechanism may involve NSAID-induced mucosal injury via prostaglandin inhibition, leading to antigen exposure and immune activation.
The pulmonary embolism was considered incidental. Although the Factor V Leiden mutation confers pro-thrombotic risk, a direct relationship between the embolic event and vasculitis could not be definitively established.
Conlusions: This case highlights an uncommon but important presentation of drug-induced systemic vasculitis with gastrointestinal and cutaneous involvement, likely triggered by NSAIDs and possibly worsened by paracetamol. The incidental finding of pulmonary embolism underlines the importance of thorough investigation in systemic inflammatory states, particularly in genetically predisposed individuals. Recognition of drug-induced vasculitis is crucial, as prompt withdrawal of the offending agent and corticosteroid therapy can lead to resolution.



B LYMPHOPROLIFERATIVE DISEASE AND ACQUIRED COAGULOPATHY: AN INSIDIOUS LINK

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Background: Acquired coagulation factor inhibitors are autoantibodies that may develop in individuals with autoimmune or neoplastic disorders and should be assessed in patients without personal or familiar history of bleeding disorders. These inhibitors most commonly target factor VIII (FVIII) or von Willebrand factor (VWF), resulting in acquired hemophilia A or acquired von Willebrand disease, respectively. However, inhibitory autoantibodies may occasionally interfere with the normal activity of other coagulation factors.
Case report: An 81-year-old female presented with recurrent episodes of anterior epistaxis and ecchymoses. She had no previous history of abnormal coagulation parameters or personal/familial bleeding disorders. Laboratory testing revealed deficiencies in vitamin K–dependent factors (except factor IX) in the absence of liver dysfunction or other known causes of coagulopathy, raising suspicion of an acquired hemorrhagic disorder mediated by coagulation inhibitors. Imaging studies revealed no hepatosplenomegaly or lymphadenopathy. Past medical history included an indolent B-cell lymphoproliferative disorder under hematological follow-up, hypertension, and mixed dyslipidemia.
Clinically, the patient exhibited persistent mucocutaneous bleeding associated with progressive anemia and transient memory deficits. Due to suspected central nervous system involvement, an MRI was performed, revealing a small hemorrhagic area in the fornix of the limbic system. At the hospital admission, coagulation studies confirmed markedly abnormal values: PT/INR 5.36 and aPTT 1.56. A mixing test showed suboptimal correction, prompting further assessment of vitamin K–dependent factors. The assay revealed the following:

Factor IX 171%, Factor II 5%, Factor VII 17%, Factor X 7%, Protein S (free) 51%, and Protein C 24%. Mixing studies for Factors II and VII demonstrated suboptimal correction, suggesting the presence of inhibitors. Antiphospholipid antibodies were not detected. According to these results, we hypnotized the presence of a polyspecific serum para-protein interfering with clotting factors. Immunosuppressive steroid therapy with prednisone was started at the time of admission. Intravenous vitamin K (Konakion 10 mg) induced a not significant resolution of PT/INR prolongation, followed by a rebound increase to 4.66 and 5.27, indicating limited or absent therapeutic efficacy. PIVKA-II levels were 41 AU/mL (negative), supporting the lack of a functional vitamin K deficiency.
Given the known lymphoproliferative disorder, the possibility of a neoplastic trigger for the coagulation abnormality was considered. Flow cytometry confirmed the presence of a B-cell clone expressing CD20, with a 2% blast count. After 15 days of steroid therapy without clinical improvement, a pharmacokinetic assessment was conducted following the administration of a 4-factor prothrombin complex concentrate (PCC, containing factors II, VII, IX, X). Factor levels were measured at baseline and several time points post-infusion (30 min, 1h, 2h, 4h, 12h, 24h). A marked decline in circulating coagulation factors was noted after 4 hours, with the greatest reduction observed for Factor II, suggesting preferential inhibitory activity against this factor, likely due to the presence of a neoplastic paraprotein.
Therapy with rituximab (anti-CD20 monoclonal antibody) was initiated at the standard dose of 375 mg/m^2 weekly to treat both the hematologic and the coagulation disorders. After the first infusion, PT/INR improved significantly (ranging between 1.6–1.9) and no further spontaneous bleeding episodes were reported.
Conclusions: This case highlights the diagnostic and therapeutic challenges posed by rare coagulation inhibitors beyond Factor VIII. Comprehensive coagulation assays and pharmacokinetic evaluations were pivotal in identifying the presence of a non-neutralizing anti–Factor II inhibitor. The successful use of rituximab underscores the relevance of B-cell–directed immunosuppression in managing such complex cases, particularly in the context of clonal B-cell disorders.

INVESTIGATING THE VARIATION OVER TIME OF THE LEFT ATRIAL VOLUME INDEX: A PROSPECTIVE COHORT STUDY

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Background: Left atrial enlargement (LAE) is a marker of adverse cardiovascular remodeling resulting from a chronic overload of pressure and/or volume and may be identified quantifying the size of the left atrium (LA). The left atrial volume index (LAVi) is a LA metric readily available in the reports of transthoracic echocardiograms (TTEs) performed in routine clinical practice. Correctly identifying the existence of LAE is relevant because it has been associated with clinically relevant outcomes such as the onset of atrial fibrillation (AF), symptomatic heart failure (HF) and stroke. Few studies, however, have investigated the variation of LA size over time and – to our knowledge – none have used the LAVi to quantify the LA size, despite the LAVi is the measure recommended by current cardiac imaging guidelines.
Methods: For this prospective cohort study, we screened reports of TTEs performed from 2010 to 2023 at three teaching hospitals in Milan (Bassini, Niguarda and San Paolo). For each eligible subject, we included two TTEs at least one year apart, both with data made available on the LAVi. Eligibility criteria included adult age and residency in the metropolitan area of Milan (so that record linkage with administrative databases could be performed). In case more than 2 TTEs were available for each subject, we included the latest available exam. Exclusion criteria were the impossibility of record linkage with the administrative databases of the Public Health Agency of Milan, known AF at the time of any of the two TTEs, and anticoagulation ongoing either at the time or in the year following each TTE. Data on eligible subjects' comorbidities and pharmacological treatments were obtained from the administrative databases maintained by the Public Health Agency of Milan. The LAVi was considered normal for values ≤34 mL/m2. LAVi variation over time was expressed as percent variation. Univariate and multivariate analyses were performed using SPSS. Two-tailed p-values below 0.05 were considered statistically significant.
Results: Of the screened TTE reports (n=296,747),15,082TTEs from7,541subjects were eligible for inclusion in the study. Females and subjects over70years of age made up44.4% and41.4% of the cohort, respectively. At the time of study inclusion,50.3% of subjects had hypertension,14.9% had diabetes mellitus,4.3% had chronic kidney disease (CKD) and12.9% had HF. Of the eligible patients,44.8% were on treatment with either an ACE-inhibitor (ACE-I) or an angiotensin receptor blocker (ARB), and32.6% were on treatment with a beta-blocker. The median baseline LAVi was28.9mL/m2 (IQR,22.7-36.7). Subjects with HF had the highest baseline LAVi (36.2mL/m2, IQR28.8-44.8), followed by subjects with CKD (34.0mL/m2, IQR26.7-42.7). Over a median follow-up of35months, the percent variation of the LAVi was5.9% (IQR, -14.3-29.7). The percent variation of the LAVi was significantly higher when the second TTE was performed at5years (7.0%, IQR -13.1-30.5) compared to2and3years (1.9%, IQR -16.8-23.2; and2.0%, IQR -16.9-28.2, respectively; p<0.0001). In subjects with none of the examined comorbidities (hypertension, diabetes, CKD and HF), the percent variation of the LAVi was3.2% (IQR, -15.5-27.9), significantly lower to that of subjects with any of those comorbidities (6.3%, IQR -13.7-30.2; p=0.03). Next, we investigated the association of relevant covariates (female sex, treatment with ACE-Is or ARBs, treatment with beta-blockers, CKD, HF, hypertension and diabetes) with a positive variation of the LAVi in univariate and multivariate analyses. To do so, we stratified the percent variation of the LAVi in5quintiles, obtaining two quintiles of negative variation (Q1-Q2), a quintile of null variation (Q3), and two quintiles of positive variation (Q4-Q5). We then compared Q4-Q5with Q1-Q2. We found that the only covariate significantly and independently associated with a less positive variation of the LAVi was HF (OR0.85,95% CI0.74-0.98; p=0.03).
Conclusions: Our results show that the LAVi increases over time, but that such increase is negligible within 3 years of the first echocardiogram. HF appeared to be the only covariate associated with a less positive increase of the LAVi over time. A possible explanation is that subjects with HF had the highest baseline LAVi, resulting in a less pronounced percent increase. Another hypothesis is that HF treatments other than those considered in this study – such as diuretics – could play a role in the reverse remodeling of the LA. In conclusion, based on the results of our study, the clinical implications of an enlarged LA appear to be valid up to 3 years since the initial echocardiogram, a time frame after which potentially clinically relevant increases of the LAVi should be expected.

BRONCHOALVEOLAR LAVAGE CULTURES IN INTERNAL MEDICINE WARD: A MONOCENTRIC PERSPECTIVE

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Background: Respiratory infections constitute a major cause of hospitalisation and are associated with high mortality rates. Empirical antibiotic therapy is guided by epidemiological data, with respiratory cultures reserved for severe cases or in the suspect of multidrug-resistant organisms. Bronchoalveolar lavage (BAL) is commonly used for specimen collection in intensive care units or in severely immunocompromised patients, although no specific guideline exists. In this study, we wanted to evaluate the characteristics of patients selected for BAL in our Internal Medicine wards, and to gather preliminary data to assess its impact in the decision-making process and on clinical outcome.
Methods: This explorative analysis leveraged on a prospective registry of consecutive patients admitted to two internal medicine departments and it was restricted to subjects with respiratory diseases and/or respiratory infections who underwent BAL culture between January2024and February2025. Collected data included demographics, comorbidity burden (Cumulative Illness Rating Scale, CIRS), risk of pressure lesions (Braden Scale) and disability (Barthel Index). Empirical estimation of benefit from intensive care was recorded in a1-3discrete scale. BAL results were defined as positive if at least one prevalent microorganism grew on culture media while negative if no microbiological agent or a mixed oropharyngeal flora was found. BAL patients were matched with patients with respiratory infections and similar clinical characteristics who did not receive BAL. We also compared BAL-positive patients with BAL-negative patients. Exclusion criteria were BAL performance in Intensive Care Units or for bronchial de-obstruction only. Antibiotic therapy was stratified into first,

second, and third-line treatments based on clinical practice and internal guidelines.
Results: We analysed 128 subjects: 46 receiving standard care along with BAL, and 82 only standard treatment. Both groups showed a higher prevalence of male patients (54% and 67%). No differences were observed in oxygen support requirements at admission between the two groups. BAL was performed in younger patients (mean age 68 vs 76, p=0.026) with lower burden of comorbidities, as reflected by the CIRS score [10 (16-13) vs 7 (4-11), p=0.034]. On admission, a higher proportion of subjects undergoing BAL were deemed sufficiently fit for moderate/high benefit from intensification of care than patients not receiving BAL (70% vs 89%, p=0.028). There were no significant differences in daily life activity scores between the two groups, both at home and at discharge. However, BAL group showed a sharper decline in Barthel score (-25 [-50–0] vs -5 [-15–0], p<0.001) following hospitalization. Concerning hospitalization outcomes, BAL patients exhibited longer hospital stays (22 vs 18 days, p=0.026) and fewer patients were discharged alive. Besides, taking only in account patients with an expected benefit from intensification of care, BAL group had a higher proportion of patients dead or referred to palliative care. Moreover, BAL patients received more frequently antifungal and second/ third-line antibiotics, such as meropenem and daptomycin. In 44% of cases, BAL cultures were positive. The most frequent pathogens were P. Aeruginosa (11%), E. Coli (9%), S. Aureus (7%), K. Pneumoniae and C. Albicans (6%). 63% of BAL patients received antibiotics in the preceding 2 weeks, with no difference in empiric therapy chosen between the BAL positive and BAL negative groups. During hospitalization, BAL-negative patients received more often azithromycin and less frequently daptomycin compared to BAL-positive patients. We observed no major therapeutic changes following BAL results.
Discussion: BAL culture was primarily performed in younger subjects with fewer comorbidities (regardless of oxygen support need) but deemed at higher potential benefit from intensive care. Nonetheless, when taken as a whole, patients undergoing BAL had longer hospital stay and no better outcomes than patients not receiving BAL. Therapeutic changes appeared non-significantly affected by BAL results, suggesting that BAL only confirmed empirical changes to second/third-line antibiotics made before obtaining the results.
Conclusion: These data might indicate that performance of BAL identifies a group of patients with acute illnesses of higher severity compared to non-BAL-patients, despite comparable or even lower background morbidity. However, BAL does not apparently affect treatment changes possibly suggesting that its role might be often limited to rule out alternative diagnoses and that other parameters should be considered to tackle potentially adverse admission outcomes. These variables would also help refine current algorithms for BAL indication, thus minimising risks and optimising identification of patients with higher expected benefit from BAL. Based on this, we believe that a prospective study aimed at developing a decision-making protocol for BAL performance could be valuable in identifying patients who may experience greater clinical benefit, while also helping to avoid unnecessary procedures.

RESOLVIN RESPONSE IN BRONCHIAL ASTHMA PATIENTS: ENDOTYPE AND CLINICAL SEVERITY

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Background: Asthma is a chronic inflammatory condition characterized by distinct endotypes. The most common is type 2 asthma, which is allergic and/or eosinophilic in nature. In contrast, non-type 2 asthma—typically neutrophilic or paucigranulocytic—often has a later onset and is more strongly associated with risk factors such as smoking, pollution, and obesity. Resolvins (Rv) are lipid mediators derived from omega-3 fatty acids, primarily eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), that can promote the resolution of inflammation in asthma.
Objectives: To determine resolvin levels in asthma patients in relation to endotype and clinical severity.
Methods: In a observational study, we enrolled thirty-nine patients with varying degrees of bronchial asthma severity (steps 3+4 and 5). Patients were also classified according to inflammatory endotype: type 2 allergic (GT2A, n = 20), type 2 non-allergic (GT2NA, n = 13), and non-type 2 (GNT2, n = 6). A control group (GC, n = 12) was also included. All participants underwent clinical assessment and lipidomic analysis focusing on D-series resolvins.
Results: Step 5 asthma patients showed significantly lower levels of RvD1 (step 3+4 vs. step 5, p = 0.018) and 17(R)-RvD1 (step 3+4 vs. step 5, p = 0.045) (Figure 1). Patients treated with the highest doses of inhaled corticosteroid/long-acting β2-agonist (ICS/LABA) had lower levels of 17(R)-RvD1. No significant differences were observed for RvD2 and RvD3 (Figure 1). The type 2 non-allergic group exhibited higher levels of RvD2 compared to both the type 2 allergic group (p = 0.040) and the non-type 2 group (p= 0.057) (Figure 2).
Conclusions: Pro-resolving mediators are produced during asthma; however, their biosynthesis appears reduced in severe and uncontrolled disease. The lower levels of RvD1 and 17(R)-RvD1 observed in patients with higher clinical severity and reduced therapy responsiveness suggest that persistent and adaptive airway inflammation may be due, at least in part, to impaired resolution mechanisms. RvD2 is known to regulate type 2 inflammatory responses, promoting resolution in murine models through RvD2–DRV2 receptor interaction. Our findings support the pro-resolving role of RvD2, highlighting its potential as a key mediator in eosinophil recruitment and activation in the type 2 endotype. Large-scale studies are warranted to further elucidate the role of resolvins in asthma pathogenesis and their potential utility as biomarkers.

Figure 1

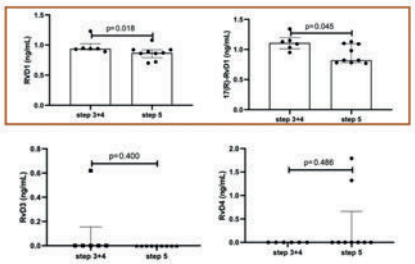
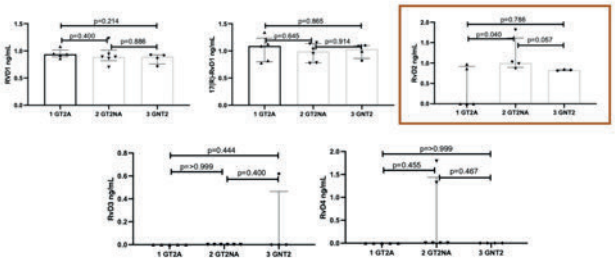


Figure 2



UNVEILING DIAGNOSES: FEVER AND RASH. A SECONDARY SYPHILIS CASE

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Introduction: Cutaneous rash with fever is a frequent presentation in Internal Medicine wards, with a broad range of differential diagnosis encompassing different causes. History-taking and epidemiological analysis are essential to guide physicians toward the most probable etiology. This report discusses the case of a 64-year-old woman, in whom diagnosis proved particularly challenging.
Case presentation: A 64-year-old woman was evaluated for diffuse erythematous rash and fever. Her medical history was notable for Polycythemia Vera, treated with hydroxyurea, aspirin and allopurinol. She reported no adverse reactions to drugs. She never smoked and she had no history of alcohol or substances abuse. She was Russian but she denied recent travels. She had been in her usual state of health until three weeks before, when she developed a lower limb rash and reduced left eyesight. Eventually, the rash spread through the body and the lesions on the lower extremities became larger and malodorous. She became febrile. On admission to the emergency ward, her vital parameters were normal, and the general examination revealed a diffuse maculopapular erythematous rash with areas of desquamation. She exhibited extended ulcerations on the lower limbs. ECG and chest x-ray were normal, as well as laboratory testing except for CRP and LDH increase. She started treatment with amoxicillin-clavulanic acid while hydroxyurea was discontinued. The patient was then

admitted to the General Medicine ward. The review of her medical history was complex due to language barriers, but she reported loss of 20kg in the last two years, night sweats and occasional episodes of low-grade fever, she denied any sick contacts. Blood and urine cultures were negative while skin biopsy of the legs was positive for C. Striatum, S. Dysagalactiae and E. Cloacae Complex, confirming superinfection. At first, she underwent a whole-body contrast-enhanced CT which tested negative. Due to reduced vision in the left eye, she underwent an ophthalmologic exam revealing a panuveitis of possible syphilitic origin. The diagnosis was supported by dermatological examination, which identified lesions consistent with secondary syphilis. Indeed, non-treponemal and treponemal tests resulted positive. Tests for other etiological agents, such as HIV, HSV1, VZV, HBV, HCV, EBV, and CMV, were negative as well as major autoantibodies for autoimmune systemic diseases as p-ANCA, c-ANCA and RF, except for nonspecific ANA positivity. She then started antibiotic therapy with intravenous Penicillin G. Her ophthalmologic symptoms indicated involvement of the central nervous system. Accordingly, cerebrospinal fluid analysis was performed, confirming the diagnosis of neurosyphilis, which prompted extension of treatment duration. Echocardiogram excluded cardiac involvement. In the following days, the patient reported major improvements, and she was discharged with indications to continue antibiotic therapy in outpatient clinic.

Discussion: The patient exhibited diffuse skin manifestations, along with a history of weight loss, night sweats, and elevated LDH. According to the clinical history, we focused on a possible lymphoproliferative disease, then excluded by a CT scan. We ruled out autoimmune conditions with cutaneous presentation and potential iatrogenic causes as drugs. We considered viruses responsible for exanthematous rashes in adults, as well as other infectious agents based on geography and exposure. Even though the patient appeared hesitant to speak about her sexual history, she denied high-risk contacts, so, given the low epidemiological probability, we waited for sexually transmitted diseases screening. Nevertheless, due to her ocular presentation, compatible with syphilitic panuveitis, we then confirmed syphilis positivity. This case carries epidemiological relevance considering insights from the2023European CDC Syphilis Epidemiological Report. It highlights that it is more common in males (M:F -7:1), especially men who have sex with men, typically within the25–34-year age group, while incidence decreases sharply after45years of age. Given these premises, the presentation suggestive of a lymphoproliferative disorder and the difficulties in obtaining clinical information, diagnosis was far from straightforward. However, her features clearly aligned with Secondary Syphilis, a sexually transmitted disease caused by the spirochete Treponema pallidum, that emerges weeks to months after the initial infection.

Conclusion: During the formulation of differential diagnosis, the physician must prioritize diagnoses based on their probability, to rule out systematically the most likely ones first. This process requires a comprehensive evaluation of factors, including the clinical presentation, detailed history taking and epidemiology. This case exemplifies the critical role of rigorous data acquisition and patient dialogue, which facilitates the consideration of less common but plausible diagnostic alternatives that might otherwise be overlooked.

MUCINOUS GALLBLADDER ADENOCARCINOMA AND CARCINOSIS: A RARE CASE OF SECONDARY RETROPERITONEAL FIBROSIS

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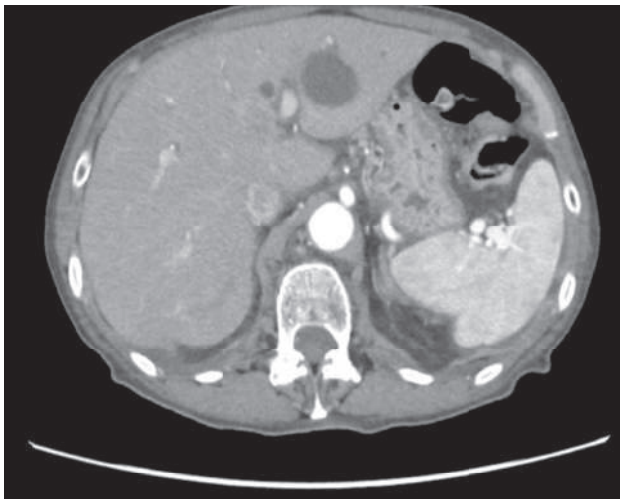
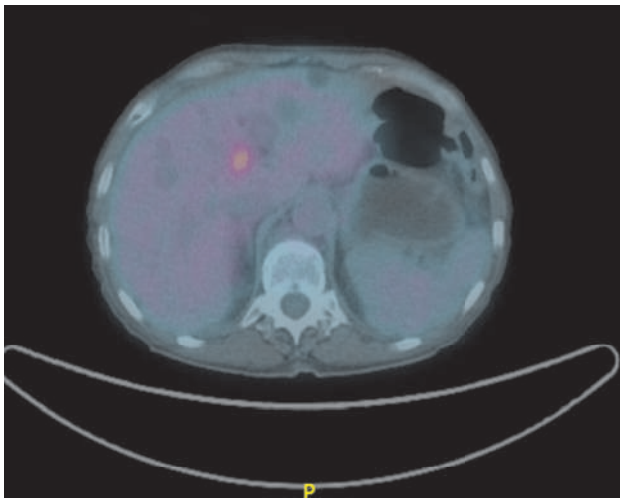
Background: Retroperitoneal fibrosis (RPF) is a rare condition marked by the development of inflammatory and fibrous tissue in the retroperitoneum, typically around the infrarenal aorta and iliac arteries, often encasing the ureters. Excluding idiopathic causes (IgG4-related or not), RPF can rarely be secondary to other diseases, including malignancies, in which case histological confirmation via biopsy may be necessary to guide treatment. We report a case of severe RPF secondary to mucinous gallbladder adenocarcinoma with carcinomatosis, itself a rare malignancy (1–2/100,000 in the US) due to anatomical location and nonspecific symptoms

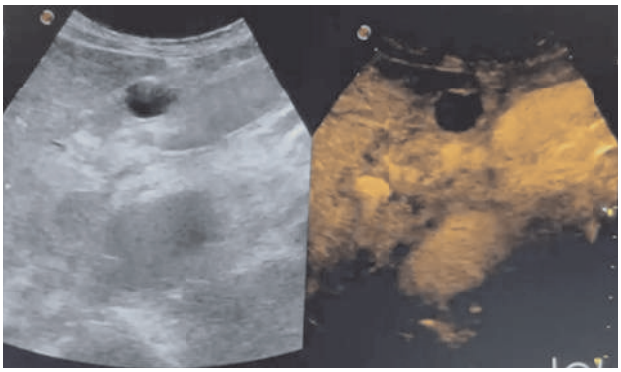
Case Description: A 68-year-old woman with no medical history presented with left lumbar pain unresponsive to analgesics, mild fever and profuse sweating. Abdominal ultrasound revealed gallstones and bilateral hydronefrosis, grade II on the left . An urography computed tomography (CT) confirmed hydronephrosis and a left ureteral stricture, leading to JJ stent placement. She was later admitted to the emergency department, where repeat imaging showed suspected RPF and areas of impaired hepatic vascularity , likely secondary to renal impairment. To exclude idiopathic RPF, a broad laboratory panel was performed (ESR, CRP, IgG including IgG4, autoimmunity, serum protein electrophoresis, free light chains), all returning within normal range. Having ruled out infection and autoimmune causes, a neoplastic origin was considered. So we performed:

Discussion: RPF is a rare disease, often with vague symptoms, and is commonly discovered after urinary obstruction or renal failure. Gallbladder cancer also poses a significant diagnostic challenge, especially when presenting with indirect symptoms. This case illustrates a complex diagnostic path that, through careful exclusion, identified a paraneoplastic cause. The diagnostic process, in fact, has been affected by some biases: the unusual nature of the disease, the difficulty of histology due to the abundant retroperitoneal fibrosis and, finally, the traditional imaging not totally conclusive. In our case the worsening clinical course with intense algic symptoms and the CEUS (through characteristic wash-out) played a critical role by revealing early suspicion of primary gallbladder cancer , although actually EFSUMB recommendations are not of a high degree.

Conclusion: This case highlights a rare association between two uncommon conditions (mucinous gallbladder adenocarcinoma and RPF) and emphasizes how a structured diagnostic approach combined to an appropriate imaging can enable early diagnosis and targeted treatment, despite the poor prognosis associated with these malignancies.







THE BURNING MED: PREDICTING BURNOUT SYNDROME I N EMERGENCY MEDICINE THROUGH A DATA-DRIVEN APPROACH

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Introduction: Burnout Syndrome(BOS) among professionals is a critical issue in healthcare, especially in emergency departments, where the prevalence of BOS has significantly increased in the last years, ranging from 40% to 68%.
This study seeks to develop a machine learning(ML)-driven predictive model for BOS risk, focusing on identifying related critical risk factors in emergency medicine.
Methods: The study is based on data collected through a survey distributed to members of the Italian Emergency Medicine Schools (ITEMS) and analyzed by different ML approaches. Burnout levels were assessed using the Maslach Burnout Inventory (MBI), while personality traits were evaluated through Positive(PA) and Negative Affect(NA) Schedule (PANAS) and the Mini International Personality Item Pool (Mini IPIP). Additional data on work history and individual anamnesis were included to provide a comprehensive analysis of burnout's multidimensional nature.
Results: Among 121 emergency medicine physicians and residents in Italy, 64% experienced emotional exhaustion but, intriguingly the 87% of them presented a lower risk of reduced personal accomplishment. Burnout risk was associated with long working hours, emotional traits, and COVID-19 unit exposure. Neuroticism increased burnout susceptibility, while extraversion and conscientiousness were protective. NA positively correlated with burnout, while PA showed an inverse relationship. ML models achieved 93% of accuracy in predicting burnout dimensions. Furthermore, feature importance analysis revealed new strategies for burnout assessment overpassing traditional methods.
Conclusion: This study highlights the potential of AI-driven assessments in monitoring burnout risk and promoting targeted interventions for healthcare professionals, with the aim of improving both well-being and patient care quality.

DIAGNOSTIC AND THERAPEUTIC MANAGEMENT OF SARS-COV-2 INFECTION IN HAEMATOLOGICAL PATIENTS: A DELPHI CONSENSUS

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COVID-19 poses a significant risk to individuals with haematological malignancies (HM), as they are particularly vulnerable to severe disease progression and hospitalization due to their compromised immune systems. Many clinical decisions regarding the management of COVID-19 in these patients are yet to be fully addressed by existing guidelines, leading to variability in care.
Based on the literature review, three areas of interest in SARS-CoV-2 in HMs were identified: 1) risk stratification for severe COVID-19 progression; 2) clinical management of SARS-CoV-2 by symptoms severity, type of active HM and specific treatment; 3) clinical management of persistent SARS-CoV-2 and COVID-19 recovered patients. A three-round Delphi anonymous survey of 28 questions was conducted through REDCap platform. Twenty-one experts were identified based on their clinical-research experience in haematology and infectious diseases by relevant international networks and scientific societies. Consensus was defined as a Total Cumulative Consensus above 79%, and its strenght by the 6-point Likert scale categorised into four tiers (strong disagreement, moderate disagreement, moderate agreement, strong agreement). Final statements were generated on questions achieving consensus.
Fifteen statements were generated: three regarding the risk of severe COVID-19, ten regarding COVID-19 management in active HM patients, two regarding clinical management of persistent SARS-CoV-2 and COVID-19 recovered HM patients. HM type and treatment and the vaccinal status should be considered in the infection therapeutic management decisions. Early antivirals or effective anti-spike monoclonal antibodies are strongly recommended in all HM patients with active disease, irrespective of the COVID-19 symptoms' severity. Prolonging antiviral therapy should be considered in case of persistent symptoms of infection after early treatment (moderate agreement). Chemotherapy discontinuation has been strongly suggested for severe COVID-19, and discontinuation of HM's treatment (anti-CD20 antibodies, glucocorticoids, chemotherapy) should be considered on individual clinical risk/benefit ratio in asymptomatic-mild COVID-19 (moderate agreement). It is strongly recommended to restart delayed-discontinued HM treatment one week after achieving SARS-CoV-2 clearance.
This Delphi consensus offers valuable support to tailored COVID-19 treatment strategies in patients with active HM. The recommendations can play also a pivotal role in driving new research questions in the HM vulnerable population for pandemic preparedness plans.

LONG-TERM SEQUENTIAL IRON CHELATION WITH DEFERASIROX AND DEFERIPRONE IN ACERULOPLASMINEMIA: A CASE SERIES OF TWO BROTHERS WITH SUSTAINED NEUROLOGICAL IMPROVEMENT

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Background: Aceruloplasminemia is a rare autosomal recessive disorder of iron metabolism caused by mutations in the CP gene that result in decrease or absent ceruloplasmin ferroxidase activity, leading to iron-restricted erythropoiesis and iron accumulation in several organs (liver, pancreas, heart, thyroid), including the central nervous system. The therapeutic approach to aceruloplasminemia is currently debated and poorly defined. Currently, no curative therapy exists, and treatment primarily relies on iron-chelating agents. While iron chelation has been employed to manage systemic iron overload, its effectiveness in addressing neurological involvement is uncertain, with limited evidence regarding long-term outcomes and optimal chelation protocols.
Case Presentation: We report the long-term follow-up of two adult brothers (Pt1 and Pt2), aged 44 and 45, with a confirmed diagnosis of aceruloplasminemia due to a homozygous nonsense mutation (c.2242C>T, p.Gln748X) in exon 12 of the CP gene. Both presented with unexplained hyperferritinemia, hepatic iron overload, diabetes mellitus, and were initially misdiagnosed with hemochromatosis. Over time, they developed progressive neurological symptoms including memory impairment, parkinsonism, dystonia, and ataxia, which raised the suspicion of Wilson disease. At this point, they were referred to our center for further evaluation of disorders related to iron and copper metabolism. Before our evaluation, Pt1 had previously received deferoxamine (DFO) and deferiprone (DFP) both discontinued due to adverse events and poor compliance. Pt2 underwent phlebotomy/ erythroapheresis for 8 years until anemia precluded continuation. At the time of referral, both patients had advanced hepatic siderosis and mild to moderate liver fibrosis, confirmed by biopsy and T2-weighted magnetic resonance imaging (MRI).
Pt1 exhibited impaired constructive praxis, executive function deficits, and spatial/verbal anterograde memory impairment, with neurological signs including mild polyneuropathy, minimal sensory ataxia, and bradykinesia. Pt2 had a more severe neuropsychiatric syndrome with signs of basal ganglia dysfunction (facial hypomimia, dystonia, dyskinesias), extrapyramidal features (rigidity, bradykinesia), ataxia, pyramidal signs, and mild cognitive and affective symptoms. Both had mild sensorineural hearing loss and electromyographic evidence of peripheral nerve involvement. Brain MRI showed widespread cerebral siderosis involving basal ganglia, cerebellar cortex, and hypophysis.
A treatment strategy combining two iron chelators—initial intensive chelation with deferasirox (DFX), followed by long-term maintenance with DFP—was implemented sequentially in both patients. DFO was not considered in the intensive treatment phase, due to previous adverse events (Pt1) and lack of compliance (Pt2).
Outcomes: DFX at low-to-moderate doses led to significant reductions in liver iron concentration (LIC) and serum ferritin (< 500 ng/ml), accompanied by a marked regression of neuropsychiatric symptoms, particularly in Pt1. After reduction and stabilization of systemic iron stores, both patients were transitioned to medium-low doses of DFP (30–70 mg/kg/day), leveraging its capacity to cross the blood-brain barrier and its successful use in case series of Neurodegeneration with Brain Iron Accumulation (NBIA) (Dusek et al., 2016; Kakhlon et al., 2010, Forni et al. 2022), for continued cerebral iron clearance. After 9 years of therapy, Pt2 developed unexplained syncopal episodes: neurological, cardiologic and endocrinological causes were ruled out as well as overt autonomic dysfunction. These unexplained symptoms prompted evaluation for potential DFP-induced seizures; however, no definitive link was established, and DFP was continued without further clinical deterioration. Over a follow-up period of more than 10 years, both patients demonstrated sustained clinical improvement and stabilization of brain MRI findings, with no evidence of progressive neurological damage. Notably, this represents one of the longest reported treatment periods with DFP in aceruloplasminemia, with excellent therapeutic adherence and good tolerability.
Conclusions: This case series provide novel evidence supporting the long-term use of a sequential dual chelation regimen (DFX followed by DFP) in overtly symptomatic aceruloplasminemia. In particular, DFP may effectively halt or even reverse neurological progression when used as a maintenance therapy. The observed clinical improvement and long-term stabilization of brain iron overload, which were particularly evident under DFP chelation, underscore its relevant role in managing the cerebral component of iron accumulation. These findings contribute to the limited but growing evidence supporting tailored chelation strategies in aceruloplasminemia once systemic iron overload occurs, and suggest that deferiprone may be a valuable long-term option for maintaining neurological stability.

A COMPLEX CASE OF INFECTIVE ENDOCARDITIS

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Introduction: Infective endocarditis (IE) is a severe microbial infection involving the endocardial surface of the heart, most commonly affecting the valves, and characterized by a heterogeneous clinical presentation that often complicates timely and accurate diagnosis. The diagnosis is based on modified Duke criteria that include 2 major criteria (positive blood cultures for typical microorganisms and imaging suggestive of IE) and 5 minor criteria (predisposing conditions, fever, embolic phenomena, immunologic phenomena, microbiologic evidence of atypical pathogens). The diagnosis is confirmed with 2 major, 1 major and 3 minor criteria, or 5 minor criteria. The main complications of IE include heart failure, persistent infection with progression to septic shock, and neurological manifestations (such as stroke, meningitis, or brain abscess). The following report outlines a complex case of infective endocarditis with significant neurological sequelae.
Clinical case: A69-year-old male patient was admitted due to generalized weakness, psychomotor slowing and a transient episode of generalized limb rigidity, without associated fever. His medical history included a recent hospitalization for ischemic stroke of unknown etiology complicated by Enterococcus faecalis bacteremia, schizophrenia, and chronic alcohol abuse. His home pharmacological therapy included paliperidone and cardioaspirin. Upon arrival at the emergency department, the patient was awake, afebrile, and hemodynamically stable, with psychomotor slowing but no signs of meningeal irritation. Routine blood tests showed no significant abnormalities. The neurological consultation recommended a brain CT scan, which excluded any acute events; an electroencephalogram (EEG), which revealed nonspecific background slowing; and a brain MRI.
The patient was admitted to the Internal Medicine ward for further evaluation. On the second day, he developed a fever and a worsening level of consciousness. Blood cultures were positive for E. faecalis, with an antibiogram similar to that from the previous hospitalization. Antibiotic therapy with ampicillin was started. Given the suspicion of complicated bacteremia, a transthoracic echocardiogram was performed, which showed no evidence of endocardial vegetations; follow-up blood cultures were negative.
Subsequently, in accordance with the prior neurological recommendation, a brain MRI was performed and revealed subtle meningeal enhancement consistent with an infectious-inflammatory or secondary neoplastic process in the bilateral frontal regions. A lumbar puncture showed decreased glucose levels, elevated protein concentration, and mild pleocytosis, without neoplastic atypia. Given the suspicion of neurological complications of infective endocarditis (IE), transesophageal echocardiography was performed, revealing vegetations on both the mitral and aortic valves.
Based on these findings, the antibiotic regimen was modified by adding ceftriaxone 2 g twice daily to the ongoing ampicillin therapy. A cardiothoracic surgery consultation was obtained, and valve replacement was recommended. Concurrently, due to the suspicion of a neoplastic nature of the brain lesions, a contrast-enhanced CT scan of the chest and abdomen was performed, revealing thickening of the bladder wall. Urine cytology showed the presence of cells compatible with high-grade urothelial carcinoma.
The clinical course was complicated by multiple episodes of tonic-clonic seizures, prompting the initiation of antiepileptic therapy with valproic acid and levetiracetam. A follow-up brain MRI demonstrated new ischemic lesions, likely related to septic emboli, along with evidence of subarachnoid hemorrhage and a small hemorrhagic infarction. Given the complexity of the clinical picture, and in agreement with the cardiothoracic surgeons, surgical intervention was deferred. Progressive clinical deterioration in the following weeks led to the decision not to proceed with cystoscopy.
Conclusion: The complexity of this clinical case highlights the importance of an accurate and timely diagnosis. Although the initial symptoms were consistent with sepsis due to uncomplicated bacteremia from E. faecalis (first echocardiogram negative for vegetations, follow-up blood cultures negative), the persistence of the clinical picture, particularly neurologically, and the presence of the same pathogen in the blood cultures, suggested the need for further investigation with brain MRI and lumbar puncture. The diagnosis of infective endocarditis (IE) was confirmed by repeating the echocardiographic examination. Neurological complications are the initial symptom in approximately[30]% of IE cases, making it essential to repeat cardiac imaging or perform second-line diagnostic tests if clinical suspicion persists.

ASSOCIATION OF CIRCULATING MIR-29B WITH MICROVASCULAR DYSFUNCTION AND DIGITAL ULCERS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Rationale: Systemic sclerosis (SSc) is a rare and complex autoimmune disease

characterized by endothelial dysfunction, immune system dysregulation, and fibrosis of the skin and internal organs. Digital ulcers (DUs) are a common and debilitating vascular complication in SSc, closely linked to disease severity and impaired microcirculation. However, the underlying mechanisms of these vascular alterations remain poorly understood and may involve dysregulation of circulating microRNAs. In particular, downregulation of microRNA-29b (miR-29b), a key regulator of fibrotic processes and vascular remodeling, has been observed in SSc and may be associated with DUs development.
This study aimed to investigate whether modulation of circulating miR-29b levels are associated with DUs (history and recurrence) and digital perfusion impairment as assessed by the proximal-distal gradient (PDG) using laser speckle contrast analysis (LASCA).
Methods: In this retrospective observational study, 29 patients with SSc [26 female, median age 55 years (IQR 45-66)] were enrolled. Clinical data were collected, including DUs history and recurrence. Perfusion images of the dorsal hand were obtained using LASCA and divided into three regions of interest (ROIs): ROI1: second, third, and fourth fingertips distal to the proximal interphalangeal joints; ROI2: area between the proximal interphalangeal and metacarpophalangeal joints; ROI3: the dorsal surface of the hand. The PDG was calculated as the perfusion difference (in perfusion units, pU) between ROI1 and ROI2. A PDG<30pU was considered indicative of significant distal microvascular impairment. Fasting blood samples were collected and circulating levels of miR-29b were quantified using real-time quantitative PCR (RT-qPCR).
Results: We observed significant downregulation of circulating miR-29b in SSc patients with a history of DUs (n=15;51.7%) compared to those without (n=14; 48.3%) (p<0.05). Similarly, miR-29b levels were significantly lower in SSc patients with recurrent DUs (n=10;34.5%) than in those with no recurrence (n=19; 65.5%) (p<0.05). When SSc patients were stratified based on PDG values, those with PDG<30pU (n=21; 72.4%), reflecting impaired distal perfusion, showed significantly reduced miR-29b levels compared to SSc patients with PDG ≥30pU (n=8; 27.6%) (p < 0.05).
Conclusion: Our data demonstrated a consistent downregulation of miR-29b in SSc patients with more severe digital vascular involvement. Further investigations are warranted to clarify whether miR-29b may contribute to the pathophysiology of SSc-related vasculopathy and could represent a potential biomarker or therapeutic target for preventing microvascular complications and improving clinical outcomes in SSc.

NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN AS A BIOMARKER OF SUBCLINICAL RENAL INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Rationale: Systemic sclerosis (SSc) is a rare and complex autoimmune disease characterized by endothelial dysfunction, immune system dysregulation, and fibrosis of the skin and internal organs. Subclinical renal involvement is frequent in SSc patients and it is characterized by vascular damage in small and medium size vessels, probably due to renal Raynaud's phenomenon (RP) vasospasm episodes, with consequent hypoxia, vasoconstriction and increase of renal resistive index (RRI). Indeed, renal scleroderma associated-vasculopathy is characterized by vascular damage with normal estimated glomerular filtration rate (eGFR).
In hypoxic renal tissue, macrophagic infiltrates and damaged tubular cells release several inflammatory and profibrotic cytokines and chemokines such as neutrophil gelatinase-associated lipocalin (NGAL).
This study aimed to investigate the possible role of NGAL as a biomarker of subclinical renal involvement in SSc patients.
Methods: In this retrospective observational study, 42 patients with SSc [36 female, median age 54 years (IQR 46-60)] were enrolled. Clinical data were collected. Renal function was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI). Renal Doppler ultrasound was performed to analyze blood velocity from the interlobar arteries by placing the probe at 3 different positions (mesorenal, superior, and inferior) evaluating peak systolic velocity (PSV) and diastolic velocity (DV). Renal resistive index was measured as RRI=(PSV−DV)/PSV. Peripheral venous blood samples were collected and serum was separated from blood cells by centrifugation at 1500×g for 15 min at room temperature and stored at -80°C until tests were performed using ELISA kits specific for Human Lipocalin-2/NGAL Quantikine ELISA from (R&D Systems, McKinley Place, Minneapolis, MN, USA).
Results: Median eGFR was 81.4 ml/min (IQR 70.4-91) and median RRI was 0.68 (IQR 0.64-0.70). Fourteen (33.3%) SSc patients had RRI ≥ 0.70. Median NGAL was 38.3 ng/ml (IQR 20.3-53.7). A significant positive linear correlation was found between serum NGAL and RRI (r=0.489, p<0.001). Moreover, SSc patients with RRI ≥ 0.70 had statistically significant higher serum NGAL compared to SSc patients with RRI < 0.70 [61.2 ng/ml (IQR 48.1-62) vs 23 ng/ml (IQR 18.2-39.15), p<0.001].
Conclusion: Renal scleroderma-associated vasculopathy, characterized by increased RRI despite normal eGFR, releases NGAL related to chronic hypoxia due to renal RP. This suggests that NGAL might be a potential biomarker for subclinical renal involvement in SSc patients.

OBESITY SEVERITY AND CLINICAL BURDEN: STRATIFIED COMORBIDITY ANALYSIS ACROSS BMI SUBGROUPS IN A REAL-WORLD COHORT

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Background: Obesity is a well-recognised risk factor for cardiometabolic, hepatic, and respiratory diseases. Its impact extends beyond total fat mass, with visceral adiposity playing a central role in the development of insulin resistance, inflammation, and organ-specific complications. Although BMI is a widely available surrogate for excess weight, its utility in stratifying clinical burden is not consistently integrated into routine care. Mapping how comorbidities distribute across BMI strata may help refine screening protocols and enable early, targeted intervention. This study aimed to quantify the prevalence of major obesity-related comorbidities across BMI categories in a real-world multidisciplinary setting.
Methods: We conducted a retrospective cross-sectional analysis of 451 adult patients referred to the Metabolic Health Centre at IRCCS San Raffaele Hospital, Milan. Each patient had recorded anthropometric data and at least one confirmed obesity-related comorbidity. Standardised clinical assessments included medical history, anthropometry, laboratory testing (including lipid profile and glucose), and targeted instrumental diagnostics. Comorbidities evaluated were arterial hypertension, dyslipidaemia, cardiovascular disease (CVD), hepatic steatosis (assessed by abdominal ultrasound), obstructive sleep apnoea syndrome (OSAS, via polysomnography or home sleep study), gestational diabetes, and dyspepsia. Patients were grouped into BMI categories of 27–32, 32–37, and 37–42 kg/m². Prevalence was calculated per subgroup, and differences across BMI classes were analysed using Chi-square testing.
Results: Among 451 patients with complete data, hepatic steatosis showed a progressive increase with BMI: 31.8% in the 27–32 group, 38.5% in 32–37, and 47.3% in 37–42 kg/m² (p = 0.0301). OSAS followed a similar trajectory (9.8%, 17.6%, and 21.4%; p = 0.0393), reinforcing its association with excess visceral fat. Hypertension was common across all categories but peaked in the intermediate BMI group (37.1%, 50.3%, 45.5%), with no significant trend (p = 0.1015). Dyslipidaemia was consistently high (50.8%, 42.7%, 50.9%), while the prevalence of CVD remained low and uniform (2.3%, 2.1%, 2.7%; p = 0.9418). Gestational diabetes and dyspepsia were uncommon across all strata (<7%).
Conclusion: In this real-world cohort, hepatic steatosis and OSAS were significantly more prevalent in higher BMI groups, confirming their close pathophysiological link to visceral adiposity and metabolic dysfunction. Hypertension and dyslipidaemia, while highly prevalent, did not display a clear BMI-dependent pattern, suggesting additional determinants beyond adiposity alone. These findings support the inclusion of BMI-stratified screening in clinical practice and reinforce the need for structured evaluation of hepatic and respiratory complications in patients with more severe obesity. Although based on a single-centre cohort, this analysis provides actionable insights for optimising multidisciplinary obesity care and tailoring early diagnostic pathways.

IMPLEMENTATION OF A RISK MANAGEMENT-BASED MODEL sFOR THE CONTROL OF CLOSTRIDIOIDES DIFFICILE INFECTIONS IN A SOCIO-HEALTHCARE FACILITY AUTHORS

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Healthcare-associated infections (HAIs), and in particular Clostridioides difficile (CD) infections, represent a major concern for patient safety in socio-healthcare

settings. CD infection is characterized by high morbidity, potential recurrence, and significant clinical impact. According to the European Centre for Disease Prevention and Control, these infections generate substantial annual costs for the European healthcare system.
In this context, the present study—conducted in 2024 in a socio-healthcare facility (ASP) in Milan—aimed to assess compliance with institutional procedures for the management of CD infection risk and to propose structured improvement interventions, aligned with the most recent IDSA-SHEA and ESCMID-ECDC guidelines.
The study examined 50 confirmed cases of CD infection. A multidimensional methodological approach was employed, including the use of a newly developed 25-item checklist organized into thematic areas: timely diagnosis, patient isolation, use of personal protective equipment (PPE), hand hygiene, environmental management, and staff training. The data were consolidated into two databases: the first for mapping field non-conformities (NCs), and the second for calculating critical time-based indicators (e.g., time to isolation, initiation of sanitization, symptom recognition).
The results revealed a high incidence of NCs, averaging four per observed case. Key findings include:
These timeframes highlight significant operational vulnerabilities, particularly in light of the high transmissibility of CD spores. The most frequent NCs involved device management, delays in isolation and sanitization, and inconsistent staff training. Furthermore, a notable number of "not applicable" entries in the checklist revealed practical challenges in monitoring certain procedures, suggesting a need for methodological refinement.
Based on the findings, a series of targeted improvement actions were proposed, including:
This study offers a potentially transferable model for other socio-healthcare settings, representing a successful integration of field research, scientific review, and operational planning. The introduction of the checklist fostered a systemic and proactive approach to infection control, consistent with the principles of Clinical Governance and Risk Management.
The experience underscores that timeliness, action traceability, and interdisciplinary collaboration are key elements in effectively containing the risk of Clostridioides difficile infection, particularly in high-dependency environments with vulnerable populations.

LONG-TERM ALBUMIN TREATMENT IMPROVES OUTCOMES IN PATIENTS WITH CIRRHOSIS AND ASCITES

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Background: and Aims: While the ANSWER trial has demonstrated improved survival with long-term albumin treatment in patients with ascites, a benefit was not observed in some other studies. Study design, heterogeneity in study cohorts and albumin dose have been hypothesized to explain these discrepancies. We aimed to assess the effects of long-term albumin treatment – administered in a real-life outpatient setting – on liver-related mortality in cirrhosis patients with ascites.
Methods: 878 cirrhosis patients with ascites as index decompensation between 2003-2024 from four tertiary care centers in Europe were included. 106 patients (11.7%) receiving longterm (i.e., more than > 30 days) i.v. albumin therapy. Patients were characterized from time of albumin treatment initiation or first decompensation. We performed inverse probability of treatment weighting (IPTW) adjusting for age, sex, MELD-Na and etiologic cure to account for differences in disease severity in multivariable cox regression analyses of liver-related mortality.
Results: The main patient characteristics were balanced between patients receiving long-term albumin [ivALB (+)] and those w/o albumin treatment [ivALB(-)]: median age: 60.2 vs 56.9 years (p = 0.008) and MELD-Na 14 vs 15 (p = 0.231). Median ivALB(+) treatment dose was 40 grams per week (mostly 20% 200mL) and patients were treated for 11.1 (IQR: 5.0 – 20.3) months. During a median follow-up of 46.5/36.4 months in ivALB(-)/ivALB(+) patients, 44.4%/35.9% died including 39.0%/27.2% liver-related deaths, and 12.3%/17.5% underwent liver transplantation (LT). Incidence of liver-related mortality at 36 months was 38.8% in the ivALB(-) vs. 34.4% in the ivALB(+) patients (log-rank p = 0.100). Cox proportional hazards regression with IPTW for ivALB(+) treatment showed that next to age (aHR per year: 1.04 [95%CI: 1.02-1.06]; p < 0.001), MELD-Na (aHR per point: 1.07 [95%CI: 1.04-1.10]; p < 0.001), female sex (aHR: 0.58 [95%CI: 0.42-0.81]; p = 0.001) and etiologic cure (aHR: 0.56 [95%CI: 0.36-0.88]; p=0.012) - long-term ivALB(+) therapy was associated with significantly reduced risk of liver-related death (aHR: 0.65 [95%CI: 0.42-0.99]; p = 0.048).
Conclusions: Acknowledging the limitations related to retrospective design and nonstandardized treatment schedules, long-term ivALB(+) treatment significantly reduced liverrelated mortality in our cohort of cirrhosis patients with ascites.

SUICIDE RISK ASSESSMENT IN A MILANESE SOCIO-HEALTHCARE AGENCY: ANALYSIS OF PATIENT INTAKE PROCEDURES

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Suicide represents a major public health issue, not only due to its severity and incidence, but also for its significant impact on the healthcare system and society as a whole. According to the World Health Organization, over 700,000 people die by suicide each year, with many more attempting it—highlighting a profound underlying vulnerability. In hospital settings, suicide is classified as a sentinel event: a serious, preventable adverse event that can undermine public trust in the healthcare system. The Italian Ministry of Health has addressed this issue through Ministerial Recommendation No. 4, which provides operational guidelines for suicide prevention in hospitals, urging the implementation of standardized procedures for suicide risk assessment—especially in high-vulnerability contexts such as oncology wards.
This study aims to evaluate the application of these recommendations within a socio-healthcare agency in Milan (ASP), through a retrospective analysis of 48 clinical records of patients hospitalized in an oncological rehabilitation ward, combined with direct observation of patient intake interviews. The sample was selected to represent a particularly vulnerable population, as identified in Recommendation No. 4. A structured 15-item checklist was used, divided into six sections (personal information, medical history, sociodemographic characteristics, clinical condition, chronic alcoholism/withdrawal/blood alcohol levels, and other warning signs) to verify whether healthcare professionals systematically explored risk areas during the initial assessment.
The results revealed several critical issues: in over 50% of cases, key areas such as self-harming behavior, family history of suicide, social isolation, and sexual abuse were neither investigated nor documented. Qualitative analysis of the observed interviews confirmed a frequently unstructured approach, with insufficient and fragmented documentation in clinical records. In several cases, psychological support was activated only when obvious distress was present, without any systematic preventive assessment. Furthermore, risk evaluations were rarely repeated or updated in relation to the patient's evolving clinical condition.
Based on these findings, a number of improvement actions are proposed, including: the mandatory use of validated suicide risk assessment tools (e.g., NGASR, SSI, SIS), revision of the initial intake protocol, targeted staff training, integration of checklists into electronic health records, and reinforcement of the role of Risk Management. The value of a multidisciplinary approach is also emphasized, involving collaboration among physicians, psychologists, nurses, public health professionals, and caregivers to ensure comprehensive and personalized care for at-risk patients.
The study also explored the role of Public Health Officers and Risk Management services in prevention efforts, identifying the need to foster a culture of safety focused on prevention, effective communication among professionals, and implementation of evidence-based decision-making tools. Particular attention was given to clinical documentation, which must explicitly record all assessments

conducted during intake interviews to ensure traceability and continuity of care.
In conclusion, the findings underscore the need for a standardized operational model aligned with Ministerial Recommendations to enhance the quality and safety of care. The adoption of a specific suicide risk assessment protocol represents not only an ethical and professional obligation, but also a tangible opportunity to reduce sentinel events, improve care quality, and protect the most vulnerable patients.

ACCURATEZZA DELLA SEMEIOTICA ECOGRAFICA NELL'IDENTIFICAZIONE DEL FOCUS INFETTIVO NEL PAZIENTE ANZIANO RICOVERATO PER SEPSI: LA NOSTRA ESPERIENZA

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Introduzione: La sepsi è una complessa sindrome clinica pericolosa per la vita caratterizzata da una disfunzione d'organo causata da una risposta disregolata dell'ospite alle infezioni. È caratterizzata da anomalie fisiologiche, biologiche e biochimiche causate dalla risposta infiammatoria che ne consegue che possono portare anche alla sindrome da disfunzione d'organo multipla e alla morte. È una patologia "tempo dipendente", il cui esito clinico dipende dalla rapidità del riconoscimento e dall'efficacia della gestione clinica a partire dalla prima ora. È potenzialmente letale specialmente nei pazienti anziani. La difficoltà diagnostica è amplificata dai sintomi atipici di presentazione nell'anziano e dall'assenza di test diagnostici specifici. Nonostante le campagne di sensibilizzazione, la mortalità rimane elevata, con un'incidenza crescente legata a fattori demografici e clinici come l'invecchiamento della popolazione e le comorbidità.
Materiali e Metodi: L'ecografia point-of-care (POCUS) si sta affermando come strumento cruciale nell'identificazione precoce del focus infettivo e nel monitoraggio emodinamico dei pazienti. La POCUS migliora l'accuratezza diagnostica nei pazienti critici grazie alla possibilità di valutare i principali distretti anatomici quali apparato respiratorio, addominale, cardiaco e vascolare. Inoltre, è di fondamentale ausilio nell'esecuzione di procedure bedside come il posizionamento di drenaggi e di accessi venosi, riducendo notevolmente i tempi di intervento. Alla luce della letteratura scientifica, è stata effettuata una revisione dei pazienti ricoverati nel reparto di Alta Intensità di Cura dell'Ospedale di Guastalla da gennaio 2023 a dicembre 2023 con diagnosi d'ingresso di sepsi, focalizzando l'attenzione su quale ruolo ha svolto l'Ecografia Point-of-Care (POCUS) nella ricerca del focus infettivo. La diagnosi di sepsi è stata stabilita secondo i criteri della Surviving Sepsis Campaign. I pazienti sono stati esaminati da personale medico formato all'esecuzione dell'ecografia point-of care. L'ipotesi diagnostica formulata dopo l'esecuzione della POCUS è stata confrontata con la diagnosi di dimissione ottenuta attraverso il work-up diagnostico standard (che includeva esami ematici, colturali, imaging radiologico di secondo livello).
Risultati: Il campione totale di pazienti esaminati era composto da 84 soggetti, di cui 49 maschi e 35 femmine, con un'età media di 73,9 anni. La fonte infettiva è stata identificata nel 90% dei pazienti (76 su 84). Le fonti principali di sepsi sono state: urinaria, polmonare, addominale, cardiaca, cutanea, osteoarticolare e tessuti molli. Al momento dell'ingresso in reparto la POCUS è stata eseguita su 59 degli 84 pazienti (70,2% dei casi). La diagnosi formulata attraverso la POCUS coincideva in 22 pazienti (37,3%) con la diagnosi di dimissione, mentre non coincideva in 35 pazienti (62,7%). In particolare, è stata eseguita in 29 su 44 pazienti con sepsi urinaria (66%) ed è risultata diagnostica in 6 casi (20%), in pratica in tutti i casi con sepsi a componete ostruttiva del case-mix. È stata utilizzata in 11 su 13 casi di sepsi polmonare (84,6%) risultando diagnostica in 8 casi (73%). In presenza di polmonite batterica, è stata diagnostica in 8 casi su 9 (89%). È stata inoltre eseguita in 8 su 10 pazienti con sepsi addominale (80% dei casi) risultando diagnostica in 6 casi (75%). Nei casi di colecistite acuta litiasica, la POCUS iniziale è risultata diagnostica in 4 casi su 4 (100%). Nel sottogruppo di pazienti con ascessi endoaddominali (3 casi) non è mai risultata diagnostica richiedendo l'utilizzo di esami radiologici di secondo livello. Nei casi di endocardite batterica, la POCUS iniziale è risultata diagnostica in 2 casi su 2 (100%).
Conclusion: I risultati della nostra esperienza suggeriscono come la POCUS sia uno strumento utilissimo nella valutazione dei pazienti con sepsi nei reparti di Alta Intensità Medica. In particolare, ha mostrato una buona capacità diagnostica nei casi di colecistite acuta litiasica, nelle polmoniti batteriche, nelle infezioni urinarie con componente ostruttiva e nelle endocarditi. L'utilizzo della POCUS nella ricerca del focus infettivo contribuisce a migliorare la gestione clinica dei pazienti ricoverati con diagnosi di sepsi consentendo di intraprendere precocemente una terapia antibiotica empirica il più possibile mirata secondo il sospetto diagnostico, nel monitoraggio emodinamico e nella valutazione dell'eventuale necessità di procedure interventistiche e/o interventi chirurgici potenzialmente fondamentali per l'outcome dei pazienti.

Tabella 6: *Fonti settiche individuate*

	No.	%
SEPSI URINARIE	44	52,4
Senza idronefrosi	38	86,4
Con idronefrosi	5	11,4
Con pielonefrite	1	2,3
SEPSI POLMONARI	13	15,5
Polmoniti	9	69,2
Inalazioni	4	30,8
SEPSI ADDOMINALI	10	11,9
Colecistite litiasica	4	40
Ascessi	3	30
Colangiti	3	30
SEPSI CARDIACHE	2	2
Endocarditi	2	2
SEPSI A PARTENZA DA CUTE E TESSUTI MOLLI	5	6
Ulcera piede	1	20
Flemmone parete addominale	1	20
Fascite gamba	1	20
Ascesso vulvare	1	20
Ascesso perineale	1	20
SEPSI OSTEO-ARTICOLARI	2	2,38
Osteomielite del piede	1	50
Artrite settica ginocchio	1	50
SEPSI INDETERMINATE	8	9,5
FONTE SETTICA INDIVIDUATA	76	90,5%
FONTE SETTICA NON INDIVIDUATA	8	9,5%
TOTALE	84	

A MASKED DIAGNOSIS: WHEN A STUBBORN CHOLECYSTITIS HIDES SOMETHING MORE

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Acute acalculous cholecystitis is a rare and under-recognized manifestation of systemic lupus erythematosus (SLE). Even more exceptionally, this condition can represent the first clinical sign of
the disease, making the diagnosis particularly complex and the initial treatment often inadequate. Literature reports few similar cases, with a higher prevalence in immunocompromised patients or in
the presence of other autoimmune comorbidities. Between 1983 and 2020, only 15 case reports ofacute acalculous cholecystitis in SLE patients were described, confirming the rarity of this clinical
presentation. A timely recognition of this atypical form is essential to prevent complications and
ineffective treatments.
We report the case of a 68-year-old woman who presented at the Emergency Department for a syncopal episode, intermittent fever peaking at 38°C, and right upper quadrant abdominal pain.
Her recent medical history included hospitalization at another facility for similar symptoms, treated with broad-spectrum antibiotics with transient benefit. Nevertheless, just a few weeks after
discharge she complained of symptoms recurrence. Upon admission to our Unit, blood tests proved neutrophilic leukocytosis (WBC 24700/μL; R.R. 4000-10000/μL), elevated CRP 31 mg/dl
(R.R. < 0,5 mg/dl) and ESR 47 mm/h (R.R. < 30 mm/h). Abdominal ultrasound revealed a distended gallbladder with thickened walls, positive sonographic Murphy's sign, and no stones,
consistent with acute acalculous cholecystitis.
Broad-spectrum antibiotic therapy was started according to guidelines for suspected intra- abdominal infections. However, despite partial initial

improvement, the patient's clinical condition
worsened, with increased abdominal pain, persistent fever, and rising inflammatory markers, despite multiple antibiotic changes. Given the failure of antimicrobial therapy and a history of
rheumatoid arthritis and Sjögren's syndrome, an autoimmune origin of the cholecystic pathology
was suspected.
While awaiting immunological test results, corticosteroid therapy (methylprednisolone 40 mg IV/day) was started ex adiuvantibus. Within 48 hours, a marked clinical improvement was
observed, with resolution of fever, reduced pain, and a significant decrease in inflammatory markers. Subsequent immunological tests confirmed the SLE diagnosis according to the 2019
EULAR/ACR criteria, with high-titer positive ANA (1/640), hypocomplementemia, C3 47 mg/dl (R.R. 80-185 mg/dl) and C4 2,9 mg/dl (R.R. 15-53 mg/dl), lupus anti-coagulant positivity,
autoimmune hemolytic anemia (positive direct Coombs test, schistocytes on peripheral blood smear and increased markers of tissue damage and cytolysis), serositis (pleural and pericardial
effusion), and proteinuria > 0.5 g/24 hours. The patient started oral therapy with prednisone 25 mg/day (for 10 days, then tapered) and
hydroxychloroquine 200 mg twice daily, leading to complete resolution of symptoms and normalization of gallbladder ultrasound findings. One-month follow-up confirmed full clinical and
biochemical recovery (WBC 6650/µL; CRP 0,3 mg/dl). Our case highlights that in the presence of acute acalculous cholecystitis unresponsive to antibiotic therapy, especially in patients with a history or suspicion of autoimmune diseases, an autoimmune etiology should be suspected. In such cases, corticosteroids are an effective therapeutic strategy,
able to avoid prolonged ineffective treatments and potentially unnecessary surgical procedures. Awareness of this rare but significant manifestation of SLE can improve the diagnostic and
therapeutic approach in similar cases.

Entry criterion
Antinuclear antibodies (ANA) at a titer of ≥1:80 on HEp-2 cells or an equivalent positive test (ever)

↓

If absent, do not classify as SLE
If present, apply additive criteria

↓

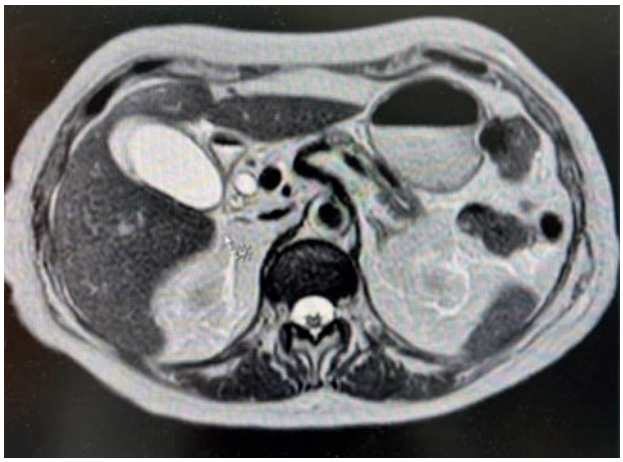
Additive criteria
Do not count a criterion if there is a more likely explanation than SLE.
Occurrence of a criterion on at least one occasion is sufficient.
SLE classification requires at least one clinical criterion and ≥10 points.
Criteria need not occur simultaneously.
Within each domain, only the highest weighted criterion is counted toward the total score§.

Clinical domains and criteria	Weight	Immunology domains and criteria	Weight
Constitutional		***Antiphospholipid antibodies***	
Fever	2	Anti-cardiolipin antibodies OR	
Hematologic		Anti-β2GP1 antibodies OR	
Leukopenia	3	Lupus anticoagulant →	2
Thrombocytopenia	4	***Complement proteins***	
Autoimmune hemolysis	4	Low C3 OR low C4	3
Neuropsychiatric		Low C3 AND low C4 →	4
Delirium	2	***SLE-specific antibodies***	
Psychosis	3	Anti-dsDNA antibody* OR	
Seizure	5	Anti-Smith antibody	6
Mucocutaneous			
Non-scarring alopecia	2		
Oral ulcers	2		
Subacute cutaneous OR discoid lupus	4		
Acute cutaneous lupus	6		
Serosal			
Pleural or pericardial effusion →	5		
Acute pericarditis	6		
Musculoskeletal			
Joint involvement	6		
Renal			
Proteinuria >0.5g/24h →	4		
Renal biopsy Class II or V lupus nephritis	8		
Renal biopsy Class III or IV lupus nephritis	10		

Total score:

↓

Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.



PREVENTION OF VIOLENCE AGAINST HEALTHCARE WORKERS: ASSESSMENT OF THE PHENOMENON WITHIN A SOCIO-HEALTHCARE FACILITY

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Violence against healthcare workers represents an alarming and increasingly prevalent issue, recognized as a priority at both national and international levels. This study investigates the phenomenon within a socio-healthcare organization in Milan, in accordance with Ministry Recommendation No. 8 and regional guidelines.
An anonymous online questionnaire was administered to all healthcare and social-healthcare personnel within the facility. The survey explored the frequency and types of violent incidents, the settings in which they occurred, the individuals involved, and the preventive measures perceived as necessary. A total of 74 out of 867 eligible staff members responded. Of these, 55% reported experiencing at least one episode of violence, with verbal abuse being the most frequent, followed by psychological and physical aggression. The primary perpetrators were patients (46%) and family members (31%), though cases involving colleagues and supervisors were also reported.
Findings indicate significant underreporting of incidents. When asked, "If you experienced violence, did you report the episode to management?", 80% of respondents stated they did not formally report the event. This highlights cultural and organizational barriers that discourage reporting, exacerbating the victims' sense of isolation. Key risk factors identified include the presence of patients with behavioral disorders, communication issues with patients and families, lack of training on managing violent behavior, overcrowding, and inadequate environmental safety.
The data are consistent with findings in the literature: verbal violence is the most common form, and lack of ongoing training is a significant vulnerability. Gender and professional experience also influence exposure: most victims are women, frequently working in high-interaction settings such as long-term care facilities and intermediate care units.
These results underscore the urgent need to implement integrated programs for the prevention, monitoring, and management of violent incidents within socio-healthcare settings. Such programs should include systematic risk assessment, mandatory training, the activation of secure reporting channels, and immediate psychological support for victims.

ALLOIMMUNIZATION AND HEMOLYTIC TRANSFUSION COMPLICATIONS AMONG AN ITALIAN COHORT OF SICKLE CELL DISEASE PATIENTS: BEYOND ETHNIC DIFFERENCES.

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Red Blood cell (RBC) transfusion is a key intervention in decreasing morbidity and mortality in patients with Sickle cell disease (SCD), with approximately 90% of adults requiring at least one blood transfusion in their lifetime. However, RBC transfusion withholds several complications, among which alloimmunization is a major concern. Alloimmunization prevalence in SCD patients is the highest of any transfused patient population, ranging from 7% to 59%, and increases the risk of hemolytic transfusion complications and delays in identifying compatible RBC units. Knowledge on these conditions is limited and mainly derives from patients with SS genotype, with a significant knowledge gap for sickle-thal patients.

We retrospectively analyzed the characteristics of 52 patients referred to our attention for an acute event that required transfusion between 2018 and 2024 to evaluate the prevalence of alloimmunization among this population. 32/52 (61.5%) were females. The mean age was 35 years. 50% of patients were SS homozygous and 50% had a βS genotype. 44.2% were Caucasian, while 34.6% were Sub-Saharan African. 84.62% of sickle-thal patients were Caucasian, while all Sub-Saharan Africans had the SS genotype; only 1 Caucasian was HbSS. The prevalence of alloimmunization was 44.2% with no difference between the 2 genotypes. The immunohematologic characteristics of patients are summarized in Table 1. We recorded 188 acute events requiring hospital access, among which 140 were treated with blood transfusion. Most of them were vaso-occlusive crises with osteo-muscolar involvement, followed by acute worsening of anemia and acute chest syndrome. 5 acute ischemic strokes were reported, all of them in sickle-thal patients (p=0.012). Several other episodes of acute thrombosis were observed, the majority of which in the same population (5/6 events; p=0.054). The main trigger of acute events was infection. Clinical presentation was heterogeneous. 1/3 presented with organ damage (39 had respiratory failure, 4 required admission to the intensive care unit [ICU], and 3 developed multiorgan failure [MOF]). 3 events led to death. New alloantibodies developed in 10 cases (7.3%) after a transfusion during the acute event, all in 10 different patients. 3 patients developed more than 1 antibody and 2 patients developed allo- and auto-antibodies. We recorded 11 cases of hemolytic transfusion complications (7.9%) involving 9 patients: 6 delayed hemolytic transfusion reactions (DHTR) and 5 hyperhemolysis syndromes (HS). Among them, 6 patients already had allo/autoantibodies, while in 5/11 cases we did not found any new allo- or auto-antibody. The median estimated time from transfusion was 5 days. Clinical manifestations and severity of DHTR/HS were heterogeneous: 6 progressed to organ dysfunction (mainly respiratory failure) and 2 patients were hospitalized in the ICU. 1 event led to the death of a 40-year old patient. Management of DHTR/HS consisted mainly of supportive therapy (hydration, oxygen, analgesia). In 5 cases high-dose steroids were used, while eculizumab and intravenous immunoglobulins were used in one single patient respectively. In 8/11 DHTR/HS additional transfusions were used, with worsening of Hb value in 6 cases and stability in 2. As already known, we found a strong correlation between alloimmunization and DHTR/HS but no other risk factor. No significant difference was found between the 2 genotypes. Our study confirms that alloimmunization and DHTR/HS are important complications of transfusion therapy in SCD. We need further studies to identify possible risk factors for these complications to prevent them. Moreover, we need a better characterization of the sickle-thal population as it may have some peculiarities among the spectrum of SCD.

Patient	Alloantibody specificity	Autoantibody specificity	DHTR/HS
1	Anti-C, **anti-E, anti-Js(a), anti Fy(5), anti-Cw***		**HS**
2	Anti-C, anti-Fy(a), anti-Bga		
3	Anti-C, anti-E, anti-Kp(a), anti-Jk(a), anti-Bga	Anti-pdl	
4	Anti-c, anti-E, anti-Wra, anti-Lua, anti-Cw		
5	Anti-E		**HS**
6	**Anti-E, anti-Lua***	**DAT positive (antibody specificity not known)***	**HS**
7	Anti-E, anti-Fy(a), anti-Bg, anti-Cob		
8	Anti-E		
9	Anti-e, anti-Kp(a), anti-Jk(a), anti-Bga	DAT positive (antibody specificity not known)	
10	Anti-K		
11	Anti-K, anti-Kp(a)	Anti-pdl	**HS**
12	Anti-K		
13	Anti-Kp(a), anti-Cw		
14	Anti-Fy(a)	Anti-pdl	
15	**Anti-Jk(b), anti-Wra, anti-Ytb***	Anti-pdl	**DHTR, HS**
16	Anti-M		**DHTR**
17	Anti-M, anti-Lua		
18	Anti-Bga		
19	Anti-bg, antibodies not identified	Anti-pdl	
20	Anti-Wra, anti-Sc2		
21	Anti-Cw, anti-Bg		
22	**Antibodies not identified***		**HS**
23	**Antibodies not identified***	**Anti-C3d***	**DHTR**

*Picture 1. Immunohematologic characteristics of alloimmunized patients. In the column on the right we highlighted which patients developed a hemolytic transfusion complication. *In bold the new alloantibodies and autoantibodies found during a hemolytic transfusion complication.*

EXPLORATION OF CIRCULATING PROTEOME TOWARD THE IDENTIFICATION OF ACCESSIBLE BIOMARKERS FOR SARCOPENIA: INSIGHTS FROM A PILOT STUDY

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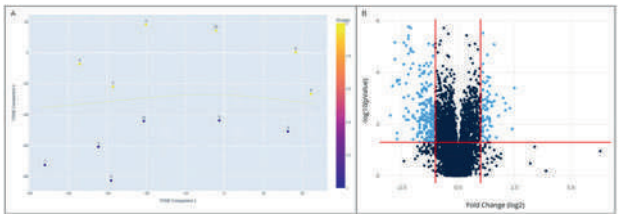
Background: Aging leads to a decline in muscle quality and strength, ultimately contributing to sarcopenia, a condition characterized by increased frailty and risk of falls. With projections indicating that 16% of the global population will be elderly by 2050, sarcopenia represents a major public health concern. However, its assessment remains challenging due to its multifactorial pathogenesis and lack of consensus among diagnostic guidelines. In this context, a deeper understanding of the molecular features of sarcopenia and the identification of accessible biomarkers are urgently needed, especially for use in clinical and hospital settings.

Materials and methods: We conducted a pilot study on serum samples from twelve individuals: six with no or mild sarcopenia (mean age: 60.5 ± 10.0 years) and six diagnosed with sarcopenia (mean age: 62.3 ± 4.8 years). Sarcopenia was assessed through clinical evaluation, functional tests, and imaging (ultrasonography/CT scan). Sera were analyzed using the Somascan 7k proteomic platform (Somalogic). Proteomic data were normalized and statistically analyzed as per the manufacturer's guidelines. Dimensionality reduction was performed using 2D t-SNE to visualize group differences (Figure 1A). Proteins with a fold change ≥ 1 and p-value < 0.05 were considered significant (Figure 1B). Enrichment and protein–protein interaction analyses were carried out to explore involved biological processes.

Results: The 2D t-SNE analysis revealed clear clustering between sarcopenic and non-sarcopenic subjects, indicating distinguishable proteomic profiles (Figure 1A). A total of 252 downregulated and 83 upregulated proteins were identified in sarcopenic individuals (Figure 1B). Downregulated proteins were significantly enriched in pathways related to protein metabolism (GO:0019538, $p = 1.7\times10^{5}$), muscle tissue development (GO:1901861, p = 0.03), and vesicle-

mediated transport (GO:0016192, p = 5.6×10^{4}), pointing out a disrupted muscle maintenance and cellular communication. Conversely, upregulated proteins were associated with immune and inflammatory responses (e.g., immune effector process, GO:0002252, p = 0.0026), cell adhesion (GO:0007155, p = 7.66×10^{5}), locomotion (GO:0040011, p = 2.7×10^{5}), and stress response (GO:0006950, p = 2.5×10^{5}), suggesting enhanced inflammation and altered cellular homeostatic mechanisms.
Conclusion: This pilot study identifies distinct circulating proteomic signatures associated with sarcopenia, reflecting the dysregulation of biological pathways implicated in its pathophysiology. Importantly, the identified signatures highlight the involvement of immune and inflammatory processes, along with perturbations in cellular communication and homeostasis, underscoring their potential mechanistic relevance. If validated in larger cohorts, these biomarkers could serve as accessible tools for monitoring sarcopenia and its progression, particularly in elderly and hospitalized populations.



ORCHESTRA DELPHI CONSENSUS: DIAGNOSTIC AND THERAPEUTIC MANAGEMENT OF POST-COVID-19 CONDITION IN VULNERABLE POPULATIONS

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Background: Post-COVID condition (PCC) remains poorly understood, especially in clinically vulnerable groups. Within the ORCHESTRA Project, we applied the Delphi approach to drive recommendations for the diagnosis, management, and prevention of PCC in people living with HIV (PWH) and patients affected by rheumatological diseases (RD) and haematological malignancies (HM).
Methods: Based on literature review, three areas of interest in PCC in PWH, HM, and RD were identified: 1) features and risk factors; 2) diagnosis and management; and 3) prevention. A three-round Delphi anonymous survey consisting of 15 questions was conducted including 69 experts. Consensus was measured by the 6-point Likert scale categorised into four tiers: strong disagreement, moderate disagreement, moderate agreement, and strong agreement. Statements were generated on questions achieving consensus.
Results: Eleven statements were generated: six on features and risk factors of PCC in clinically vulnerable populations, two on diagnosis and management, and three on prevention. Chronic fatigue was identified as the most frequent presentation of PCC in PWH and RD populations. A different case definition of PCC is required for RD population, as symptoms of PCC and autoimmune disorders may overlap. Risk factors for PCC include age>65, severity of COVID-19, and female sex; this latter is also associated with increased smell/taste impairment. A clinical assessment or a routine laboratory test performed three months after acute infection is not suggested to diagnose PCC in PWH. PWH and RD should be screened to exclude additional autoimmune disorders in case of chronic fatigue/arthralgia of new onset. Full-course vaccination and early treatment for COVID-19 should be promoted to prevent PCC, while corticosteroids during acute infection are not recommended.
Conclusion: Diagnosis, management and prevention of PCC are still under discussion. This Delphi offers valuable insights on PCC in selected clinically vulnerable populations and suggests a tailored approach in vulnerable populations.

ROLE OF URINARY 11-DEHYDRO-THROMBOXANE B2 AS A PREDICTOR OF PREECLAMPSIA IN PREGNANT HIGH-RISK WOMEN ON LOW-DOSE ASPIRIN TREATMENT

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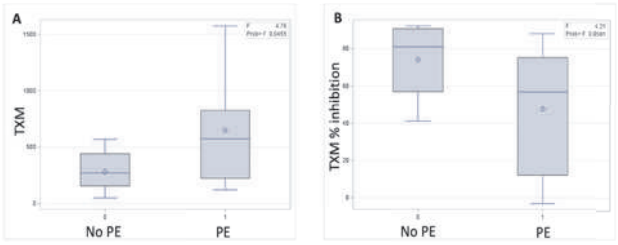
Background: Pre-eclampsia (PE) is the leading cause of adverse cardiovascular (CV) outcomes during and after pregnancy. Thromboxane (TX)-dependent platelet activation plays a key role in PE pathogenesis. Urinary 11-dehydro-TXB2, a major TX metabolite (TXM), is reduced by at least 75% by low-dose aspirin (ASA) treatment and predicts the occurrence of CV events and mortality in individuals with and without CV disease on ASA. Low-dose ASA showed to effectively prevent PE, even though an interindividual variability in ASA responsiveness exists.
Purpose: Our aims were to identify platelet and circulating biomarkers and clinical predictors of PE in patients at high risk for PE.
Methods: We enrolled 24 women with pregnancy at high risk for PE and 11 women with physiological pregnancy in an ongoing study. At first visit and every trimester, women underwent clinical evaluation, CV imaging, blood and urine sampling for biochemical markers of platelet activation. Based on the slope of sTXB2 between 10 and 24 hours after ASA intake, which indicates the recovery rate of COX-1 activity, women at risk for PE were stratified into tertiles.
Results: At baseline, the two groups did not differ in parameters except for higher glucose and cholesterol levels, lower PAPP-A and PLGF in pregnancies with high PE risk. TXM and circulating P-selectin were not different between groups at baseline, while, as expected, were significantly reduced during ASA treatment compared to healthy women, consistent with the predominant platelet source of TXM. Higher levels of TXM during the II trimester characterized women at high PE risk with serumTXB2 slope in the third vs. I tertile. Six patients at high PE risk experienced childbirth with PE. Compared to high PE risk women who did not develop events (no PE), women who developed PE were more hypertensive (p=0.01), had higher basal body weight (p=0.056), family history of coronary artery disease (p=0.031), lymphocyte count, C-reactive protein (CRP) [I, p=0.028 and III trimester, p=0.042)], higher percentage of immature platelets, higher urinary TXM (p=0.020) and a higher percentage of platelet P-selectin (p=0.072) in the II trimester.
Interestingly, patients who developed PE had a suboptimal, lower than 75% TXM percent inhibition (p=0.058) during II trimester of pregnancy (mean 57% vs. 87%, Fig B). Women with TXM<75% have an odds ratio 2.40 (95% CI: 0.30 to 19.04; P = 0.41) of developing PE.
Finally, TXM during II trimester, adjusted for baseline values, predicted the development of PE despite ASA, among at-risk patients (p=0.035) (Fig A).
Conclusions: Residual, TX-dependent platelet activation is associated with a shorter duration of ASA effect over the 24-hour dosing interval and may predict the occurrence of PE, despite prophylaxis with low dose ASA. Studies with a larger sample size are needed to validate the role of urinary TXM as a circulating biomarker predicting suboptimal response to ASA and PE occurrence in pregnant women at high risk for PE.

Distribution of TXM levels and TXM percentage of inhibition in high risk preclampsia patients with or without preeclamptic complications



RELATIONSHIP BETWEEN BASELINE SERUM ALBUMIN CONCENTRATION AND OUTCOME OF PATIENTS WITH CIRRHOSIS AND UNCOMPLICATED ASCITES TREATED WITH LONG-TERM ALBUMIN

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Background: AND AIMS: The ANSWER trial showed that long-term administration of human albumin (LTA) improves overall survival and reduces the incidence of complications over 18 months in patients with cirrhosis and uncomplicated ascites. However, LTA remains underused outside Italy, mainly due to logistical and economic concerns. In this context, the identification of criteria that allow the identification of patients who will benefit most from the treatment represents an unmet research need. To this end, we performed a post-hoc analysis of the ANSWER trial, evaluating the relationship between pretreatment serum albumin (SA) concentration and 18-month survival, with the aim of identifying the threshold of baseline SA associated with the greatest survival benefit achievable with LTA.

Methods: This is a post hoc analysis of the ANSWER trial, a multicenter, randomized, controlled, open-label study. The trial enrolled 431 patients with cirrhosis and uncomplicated grade 2 or 3 ascites. Patients were randomized to receive either standard medical treatment (SMT) or SMT plus human albumin (SMT+HA, 40 g twice weekly for two weeks, followed by 40 g weekly) for up to 18 months. The relationship between baseline SA and survival was analyzed according to the Kaplan Meier method, while the best cut-off was defined as the SA level associated with the lowest p-value at the Log-Rank test. The incidence of complications in the two arms was assessed by calculating their incidence rates (IRs) and compared by the incidence rate ratios (IRRs) in which SMT group was used as the reference category.

Results: Patients randomized to the two arms did not differ for baseline SA concentration (SMT 3.1±0.5 vs. 3.1±0.6 g/dL, p=0.857). The baseline SA cut-off associated with the highest survival benefit was 3.2 g/dL. Overall, 275 patients (64%) had baseline SA ≤3.2 g/dL, 132 in the SMT arm and 143 in the SMT+HA arm. In the subgroup of patients with baseline SA ≤3.2 g/dL, no differences have been observed in baseline characteristics between SMT and SMT+HA arms. Nevertheless, in this subgroup of patients LTA was associated to a significantly greater survival than patients in the SMT arm (74% vs 53%, p=0.0021). Conversely, in patients with baseline SA >3.2 g/dL, no differences in 18-month survival rate were observed between the SMT and SMT+HA arms (p=0.927). The cumulative incidence of paracentesis was significantly lower in the SMT+HA group compared to SMT both in patients with SA ≤3.2 g/dL (HR 0.45 95% CI 0.31-0.65, p<0.001), and in those with SA>3.2 g/dL (HR 0.52 95% CI 0.32-0.87, p=0.010). The cumulative incidence of refractory ascites was lower in the SMT+HA group compared to SMT in patients with SA ≤3.2 g/dL (HR 0.36 95% CI 0.22-0.58, p<0.001), while the difference was not statistically significant in patients with baseline SA >3.2 g/dL (HR 0.55 95% CI 0.30-1.03, p=0.060). Finally, the IR of complications of cirrhosis was lower in the SMT+HA group as compared to SMT irrespective of the baseline SA level (spontaneous bacterial peritonitis [SBP] IRR 0.34 [95%CI 0.18-0.60], p<0.001 in the SA≤3.2 g/dL group and IRR 0.15 [95%CI 0.02-0.63], p=0.003 in the SA>3.2 group; non-SPB infections IRR 0.67 [95%CI 0.50-0.91], p=0.007 in SA≤3.2 g/dL group and IRR 0.58 [95%CI 0.34-0.96], p=0.026 in SA>3.2 group; grade III/IV hepatic encephalopathy: IRR 0.50 [95%CI 0.37-0.67], p<0.001 in SA≤3.2 g/dL group and IRR 0.28 [95%CI 0.14-0.52], p<0.001 in SA>3.2 group). There were no significant differences in gastroesophageal variceal bleeding between the two arms in both groups.

Conclusion: In this post-hoc analysis, a pretreatment SA concentration of 3.2 g/dL identify the subgroup of patients with greater benefit from LTA in overall survival at 18 months. Nevertheless, treatment with HA was associated with better ascites management and lower incidence of complications irrespective of baseline SA level.

FRANTZ TUMOR AS A DIAGNOSTIC CULPRIT IN FEVER OF UNKNOWN ORIGIN: A CASE REPORT

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Background: Fever of Unknown Origin (FUO) remains one of the major challenges for internists, with the etiology remaining unidentified in 20–50% of cases [1]. The diagnostic process is complex and often leads to three main etiologies: infectious, rheumatologic, and neoplastic. We present the case of a young woman referred to our Internal Medicine Department with FUO.

Case report:

- History and Physical Examination: 19-year-old female, unremarkable family history, adenoidectomy in childhood. For the past two months, febrile episodes 3–4 times/week, temperatures up to 39°C with flu-like symptoms, self-managed at home with several cycles of oral antibiotics with no benefit. Transient response to paracetamol/NSAIDs. A few months prior: recurrent vomiting episodes → EGD was negative. General condition: good. Murphy's and Giordano's signs negative. No cardiac murmurs. POCUS unremarkable. Initial labs: mildly elevated CRP, no leukocytosis.
- Infectious Disease Work-up: Urine and blood cultures, ASO titer, throat swab for GAS, MRSA swab, serologies for EBV, CMV, HSV, VZV, HBV, HCV, brucellosis, leptospirosis, Quantiferon TB, syphilis, HIV – all negative.
- Endocrine/Hematologic/Rheumatologic Work-up: ANA reflex, ANCA, ENA reflex, antiphospholipid antibodies, rheumatoid factor, celiac panel, lymphocyte typing, Ig levels, TSH, fT3, and fT4 – all normal/negative.
- Imaging: Chest X-ray: negative. Abdominal ultrasound showed a possible left mesorenal pyelonephritic focus, but contrast-enhanced CT ruled out pyelonephritis and showed a pancreatic mass in the body-tail (Figure 1, A, B, C) exerting mass effect on splenic vessels. An EUS with FNA was performed (Figure 1, D), suggesting Solid Pseudopapillary Neoplasm (SPN).

Discussion: A stepwise clinical work-up led to the diagnosis of **Solid Pseudopapillary Neoplasm (Frantz tumor)**[2], a **low-grade malignant pancreatic tumor**:

- Represents 1–2% of all pancreatic neoplasms.
- Female/male ratio 10/1, mean age at diagnosis: 28 years[3]
- Often presents with nonspecific symptoms (e.g., upper quadrant abdominal pain). May grow >10 cm over time, eventually causing compressive GI symptoms: nausea, vomiting, early satiety (partially present in our case, predating fever onset, possibly due to splenic perfusion impairment – see Figure 1, B and C)
- Treatment is surgical.

Conclusion: Histology confirmed SPN with extension to peripancreatic adipose tissue and infiltration of some intraparenchymal nerve branches, without vascular invasion. Surgical margins and lymph nodes were free of disease.

Follow-up: Oncologic and imaging-based surveillance due to risk of recurrence.

References:

[1] Wright W F, Durso S C, Forry C, Rovers C P. Fever of unknown origin BMJ2025;388:e080847doi:10.1136/bmj-2024-080847

[2] Berretta S., Barbagallo E., D'Agata A., Berretta M. Il carcinoma pancreatico solido-cistico-papillare di Frantz. Minerva Chirurgica2001August;56(4):413-20.

[3] Navale P, Savari O, Tomashefski JF, Vyas M. Solid pseudopapillary neoplasm. PathologyOutlines.com at https://www.pathologyoutlines.com/ topic/pancreas-solidpseudo.html

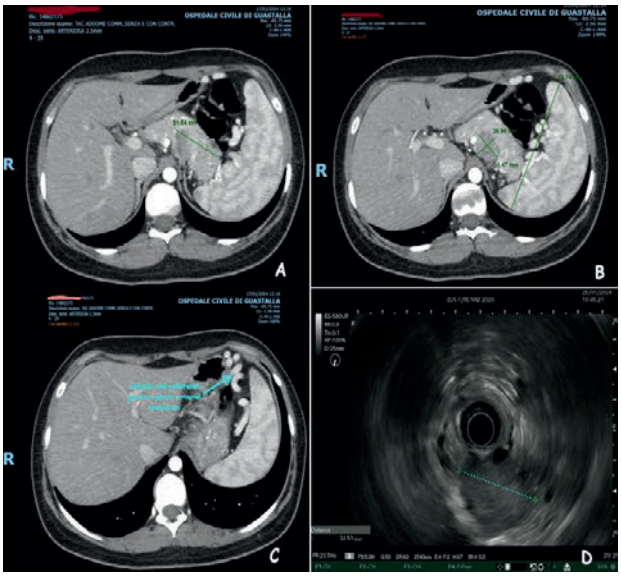

Figure 1. A, B, C: Contrast-enhanced abdominal CT (arterial phase): A. Pancreatic mass (max diameter: 51 mm) with irregular but defined margins, signs of internal neoplastic vascularization. B. Spleen with 13.7 cm bipolar diameter, diffuse intrasplenic and hilar vascular alterations. C. Ectasia and collateral gastro-splenic arterial circulation. D. Endoscopic ultrasound image of the pancreatic lesion during FNA, which led to the diagnosis.

ROLE OF TECHNOLOGY IN THE GLUCOSE CONTROL OF AGED PATIENTS WITH DIABETES IN DIALYSIS

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Diabetic patients on dialysis are at an increased risk of cardiovascular diseases, are normally older than the non-diabetic ones and have a worse quality of life than the non-diabetic ones. The primary objectives of this analysis were to describe the baseline and the follow-up characteristics of a cohort of people with type 1 (T1D) or type 2 (T2D) insulin-treated diabetes under dialysis who started to use an advanced hybrid closed loop (AHCL) system and to describe the main glycemic outcomes observed. Moreover, a Quality of Life (QoL) analysis will be described.
This is a retrospective analysis of individuals with T1D and T2D undergoing dialysis who began using the Medtronic MiniMedTM 780G system to optimize glycemic control. Both subjects under peritoneal and hemodialysis were included in the present analysis. Glucose metrics were collected at baseline, 3, 6, and 12 months after activating the SmartGuardTM feature. The baseline was considered a 14-day run-in period during which the subjects used the device in manual mode. Data were extracted from the Medtronic-dedicated web-cloud platform CareLinkTM. The WHOQoL-Bref questionnaire was administered at the last follow-up to evaluate the QoL.
Fourteen patients undergoing dialysis were included in this analysis. The average age was 60.6 years, with females comprising 21.4% of the cohort. The average duration of diabetes was 21.9 years. Most of the subjects are affected by T2D (85.7%). Most of them have at least one complication; in particular, 71.4% of the subjects had a history of cardiovascular disease, and 50% had retinopathy. 13 subjects underwent hemodialysis, and one underwent peritoneal dialysis. The average duration of dialysis was 4.3 years, and the majority followed a three-times-week dialysis rhythm (92.3%). Out of the 14 people considered in this analysis, 8 reached 1-year follow-up, whilst 2 did not yet reach the three months of follow-up. Time in Range (TIR, 70-180mg/dL) increased from 63% at baseline to 69% at 12 months, Time Below Range <70mg/dL (TBR70) decreased from 0.3% to 0%, and Time Above Range >250mg/dL (TAR250) decreased from 6.7% to 3.9%. Seven out of eight subjects who reached a 12-month follow-up achieved all three glycemic targets for this fragile population (TIR>50%, TBR70<1% and TAR250<10%). In subjects (n=11) who underwent hemodialysis and had at least a follow-up, the glycemic parameters during the non-dialysis days were compared with the dialysis days in the last 14 days available on CareLinkTM. The mean TIR was higher during the dialysis days vs non-dialysis as well as the TAR was lower during the dialysis days and no differences were observed in TBR. Due to the small number of patients and days considered, these results could be considered only a trend. At the last follow-up, the WHOQol-Bref questionnaire was submitted to all subjects. After starting to use AHCL system, 58.3% of the users were satisfied or very satisfied with their health status versus only 25% with the previous treatment. Moreover, 81.7% had a good, or very good QoL after starting to use the AHCL system, whereas only 8.3% had a good QoL and no one had a very good QoL with the previous treatment.
This analysis showed how the use of technology is safe and can help to improve the glycemic outcomes and the QoL of people with diabetes in dialysis.

CLINICAL IMPACT OF NON SELECTIVE BETA-BLOCKERS IN PATIENTS WITH CIRRHOSIS AND ACUTE KIDNEY INJURY: A POST HOC ANALYSIS OF THE INTERNATIONAL CLUB OF ASCITES GLOBAL-AKI STUDY

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Background: and Aims: Non-selective beta-blockers (NSBBs) are extensively used for preventing decompensation in patients with cirrhosis. International guidelines recommend NSBBs discontinuation in patients with cirrhosis and acute kidney injury (AKI). However, this recommendation is based on experts' opinion and, few studies have evaluated the effects of NSBBs on AKI outcomes.
Method: Post hoc analysis of ICA GLOBAL-AKI study, a multicenter intercontinental study that prospectively enrolled patients hospitalized for acute decompensation (AD) of cirrhosis from July 2022 to May 2023. AKI outcomes were compared between patients on NSBBs at AKI diagnosis and those who were not. A subgroup analysis further examined outcomes between patients in whom NSBBs were continued during hospitalization and those in whom were tapered/withdrawn within 48-72 hours from AKI diagnosis. Propensity score-matching (PSM, 1:1 ratio) was used to balance age, sex, MELD-Na, mean arterial pressure (MAP), presence of ascites, hepatic encephalopathy, AKI stage, acute on chronic liver failure (ACLF) grade at AKI diagnosis and whether patients were from low or middle-income countries. Main outcome were 28-day mortality and AKI non-resolution.
Results: 503 out of 1,238 patients with AKI were on NSBBs treatment at AKI diagnosis (propranolol 55%; carvedilol 45%). Most of patients were receiving less than 80 mg of propranolol and ≤12,5 mg of carvedilol (89%). Before PSM, patients on NSBBs were older and had significantly lower MAP, MELD- Na score and significantly lower prevalence of grade 2 and 3 ACLF. After PSM, all covariates were balanced between the two groups (standardized mean difference [SMD] <0.1). Patients on treatment with NSBBs had lower white blood cells count than those without (9.2 vs 7.4 x109/l; p<0.001). In PSM analysis, patients on NSSBs had lower risk of AKI non-resolution (OR=0.65, p=0.001) and lower risk of 28-day mortality (sHR=0.68; p=0.005). During the first 48/72 hours of hospitalization, NSBBs were continued in 123 patients (26%) and tapered/withdrawn in 350 (76%). Data about NSBBs management were missing in the remaining 37 patients. After PSM, all covariates were balanced between the two groups ([SMD<0.1). Continuation of NSBBs was neither associated with AKI non-resolution (OR=1.00; p=0.999) nor with 28-day mortality (sHR=0.56; p=0.190). Subgroup analyses in patients with MAP<70 mmHg, serum Na<130 mmol/l and ACLF confirmed the findings.
Conclusion: NSBBs treatment at AKI diagnosis is associated with higher resolution of AKI and lower 28-day mortality in patients with cirrhosis and AKI. Continuation of treatment with NSBBs in patients with cirrhosis and AKI does not seem to be harmful in these patients.

SGLT-2 INHIBITORS AND THE EFFECT ON RENAL RESISTANCE INDEX (RRI) IN PATIENTS WITH CHRONIC HEART FAILURE: PRELIMINARY DATA OF A PERSONAL CASE STUDY

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Introduction: Sodium-glucose cotransporter 2 (SGLT-2) inhibitors are a class of oral antidiabetic agents that inhibit glucose reabsorption in the proximal convoluted tubules of the kidney. They exert also positive effects on the cardiovascular and renal system such as decreased blood pressure and triglycerides, natriuresis, improved endothelial dysfunction and preservation of renal function. For these reasons, empagliflozin and dapagliflozin can be prescribed in patients with heart failure with preserved (HFpEF), intermediate (HFmrEF) or reduced (HFrEF) ejection fraction [1].SGLT-2 inhibitors have shown promising results in reducing arterial stiffness and, consequently, the risk of progression of cardiovascular and renal diseases.Nephroangiosclerosis can be assessed by Power-Doppler measurement of the renal resistance index (RRI), that expresses the percentage of reduction of telediastolic blood flow in the renal vessels in relation to the maximum systolic blood flow. The normal value is 0.47-0.70, but increases with age with a variability between the two kidneys of less than 5%.The aim of this study is to investigate the relationship between the use of SGLT-2 inhibitors and RRI in patients with chronic heart failure after 24 weeks of therapy.
Patients and methods We enrolled patients admitted to the General Medicine Unit of the Santa Rosa Hospital in Viterbo for acute-on-chronic heart failure. All patients were screened to determine BNP, albumin/creatinine ratio and estimated glomerular filtration rate (eGFR) by CKD-EPI, staged according to KDOQI classification. After obtaining informed consent, an ultrasound examination was performed for echo-color-Doppler with a 1-5 MHz convex probe on the interlobar arteries for three determinations bilaterally (2-4 mm Doppler sample volume, with an insonation angle less than 60°), finally recording the average RRI value.The primary outcome includes the change in RRI value after 24 weeks of therapy with empagliflozin or dapagliflozin. We also evaluated the variation of BNP values, albumin/creatinine ratio and renal filtration rate. **Results**We enrolled 30 patients, 11 men and 19 women, with a median age of 82 [range 62-91]. Eleven patients were diabetic, twenty-two patients were hypertensive. All patients had chronic heart failure: 7 with HFrEF (23.3%), 12 with HFmrEF (40%), 11 with HFpEF (36.7%). All patients had chronic kidney failure: 2 patients (6.7%) at baseline at I stage chronic renal failure, 12 patients (40%) at II stage, 9 patients (30%) at IIIa stage, 6 patients (20%) at IIIb stage, 1 patient (3.3%) at IV stage. The median eGFR was 55 ml/min [range 30 ml/min – 90 ml/min]. At the baseline, the median BNP was 642 pg/ml [range 299-1088 pg/ml], the median albumin/creatinine ratio was 150 mg/g [range 25-300 mg/g]. The median RRI at the baseline was 0.82 [range 0.72 – 0.93]. None of the patients had ever taken a gliflozin before being enrolled in the study; none of the patients added any new medications during the study period. We are still in the 24-week data collection phase. At the moment, we have collected data from 18 patients. Two patients stopped empagliflozin before 24 weeks due to recurrent urinary tract infections. A patient died after four months due to sepsis. The median value of RRI at 24 weeks is 0.77 [range 0.68 – 0.89]. The median eGFR is 67 ml/min [range 44 – 85 ml/min]. At 24 week 2 patients have I stage chronic kidney failure, 8 patients II stage, 4 patients IIIa stage, 4 patients IIIb stage. The median BNP after 24 weeks is 375 pg/ml [range 186 – 568 pg/ml]; the median albumin/creatinine ratio is 85 mg/g [range 25 – 300 mg/g].
Discussion: Preliminary data from our study show that SGLT-2 inhibitors prescribed in patients with chronic heart failure are able to determine an increase in renal filtration that is reflected in the reduction of the RRI. However, a possible limitation of this study is the absence of a control group.RRI is already considered a good indicator of the renal angiological status: a high renal resistance index is associated with renal arteriosclerosis and adverse cardiovascular events [2]. However, it is not only an index of purely nephrological interest. Several studies have investigated its role in patients with heart failure; in this context it has shown an independent and incremental role in predicting the progression of heart failure in relation to renal impairment in cardio-renal syndrome [3], and our study seems to confirm this aspect. So, RRI could be useful in the internal medicine approach in the multimorbid patients, because it is able to predict the course of chronic cardio-renal disease.

NINTEDANIB RESTORES ENDOTHELIAL FUNCTION IN PATIENS WITH SISTEMIC SCLEROSIS: PRELIMINARY FINDINGS OF A MONOCENTRIC STUDY

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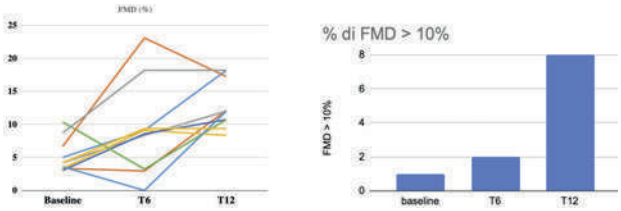
Background: Il nintedanib è stato approvato per il trattamento delle pneumopatie infiltrative diffuse (ILD) associate alla sclerosi sistemica (SSc). Alcune evidenze sperimentali supportano l'ipotesi che il nintedanib possa agire sulla vascolarizzazione riducendo il rimodellamento vascolare e migliorando l'architettura microvascolare, nonostante questi effetti rimangano tutt'ora poco chiari.
Obiettivi: Lo scopo di questo studio è stato quello di valutare l'effetto del nintedanib sul microcircolo sistemico e sulla funzione endoteliale valutata mediante la dilatazione flusso-mediata dell'arteria brachiale (FMD) in pazienti con SSc-ILD.
Metodi: In questo studio prospettico osservazionale sono stati arruolati consecutivamente 10 pazienti affetti da SSc-ILD, secondo i seguenti criteri di inclusione: 1. età > 18 anni; 2. malattia progressiva secondo i criteri INBUILD; 3. indicazione alla terapia antifibrotica con nintedanib; 4. firma del consenso informato. Non vi erano criteri di esclusione.
Per ogni paziente sono stati raccolti i dati clinico-demografici, tra cui: sesso, età, durata e localizzazione della malattia, sottogruppo di malattia (sottogruppo cutaneo limitato o diffuso), specificità anticorpale, punteggio cutaneo secondo Rodnan modificato (mRSS), pattern capillaroscopico (early, active o late), terapia pregressa e in atto.
Tutti i pazienti sono stati valutati al basale, a 6 mesi e a 12 mesi con i seguenti

test: FMD, videocapillaroscopia periungueale (VCS), ecografia cutanea a frequenza ultra-elevata (HFUS), spirometria e DLCO, 6 minute walking test (6MWT) ed ecografia polmonare. I dati sono stati analizzati con il test dei segni per ranghi di Wilcoxon.
d. Risultati
Dei 10 pazienti arruolati (10 F, età mediana 60,5 anni), 5 avevano una SSc diffusa e 5 una SSc limitata, con un mRSS mediano di 4,5 e una durata mediana della malattia di 12 anni. Tutti i pazienti hanno ricevuto nintedanib 150 mg BID. Due pazienti hanno ridotto il dosaggio a 100 mg BID (rispettivamente dopo 6 e 9 mesi), mentre un paziente ha interrotto definitivamente il trattamento dopo 6 mesi a causa di effetti avversi gastrointestinali persistenti (diarrea e nausea).
Al basale, il 90% dei pazienti aveva valori di FMD inferiori al 10% (soglia al di sopra della quale i valori di FMD sono considerati normali) con un valore mediano del 4,16% (3,03 - 10,34). A 6 mesi, i valori di FMD sono aumentati nel 70% dei pazienti, anche se nell'80% dei casi i valori sono rimasti inferiori al 10%, con un valore mediano dell'8,83% (0 - 23,07). A 12 mesi, i valori di FMD sono aumentati in tutti i pazienti rispetto al basale, con un valore mediano del 12% (9,37-18,18) ($p < 0,05$) (Figura).
Non sono state osservate differenze statisticamente significative nei parametri capillaroscopici (cioè numero mediano di capillari e megacapillari) al basale e dopo 6 e 12 mesi. Inoltre, non sono state rilevate differenze statisticamente significative per quanto riguarda il valore di mRSS e le valutazioni ecografiche di cute e polmoni. Il nintedanib è stato in grado di stabilizzare (declino < 10%) o migliorare la FVC a 12 mesi nel 60% dei casi e la TLC nel 90% dei casi. Tuttavia, nel 40% dei casi è stato osservato un calo della DLCO > 15%. Infine, si è registrato un miglioramento statisticamente significativo ($p < 0,05$) nel 6MWT a 12 mesi.
Conclusioni: Sebbene il nintedanib non abbia dimostrato un impatto significativo sul microcircolo periungueale, i dati di questo piccolo studio pilota suggeriscono un effetto positivo sulla funzione endoteliale valutata mediante FMD. Ulteriori studi dovrebbero esplorare l'ipotesi di un effetto benefico del nintedanib sulla funzione endoteliale e sul rimodellamento vascolare.



THE FUTURE ROLE OF THE ARTIFICIAL INTELLIGENCE IN INTERNAL MEDICINE: THE RESULTS OF A DELPHI STUDY

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Premises and purpose of the study: Delphi is technique used as a way of collecting data from respondents within their domain of expertise to deal with divergent opinions to achieve consensus. Materials and methods: 30 Artificial Intelligence (AI) and Internal Medicine international experts collaboratively respond to the question: role of AI in IM. Panel assigned scores reflecting the perceived value, considering the balance between strengths (S) and weaknesses (W), and the potential risks (R), considering threats (T) and opportunities (O). Scores were evaluated on a Likert scale. For X and Y axes were considered the median value from all the answers (SD +/- 1). Results: Delphi results generated the SWOT Analysis. AI in IM is considered an opportunity, generating a shared consensus. S, W and T are perceived differently depending on the experience of using AI by the panelists: application in daily practice is seen as a natural consequence of the current development of the technology by those who already use it, while more cautious appear those who are in an initial phase of AI use. Panel highlighted few opportunities, compared to the other domains (S-W-T), with a deep extremization of the items in each domain. This is typical of all discoveries that revolutionize their field of application. Conclusions: To promote the ever-increasing use of AI in IM, the role of scientific societies appears to be fundamental in promoting training, the exchange of good practices and the creation of models for the use of AI in clinical, therapeutic and diagnostic practice in IM.

HERAPEUTIC INERTIA DOES NOT APPLY EXCLUSIVELY TO LIPID CONTROL IN SECONDARY PREVENTION

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Introduction/Background: Suboptimal control of key metabolic parameters (such as blood pressure, lipid profile, body weight, and blood glucose) has been consistently associated with an increased risk of cardiovascular events. Cardiovascular risk refers to the probability of an individual developing a major cardiovascular event, such as myocardial infarction or stroke, over a defined period, based on the presence and severity of modifiable and non-modifiable risk factors. In the context of **secondary prevention**, which targets individuals with a history of cardiovascular disease, the management of these risk factors becomes even more critical. The aim of secondary prevention is not merely to delay disease progression but to actively prevent recurrent events and reduce mortality through aggressive risk factor modification, pharmacological interventions, and lifestyle optimization. Despite well-established guidelines, comprehensive metabolic assessment (an essential component for individualized risk stratification and therapeutic adjustment) remains underutilized in routine clinical practice. This gap underscores the need for a more systematic approach to metabolic monitoring in patients with established cardiovascular disease. This study aimed to characterize the metabolic profile of individuals with a documented history of cardiovascular events attending a tertiary-care dyslipidemia center.
Methods: A cross-sectional analysis was conducted on patients consecutively evaluated at the Metabolic Health Clinic of San Raffaele Hospital, Milan, between February 2022 and January 2025. Comprehensive data collection included detailed medical history, current pharmacological treatments, anthropometric measurements (including body mass index and waist circumference), and a panel of biochemical parameters, such as fasting plasma glucose, lipid profile, and blood pressure values. The metabolic profile was assessed according to the harmonized criteria for metabolic syndrome, and individuals were classified as having a "metabolically at-risk" phenotype if they met at least two out of five diagnostic components: elevated waist circumference, elevated triglycerides, reduced HDL cholesterol, elevated blood pressure, and impaired fasting glucose.
Results: A total of 60 patients were included in the analysis. Median IQR age was 70 years (65, 73); 58% male. Only 23% of the cohort achieved LDL-C target levels. Median Body Mass Index (BMI) and Waist to Height ratio (WHR) baseline were 25.5 (IQR 21.94, 27,41) and 0.55 (IQR 0.53, 0.61) respectively, and the median systolic blood pressure was 130 mmHg (IQR 120,140). Nearly half of the population reported intolerance to lipid-lowering therapy, although failure to reach LDL-C targets was not significantly associated with this condition ($p=0.091$). Conversely, patients achieving target LDL-C levels were more frequently treated with statin-ezetimibe combination therapy at baseline ($p<0.001$). Anthropometric parameters (BMI and WHR) and overall metabolic profile did not differ significantly between patients at target and those above target LDL-C levels. A high-risk metabolic profile was present in 52% of participants, with a comparable distribution between groups ($p=0.35$). Notably, lower systolic blood pressure values were observed in those reaching LDL-C targets (120 vs. 130 mmHg, $p=0.006$), suggesting a potential association between hemodynamic control and lipid profile optimization. No significant correlation was found between Lp(a) levels and metabolic or hemodynamic parameters.
Conclusion: Therapeutic inertia continues to be a significant challenge, even in patients at very high cardiovascular risk, and is not limited to lipid control alone. Optimizing treatment strategies alongside comprehensive metabolic assessment is essential to enhance secondary prevention, ensuring a holistic and personalized approach to patient management. Importantly, metabolic risk control should be prioritized, irrespective of LDL-C and Lp(a) levels.

IMPACT OF COVID-19 IN PATIENTS WITH HEART FAILURE HOSPITALIZED IN AN ITALIAN THIRD-LEVEL ACADEMIC MEDICAL CENTER

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Introduction: Coronavirus Disease 2019 (COVID-19), caused by SARS-CoV-2, since its first cases in December 2019 had a rapid expansion worldwide. COVID-19 encompassed a large variety of clinical manifestations, ranging from paucisymptomatic forms to severe pulmonary involvement with elevated mortality rates. Approximately one in three COVID-19 patients had at least one comorbidity, including chronic respiratory and cardiovascular diseases (e.g., heart failure, HF). Our study evaluates the impact of COVID-19 in patients with HF admitted to an academic medical center during SARS-CoV-2 pandemic.
Methods: This retrospective monocentric observational study was conducted in an Italian third-level academic medical center in Rome (Fondazione Policlinico Agostino Gemelli—IRCCS). The analysis includes patients who presented to the Emergency Department between March 2020 and January 2023. All patients were positive for the SARS-CoV-2 RT-PCR test on nasopharyngeal or oropharyngeal swabs. Data concerning the clinical outcomes of COVID-19 in patients with diagnosis of HF were compared to data collected from COVID-19 patients without HF (control group), using a propensity score matching (PSM) technique. Patients were matched in a 1:1 ratio by gender, age, number of comorbidities, and vaccination status. The selected outcomes were in-hospital death, 30-day mortality, and intensive care unit (ICU) admission. We used a multivariate logistic regression analysis to identify the variable independently associated with the outcomes.
Results: The analysis includes 886 patients (444 men and 442 women, mean age 80 ± 10 years). The outcomes of 189 HF patients were compared to the outcomes of 189 matched controls. Overall, HF patients had a higher prevalence of valvular disease ($p = 0.004$), atrial fibrillation ($p = 0.003$), use of anticoagulants ($p = 0.001$), chronic obstructive pulmonary disease ($p = 0.03$) and chronic kidney disease ($p = 0.001$). On the other hand, controls showed a higher prevalence of arterial hypertension ($p = 0.04$), higher lymphocyte counts and higher PaO2/FiO2 ratio. During hospitalization, HF patients were more frequently treated with high-flow nasal cannulas (18 vs. 9%; $p = 0.01$), were more commonly referred to ICU (19 vs. 12%; $p = 0.04$), and exhibited a higher mortality rate (39 vs. 1%; $p = 0.0001$) than patients without HF.
Conclusions: Our study reveals a higher mortality and clinical severity of COVID-19 in patients with a pre-existing diagnosis of HF. After adjustment for age, gender, number of comorbidities, and vaccination status, HF was the only independent risk factor for ICU admissions and death in COVID-19 patients.

PREVALENCE OF VENOUS THROMBOEMBOLISM IN PATIENTS WITH GYNECOLOGIC CANCERS UNDERGOING SYSTEMIC ANTINEOPLASTIC TREATMENT: GYNCAT STUDY – INTERIM ANALYSIS

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Background: Venous thromboembolism (VTE) is the second leading cause of death in cancer patients. The Khorana score is the most widely used tool to stratify VTE risk in oncology outpatients. International guidelines suggest a cut-off of 2 points, but in Italy pharmacological thromboprophylaxis is only reimbursed for scores ≥3. This prospective observational study analyzes the prevalence of VTE in patients with gynecologic cancers undergoing active chemotherapy who did not receive pharmacological thromboprophylaxis.
Methods: Data were collected over a 6-month period from 235 patients with gynecologic malignancies who were about to start a new chemotherapy cycle. The Khorana score was calculated for all patients. Thromboprophylaxis was prescribed according to guidelines and clinical judgment. Clinical and epidemiological data, VTE incidence, and the predictive validity of the Khorana score were analyzed.
Results: The most frequent cancers were ovarian (61%), uterine (21%), and cervical (16%). 60% of patients had a Khorana score of 1, 26% had a score of 2, and 14% had a score ≥3. Low-molecular-weight heparin thromboprophylaxis was prescribed 19% of the times. During a median follow-up of 6 months, 24 thromboembolic events occurred, of which 21 (87%) were in patients who did not receive pharmacological prophylaxis. The cumulative incidence of VTE among patients not receiving pharmacological prophylaxis was: 5.4% in the Khorana 1 group, 22.8% in the Khorana 2 group, and 33% in the Khorana ≥3 group. A Khorana score ≥2 was significantly associated with increased VTE risk (OR 2.86, 95% CI 1.24–6.70).
Conclusions: In the absence of pharmacological thromboprophylaxis, the risk of VTE increases with higher Khorana scores. In our study, a Khorana score ≥2 was significantly associated with increased VTE risk. The development of predictive models specific to this patient population is desirable in order to optimize prevention strategies.

ADVERSE EFFECTS OF FLECAINIDE DURING TREATMENT OF PAROXYSMAL ATRIAL FIBRILLATION IN A SUBJECT WITH NO EVIDENCE OF ORGANIC HEART DISEASE: A CASE REPORT IN A PATIENT WITH MULTIPLE COMORBIDITIES

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Case presentation: A 67-year-old Caucasian woman presented at least six recorded episodes of atrial fibrillation within two months. The ventricular rate during these episodes never exceeding 110 bpm, and the episodes spontaneously resolved within minutes to hours. Her baseline ECG had shown sinus bradycardia (48-52 bpm) and first-degree AV block for years. An echocardiogram revealed a normal left atrial volume (anteroposterior diameter: 35 mm), with an EF of 70%. Her medical history included a family history of bradycardia and atrial fibrillation, and she was non-smoker without diabetes, no alcohol intake, overweight. She had combined familial dyslipidemia, arterial hypertension, mild carotid atheromasia. Other conditions included spondyloarthrosis, hypovitaminosis D, chronic low back pain, fibromyalgia, carpal tunnel syndrome, occasional recurrent urticaria, and hereditary-familial LDH deficiency (lower activity of LDH-1 and LDH-2 isoenzymes) (1), as well as a chronic cough. She reported adverse reactions to tramadol and the Comirnaty vaccine. She also had an intolerance to calcium antagonists. Her continuous medications included telmisartan 80 mg, hydrochlorothiazide 25 mg, fenofibrate 145 mg, simvastatin 40 mg, ezetimibe 10 mg, magnesium 375 mg, cholecalciferol 180,000 I.U. every month. Laboratory tests showed normal liver, renal, thyroid function, as well as normal serum electrolytes. Her LDL cholesterol was 117 mg/dl, LDH 104-99 U/l (nv: 135-214), ALP 29 U/l (nv: 43-115), uric acid 6.8 mg/dl (nv: 2.6-6.0), calcium 2.66 mmol/L (nv: 2.20-2.65), ferritin 88 µg/L, magnesium 0.76 mmol/L (nv: 0.75-1.05). A 24-hour Holter ECG recorded an atrial fibrillation episode lasting two hours with a maximum rate of 105 bpm, followed by spontaneous resolution. It also revealed very rare polymorphic ventricular extrasystoles, some supraventricular extrasystoles, a brief 5-beat burst of supraventricular tachycardia, a minimum heart rate 36 bpm, two non-prolonged pauses, no changes in repolarization, normal QTc. Important psycological stressors were noted as potential triggering factors. According to the HERA score classification, here symptoms were class 2a/2b. Due to the underlying bradycardia and first-degree AV block, the patient was treated with low-dose flecainide acetate (50 mg, prolonged release hard capsule). However, the drug was discontinued after eight days due to the onset of nausea, dyspepsia, and malaise. During flecainide intake, an episode of atrial flutter with a 1:1 conduction rate and a ventricular rate of 130 bpm, lasting for a few minutes, was recorded. Following drug discontinuation, three further AF episodes, confirmed by smart device (KardiaMobile AliveCor®), were succesfully treated using the "pill-in-the-pockett" strategy (flecainide 100 mg at a reduced dose of ½ tablet) according to the 2024 ESC Guidelines for the management of atrial fibrillation (Class of recommendation IIa, Level of evidence B) (2). Anticoagulant therapy with DOAC, edoxaban 60 mg o.d., was immediately initiated, considering the CHA_2DS_2-VA score of 2 (Class I, Level C) (2). Based on the integrated AF-CARE approach, her anticholesterol therapy was modified by replacing simvastatin with rosuvastatin (40 mg), and her magnesium supplementation was doubled to 750 mg daily (3). In the next three months, no further episodes of AF occurred. Follow-up laboratory tests revealed an LDL cholesterol 94.4 mg/dl, normal ALP isoenzyme, a vitamin B6 (pyridoxal-5'-phosphate) level of 103 nmol/L (nv: 51-183), and a plasmatic ACE level of 28 U/l (nv: 13-64). The low ALP level, after excluding possible pharmacological interferences, could be indicative of an oligosymptomatic form of hypophosphatasia. Further investigation, including urinary phosphoethanolamine (PEA) measurement and potential testing for ALPL gene mutations, may confirm this diagnosis (4). Conclusions: Considering the recent-onset paroxysmal AF in a patient with sinus bradycardia and no structural heart disease, and her intolerance to prolonged flecainide therapy, transcatheter ablation (Class I, A) was scheduled after a prolonged period of anticoagulation for at least three weeks (Class I, C). In the interim, modifications of risk factors and management of stressful events were implemented. In light of the low ALP level in a patient with LDH deficiency, further tests were planned to investigate

the possibility of subclinical hypophosphatasia.

References:

1) Turrin M, et al. Lactate dehydrogenase hereditary deficiency: description of the first Italian family with total LDH reduced due to lower activity of LDH-1 and LDH-2 isoenzymes. Oral communication, 118th SIMI National Congress, Rome, october 2017.
2) Van Gelder IC, et al. 2024 ESC Guidelines for the management of atrial fibrillation devoleped in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2024; 45:3314-414.
3) Khan AM, et al. Low serum magnesium and the development of atrial fibrillation in the community: the Framingham Heart Study. Circulation 2013;127: 33-8.
4) Seefried L, et al. Diagnosis and treatment of hypophosphatasia. Calcif Tissue Int 2025;116: 46.

INCIDENCE OF THROMBOEMBOLIC EVENTS IN PATIENTS WITH HEREDITARY HEMORRHAGIC TELANGIECTASIA

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Rendu-Osler-Weber disease, or Hereditary Hemorrhagic Telangiectasia (HHT), is a rare vascular disorder (prevalence approximately 1 in 5,000–8,000), inherited in an autosomal dominant pattern with variable penetrance. It is characterized by abnormal angiogenesis leading to mucocutaneous telangiectasias (most frequently involving the nasal mucosa) and visceral arteriovenous malformations (AVMs), primarily affecting the liver, lungs, brain, and gastrointestinal tract [1–5].

Although the clinical phenotype is predominantly hemorrhagic, recent evidence suggests an increased thromboembolic risk in HHT patients [9–11], likely mediated by elevated plasma levels of factor VIII and von Willebrand factor (vWF), in association with chronic iron-deficiency anemia [10–13].

The aim of this study was to assess the incidence of venous thromboembolic events (VTE) in a cohort of HHT patients followed at the HHT Care Pathway of the Fondazione Policlinico Universitario A. Gemelli IRCCS.

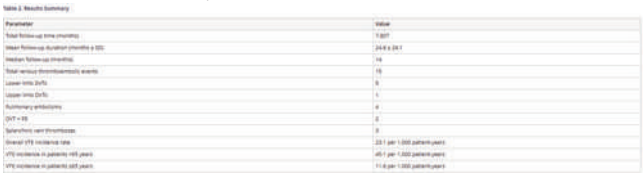
A retrospective analysis was conducted on the medical records of 315 patients with a clinical and/or genetic diagnosis of HHT, established according to the Curaçao criteria [15], with at least 6 months of follow-up.

Statistical Methods: Statistical analysis was performed using SPSS version 20.0. Descriptive statistics were used to evaluate demographic and clinical characteristics. Results are expressed as mean ± SD or as percentages. The incidence rate of thromboembolic events was calculated over the total follow-up period and expressed as the number of events per 1,000 patient-years.

Table 1. Demographic and Clinical Characteristics of the Study Population (Prospective Analysis)

The incidence of deep vein thrombosis (DVT), pulmonary embolism (PE), and splanchnic vein thrombosis was calculated as the number of events per 1,000 patient-years, both overall and stratified by age. The total follow-up time was 7,807 months (mean 24.8 months per patient); a total of 15 thromboembolic events were recorded: 5 lower limb DVTs, 1 upper limb DVT, 4 PEs, 2 combined DVT+PE, and 3 splanchnic vein thromboses. The overall incidence rate was 23.1 events per 1,000 patient-years; 45.1 in patients >65 years and 11.6 in those ≤65 years. Epistaxis was present in 97.8% of patients, and iron-deficiency anemia in 51.1%.

Table 2. Results Summary



These data confirm an increased thromboembolic risk compared to the general population [14], suggesting a potential pathogenic role for elevated FVIII and vWF levels secondary to chronic iron deficiency. Although HHT is typically considered a hemorrhagic disorder, these findings highlight the need for personalized thrombotic risk assessment and careful evaluation of anticoagulant therapy safety. This supports the rationale for prospective multicenter studies to guide evidence-based clinical recommendations.

Reference:

Hereditary hemorrhagic telangiectasia
Genet Med.
Haemophilia
N Engl J Med
Eur J Hum Genet
Laryngoscope
Am J Med Genet
Qual Life Res
World J Clin Cases
Thromb Haemost
Thorax
Br J Haematol
Blood Adv
Thromb Res.
15.Shovlin CL, et al. Am J Med Genet. 2000;91:66e7.

2IMPACT OF INDOOR AIR POLLUTION ON INFLAMMATORY PROFILE AND CARDIAC AUTONOMIC CONTROL IN PATIENTS WITH CONGESTIVE HEART FAILURE

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The present study explores the modifications of cardiac autonomic control (CAC) during sleep and of systemic inflammatory profile associated with exposure to indoor air pollution (IAP) in patients affected by chronic heart failure (HF). The study was conducted in Policlinico IRCCS Ca' Granda Hospidal of Milan, and nineteen HF patients were enrolled. Indoor levels of fine particulate matter (PM2.5), nitrogen dioxide (NO2) and volatile organic compounds (VOCs) were monitored using a portable detector for 7 days. Together, a 7-day vital signal monitoring was performed through a wireless patch that continuously recorded electrocardiogram, respiratory activity and actigraphy. Cyclic variation of heart rate index (CVHRI events/hour) during sleep, a proxy for the evaluation of the number of sleep apnoea events, was assessed for each night. After the monitoring, blood samples were collected to assess the inflammatory profile both through the assessment of plasmatic concentrations and through the evaluation of gene expression of pro- and anti-inflammatory biomarkers. Regression and correlation analysis were performed. A positive association was found in patients between average daily exposures to NO2 and the CVHRI (Δ=+0.86 events/h for 10% increase in NO2, 95% CI [0.15;1.58], p=0.022). Higher levels of daily exposure to NO2 corresponded to greater number of cyclic variations in heart rate. The other pollutants did not show effects on cardiac autonomic control in this population.

Regarding the correlation between inflammation and indoor air pollution, indoor PM2.5 exposure was positively correlated with elevated plasmatic levels of TNF-α (Δ%=17.18 for 10% increase in PM2.5, p=0.006). Lastly, regression analysis revealed that, in patients, indoor daily exposure to NO_2 was significantly associated with changes in the expression of specific inflammatory genes. A 10% increase in NO_2 levels was linked to an 8.94% increase in IL-6 gene expression and a 6.60% increase in TREM-1 gene expression, both of which are pro-inflammatory biomarkers. Notably, the anti-inflammatory gene IL-10 also showed a significant upregulation of 4.18% per 10% increase in indoor NO_2 levels.

The study highlights a possible causal relationship between IAP exposure and higher risk of sleep apnoea events, and an altered inflammatory state in patients affected by HF. The findings of this study have significant implications for both clinical practice and public health strategies, particularly in the context of

improving cardiovascular health by addressing indoor air quality. The IAP could emerge as a critical and often neglected risk factor for the public health that can be addressed through targeted preventive interventions.

CEFEPIME NEUROTOXICITY IN INTERNAL MEDICINE: A SILENT AND OVERLOOKED ADVERSE EFFECT

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A 79-year-old Caucasian woman was admitted to the ward with a clinical picture of sepsis (neutrophilic leukocytosis with 13,000/mm^3 WBCs; CRP 13 mg/dL; PCT 239 ng/mL) and was treated with empiric antibiotic therapy (piperacillin/tazobactam) and fluid resuscitation. She had a hematologic history of follicular lymphoma grade 3 and a midline central venous catheter (CVC), with chronic kidney disease (creatinine 1.1 mg/dL; body weight 38 kg; estimated creatinine clearance 25 mL/min, according to Cockcroft-Gault equation). During hospitalization, blood cultures taken from the CVC tested positive for Enterobacter cloacae complex, with susceptibility testing indicating potential resistance to the initial antibiotic; based on this, the treatment was switched to cefepime and the CVC was removed.
After approximately four days of intravenous cefepime therapy, the patient developed hypokinetic delirium followed by generalized myoclonic seizures. Brain CT excluded ischemic lesions, and since no other new medications had been introduced, serum cefepime levels were measured. Given the favorable clinical response to therapy, the antibiotic was continued for two more days despite the neurological manifestations to complete the treatment course. However, neurological symptoms did not resolve within 48 hours after discontinuation of cefepime.
During hospitalization, the patient developed anemia (Hb 8.8 g/dL) and worsening renal function (creatinine 2.08 mg/dL; CrCl of 13 mL/min, according to the Cockcroft-Gault equation), likely secondary to sepsis and cefepime toxicity. The subsequent development of an acute coronary syndrome due to supply-demand mismatch, combined with the aforementioned comorbidities, ultimately led to the patient's death. Cefepime serum levels were later found to be supratherapeutic, measuring 100 mg/L.
Cefepime is a fourth-generation cephalosporin of the beta-lactam class, widely used in internal medicine for its broad-spectrum bactericidal activity and overall safety. However, both clinical experience and literature report significant side effects, particularly neurotoxicity and nephrotoxicity.
Neurotoxicity can manifest as confusion, hallucinations, encephalopathy, myoclonus, and both convulsive and non-convulsive status epilepticus. Nephrotoxicity may involve acute interstitial nephritis, renal damage due to hemolytic anemia secondary to drug exposure, or obstructive nephropathy due to crystallization. Major risk factors for the development of encephalopathy include drug overdose (serum levels >20 mg/L), renal insufficiency, advanced age, and preexisting cerebral pathology. A 2023 observational study of 503 patients treated with cefepime reported that 4% of them developed cefepime-related neurotoxicity (CRN), with higher risk observed in those with elevated drug serum levels and impaired renal function, both independently associated with an increased risk of CRN.
During our patient's recovery, a key challenge was the definitive diagnosis of cefepime-induced encephalopathy, as no standardized criteria currently exist in the literature and the drug monitoring platform for cefepime was not routinely available in our hospital. Diagnosis is typically considered in the context of altered mental status in the absence of acute ischemic or hemorrhagic events on brain imaging (CT), elevated serum drug levels, and often concurrent anemia and renal dysfunction. EEG may show diffuse cerebral dysfunction or subclinical seizures, with high sensitivity. A meta-analysis by Payne LE et al. reported EEG abnormalities in 73% of suspected cefepime neurotoxicity cases, including non-convulsive status epilepticus, myoclonic activity, triphasic waves, and focal sharp waves.
The median onset of symptoms was around four days from therapy initiation, with resolution occurring approximately two days after clinical intervention9usually discontinuation of the antibiotic, administration of antiepileptic agents, or hemodialysis9although supporting data remain limited.
Cephalosporins, and cefepime in particular, offer broad-spectrum antimicrobial coverage; nevertheless, it is crucial to consider their potential adverse effects, especially in elderly patients or in those with multiple comorbidities, to ensure accurate differential diagnosis upon the onset of new symptoms. The limited data available presents a diagnostic and therapeutic challenge in identifying and managing this adverse effect.
References: Payne LE, Gagnon DJ, Riker RR, Seder DB, Glisic EK, Morris JG, Fraser GL. Cefepime-induced neurotoxicity: a systematic review. Crit Care. 2017 Nov 14;21(1):276. doi: 10.1186/s13054-017-1856-1. PMID: 29137682; PMCID: PMC5686900.
Maan G, Keitoku K, Kimura N, Sawada H, Pham A, Yeo J, Hagiya H, Nishimura Y. Cefepime-induced neurotoxicity: systematic review. J Antimicrob Chemother. 2022 Oct 28;77(11):2908-2921. doi: 10.1093/jac/dkac271. PMID: 35971666.

A RARE CAUSE OF ASCITES: THE HEART

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A 70-years old patient was admitted to our medicine ward for ascites and rapid atrial fibrillation. A prior episode of ascites occurred four years ago, when she underwent two paracentesis. Microbiology tests and citology came back negative. The abdomen CT showed a cirrhotic liver with a hyperdense nodule in S2, described as a probable angioma, with no splenomegaly. EGDS showed no varices. She was initially discharged with oral diuretic therapy, which the patient stopped after a few months, without developing any symptoms. In the month prior to readmission she developed significant weight gain and hard peripheral edemas, later she started experiencing exertional dyspnoea, therefore she decided to access first aid. At admission atrial fibrillation with RVR was recorded.
Patient History only included hypertension and an episode of pericarditis aproximately twenty years before.
At admission a paracentesis was repeated, draining 10 litres of trasudate. citology and cultures were negative. The abdomen ultrasound revealed an enlarged liver with irregular margins, although not clearly cirrhotic. Blood test showed no sign of advanced liver disease (normal platelets, PT, albumin, sodium).
Considering the previous investigations, all inconclusive, a primary cardiological ethiology was suspected, presumably an acute right congestive heart failure following the rapid arrythmia.
An echocardiogram was requested, which showed a mildly reduced ejection fraction, a diastolic disfunction and, of greater significance, diffuse pericardial thickening with evidence of septal bounce, a mitral PW respiratory variation >25%, medial e'>septal e', and expiratory diastolic flow reversal in the sovraepatic veins that were dilated, as the inferior vena cava. The whole picture was suggestive of constrictive pericarditis (as per the Mayo Clinic Criteria).
In order to exclude other causes of ascites, an abdominal CT scan was repeated. It showed impaired systemic venous flow with atrial blood pooling. The liver appeared enlarged and the S2 lesion seemed increased in size compared to the previous exam, with a contrast pattern suggestive of hepatocellular carcinoma (HCC). An abdominal MRI was requested which ruled out HCC revealing the lesion as an angioma. Therefore, the patient was discharged with a follow-up MRI at 6 months and an ambulatory appointment to evaluate cardiac catheterism and potential pericardiothomy. It is our thought that the atypical contrast pattern of the liver nodule may be explained by the altered hemodinamics due to constrictive pericarditis which made wash-out detection difficult.
In conclusion, constrictive pericarditis is a rare cause of ascites and cirrhosis, due to chronically altered blood flow and hepatic congestion. It should be considered in patients with unexplained ascites and a history of pericarditis, Symptoms can develop insidiously, even years after the initial episode, or abruptly if a superimposed condition worsens decompensation.
In the context of constrictive pericarditis MRI could be a better alternative to CT-scan in the evaluation of hepatic lesions.

A MAN WITH A BIG HEART

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Background: Acromegaly is a rare, acquired disorder caused by excessive growth hormone (GH) secretion, leading to increased secretion of insulin-like growth factor-1 (IGF-1). In over 95% of cases, the cause is a pituitary somatotroph adenoma. IGF-1 excess is responsible for clinical manifestations, including progressive somatic changes (primarily affecting the face and extremities) and systemic manifestations, including cardiovascular, respiratory, endocrine, and metabolic disorders. The onset and progression of acromegaly are typically insidious and slow, often leading to delayed diagnosis. Treatment depends on

the size and location of the adenoma, with transsphenoidal surgery being the first-line approach. In case of residual disease, stereotactic radiotherapy or pharmacological therapy with cabergoline (a dopamine agonist) or pegvisomant (a long-acting somatostatin analog) may be considered.
Case report: A 60-year-old man was admitted to the cardiac surgery ward for mitral valve replacement due to severe mitral regurgitation. His medical history included hypertension, diabetes, gonarthrosis, and edentulism. On admission, blood tests and vital parameters were within normal limits. At the physical examination, he presented a systolic heart murmur, macrognathia, macroglossia, and a soft, mobile mass on the right side of the neck. Echocardiography confirmed severe mitral regurgitation and showed marked cardiac hypertrophy with a "granular-sparkling" myocardial texture, suspected of cardiac amyloidosis. A total body computed tomography (CT) showed an enlarged thyroid gland, especially the right lobe, with substernal extension and carotid compression. Moreover, it showed hepatomegaly, splenomegaly, and prostate hypertrophy. Due to these findings, cardiac surgery was postponed, and the patient was transferred to our internal medicine ward for further evaluation.
Given the enlargement of the thyroid gland, thyroid function tests were conducted, showing suppressed TSH levels (< 0.005 mIU/L) with increased FT4 levels (32.2 ng/L, NV 8-17) and normal FT3 levels (3.4 ng/L, NV 2-5). Thyroid autoantibodies were negative. Upon more specific questioning, the patient reported progressive enlargement of the tongue and jaw, not present in youth, as well as a gradual increase in the size of his hands and feet. Given the clinical suspicion of acromegaly, serum IGF-1 concentration was measured and found to be elevated (35,1ug/L, VN 0-5), supporting the diagnosis of acromegaly, along with the presence of toxic multinodular goiter and other organomegalies. Additional biochemical tests were performed, which revealed hypogonadotropic hypogonadism, hyperprolactinemia, and a preserved adrenal reserve. To identify the cause of GH excess, an MRI of the pituitary gland was carried out, showing an intrasellar macroadenoma (diameter 20 mm).
Workup for amyloidosis included serum protein electrophoresis, which showed mild polyclonal hypergammaglobulinemia. Immunofixation of serum and urine was negative. Serum free light chain assays detected a slight increase in kappa chains, which was not clinically significant. Haematological consultation ruled out light-chain amyloidosis (LA). To exclude transthyretin amyloidosis, a cardiac magnetic resonance imaging (MRI) was recommended; however, in light of previous findings, the echocardiographic features were re-evaluated, and the cardiac hypertrophy was attributed primarily to acromegaly. It was therefore decided, in agreement with the cardiologist, not to carry out further tests for the time being.
A multidisciplinary team meeting, including an internist, endocrinologist, cardiac surgeon, and neurosurgeon, was held to evaluate the optimal surgical sequence. Thyroidectomy was prioritized due to the risk of thyroid storm during other surgeries. Subsequently, it was decided to carry out the operation of transsphenoidal pituitary surgery and finally mitral valve surgery, to minimize the risk of intracranial bleeding. During hospitalization, the patient remained asymptomatic for thyrotoxicosis and, in agreement with the endocrinologist, no antithyroid treatment was started.
Conclusion: Acromegaly is a rare and often underdiagnosed disorder requiring a high index of clinical suspicion. It is associated with the enlargement of many visceral organs, including thyroid, heart, liver, lungs, and kidneys. Cardiovascular complications, such as acromegalic cardiomyopathy characterized by concentric biventricular hypertrophy, diastolic dysfunction, and valvular disease, are among the leading causes of morbidity and mortality in these patients. Thyroid enlargement is also common and may be diffuse or multinodular. Thyroid function is usually normal, though subclinical hypothyroidism or, more rarely, thyrotoxicosis can occur, particularly in the context of iodine exposure, as observed in our patient.
This case highlights the importance of a careful physical examination and the integration of seemingly unrelated clinical findings, such as cardiomyopathy, multinodular goiter, and diabetes mellitus, to recognize a rare but impactful diagnosis.

SEROSAL EFFUSIONS AND HYPONATREMIA IN SYSTEMIC INFLAMMATION: CONSIDERING UNCOMMON INFECTIOUS CAUSES

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Introduction: Pleuropericardial effusion associated with severe hyponatremia is an uncommon presentation that may underlie complex systemic conditions. We describe the case of a 75-year-old woman with a complex multisystemic presentation, in whom common autoimmune, infectious, and neoplastic causes were progressively ruled out. The case highlights the importance of considering atypical etiologies in presence of nonspecific but striking clinical findings.
Case presentation: A 75-year-old woman with a medical history of arterial hypertension, atrial fibrillation, sick sinus syndrome, and Hashimoto's thyroiditis presented to the Emergency Department following a pre-syncopal episode associated with marked lower limb weakness, which occurred while attempting to stand up from the ground. Upon arrival of emergency services, she exhibited a hypertensive crisis (BP 195/140 mmHg), tachycardia, persistent dry cough. In the previous weeks she presented progressively worsening dyspnea, for which she had been prescribed azithromycin at home. Initial laboratory work-up revealed severe hyponatremia (Na 104 mmol/L), bilateral pleural effusion, and circumferential pericardial effusion up to 14 mm, without signs of cardiac tamponade. Diuretic therapy with hydrochlorothiazide was discontinued and intravenous rehydration with saline solution was initiated. During hospitalization, a systemic inflammatory response was observed, characterized by leukocytosis (WBC 18 x10^9/L), elevated C-reactive protein (CRP 43 mg/L), increased muscle enzymes (elevated CK), and troponin plateauing at 288 ng/L, without evidence of acute myocardial injury. Echocardiography confirmed a stable, non-compressive pericardial effusion, while chest CT and PET-CT revealed bilateral axillary and mediastinal lymphadenopathy with pathological uptake. Analysis of the pleural effusion indicated a transudative profile, with negative cultures and cytology. Extensive serologic and autoimmune screening was negative for major systemic diseases, except for isolated IgG positivity for Borrelia burgdorferi (IgM negative), ANA titer of 1:160, and mildly elevated serum ACE levels (68.3 U/L). The overall picture suggested a systemic inflammatory condition, with differential diagnoses including early-stage sarcoidosis or a previously unrecognized and untreated past Borrelia infection. In the absence of hemodynamic compromise, a conservative management approach was chosen, including empiric antibiotic therapy with doxycycline and reintroduction of loop diuretics for the management of generalized edema. The clinical course was favorable, with follow-up blood tests and imaging one month later showing progressive normalization of laboratory parameters, resolution of edema, disappearance of pleural and pericardial effusions, and maintenance of hemodynamic stability.
Discussion: Lyme disease, caused by Borrelia burgdorferi and transmitted by Ixodes ticks, is the most common tick-borne zoonosis in Europe, with higher prevalence in northern regions of Italy. Its clinical spectrum is highly variable and classically categorized into three stages: localized, disseminated, and late, but atypical presentations without hallmark signs such as erythema migrans often delay diagnosis. Late-stage manifestations can involve multiple systems, including the cardiovascular and central nervous systems, and in rare cases, may lead to electrolyte disturbances such as severe hyponatremia, possibly mediated by SIADH, which has been reported in some cases of neuroborreliosis. In our case, the combination of profound hyponatremia, pleuropericardial effusions, and reactive lymphadenopathy prompted a broad differential workup, excluding autoimmune, neoplastic, and common infectious causes. The only notable finding was isolated IgG positivity for Borrelia burgdorferi, in a context of systemic inflammation and mildly elevated serum ACE levels. Empirical treatment with doxycycline led to rapid clinical and radiological resolution, supporting the diagnosis of late Lyme disease with systemic atypical manifestations. This case underlies the importance of maintaining a high index of suspicion for Lyme disease in the absence of classic features, and highlights how systemic inflammation and unexplained electrolyte abnormalities may be the only clues in late-stage presentations. Literature describing such cases is scarce, emphasizing the need for awareness of Lyme disease as a clinical chameleon.

LONG-TERM EFFICACY AND SAFETY OF OPEN-LABEL SELADELPAR TREATMENT IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS: POOLED INTERIM RESULTS FOR UP TO 3 YEARS FROM THE ASSURE STUDY

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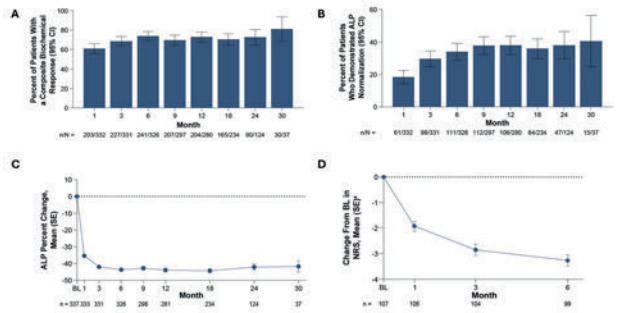
Background: ASSURE (NCT03301506) is an ongoing, open-label, long-term, Phase 3 trial of seladelpar—a novel delpar (selective PPARδ agonist)—in patients (pts) with primary biliary cholangitis rolling over from the Phase 3, placebo-controlled, registrational RESPONSE trial (NCT04620733) or with prior participation in legacy trials (Phase 3 ENHANCE [NCT03602560], CB8025-21629 [NCT02955602], CB8025-31731 [NCT03301506], CB8025-21838 [NCT04950764]). The parent studies required an inadequate response or intolerance to first-line ursodeoxycholic acid. Here, we report pooled interim efficacy and safety for all pts in ASSURE.
Methods: Using a data cutoff of January 31, 2024, pt exposure to seladelpar in ASSURE (including exposure in pts who were randomized to the active treatment arm in RESPONSE) was analyzed. Key efficacy endpoints included composite biochemical response (CBR; alkaline phosphatase [ALP] <1.67 × upper limit of normal [ULN], ALP decrease ≥15%, and total bilirubin [TB] ≤ULN) and ALP normalization. Pruritus was recorded using a numeric rating scale (NRS; 0–10) collected daily through month (M) 6; change from baseline (BL) was assessed through M6 in pts with moderate-to-severe pruritus (NRS ≥4) at BL. Exposure-adjusted adverse events (AEs) were calculated for each year on study as incidence per 100 pt-years. BL was based on first exposure to seladelpar in ASSURE or RESPONSE.
Results: 337 pts received 10-mg seladelpar daily. 34 pts reached 30M on study; 90 pts had ≥24M of seladelpar exposure. At BL, the mean (SD) age was 58.1 (9.7) years, 318/337 (94%) pts were female, mean (SD) ALP was 287.5 (128.4) U/L, mean (SD) TB was 0.75 (0.34) mg/dL, and 55/337 (16%) had cirrhosis. At M12, M24, and M30, 204/280 evaluable pts (73%), 90/124 (73%), and 30/37 (81%) met the CBR endpoint, respectively, and ALP normalized in 106/280 (38%), 47/124 (38%), and 15/37 (41%) pts, respectively. In the pruritus NRS, mean (SE) change from BL at 6M was −3.3 (0.24) among 99 evaluable pts. Outcomes are in the figure. Exposure-adjusted AEs were observed in 86, 70, and 63 pts per 100 pt-years at M12, M24, and M36, respectively. There were no treatment-related serious AEs.
Conclusion: By M30 of the long-term ASSURE study, seladelpar resulted in a durable and sustained biochemical response in 81% of pts, with an ALP normalization rate of 41%, and robust improvement in pruritus. Seladelpar continues to appear safe and well tolerated, with no new safety signals or change in frequency of AEs with up to 3 years of exposure.

(A) Composite Biochemical Response Rate Through Month 30, (B) ALP Normalization Through Month 30, (C) ALP Percentage Change From BL Through Month 30, and (D) Pruritus NRS Change From BL Through Month 6



Data cutoff: January 31, 2024.

*The pruritus NRS ranged from 0 (no itch) to 10 (worst itch imaginable).

ALP, alkaline phosphatase; BL, baseline; NRS, numeric rating scale.

ATTENUATION, NEAR RESOLUTION, AND PREVENTION OF PRURITUS IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS TREATED WITH SELADELPAR: A SECONDARY ANALYSIS OF PATTERNS OF PRURITUS CHANGE IN THE RESPONSE TRIAL

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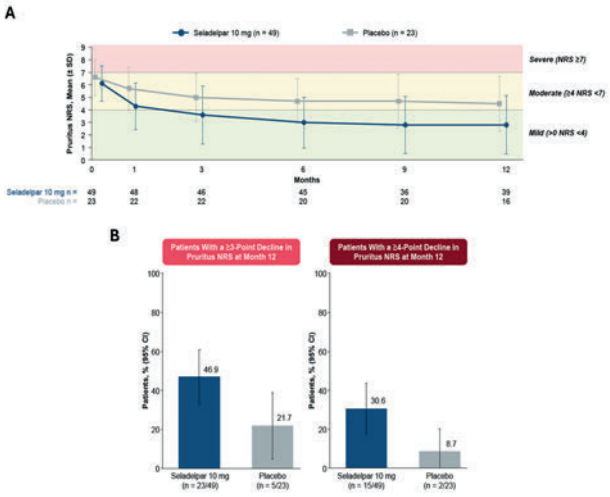
Background: Cholestatic pruritus in patients with primary biliary cholangitis (PBC) is frequently debilitating and lacks effective treatments. In the Phase 3 RESPONSE trial (NCT04620733), seladelpar, a first-in-class delpar (selective PPAR-delta agonist), significantly decreased pruritus in patients with PBC with moderate to severe pruritus (numerical rating scale [NRS] ≥4 at baseline) vs placebo. Here, we further evaluated pruritus patterns in RESPONSE.
Methods: Patients with PBC who received ursodeoxycholic acid (UDCA) for ≥12 months or were UDCA intolerant and had alkaline phosphatase ≥1.67 × upper limit of normal (ULN) and total bilirubin ≤2 × ULN were randomized 2:1 to receive daily oral seladelpar 10 mg or placebo for 12 months. We assessed trends in mean NRS over time and change in pruritus using various thresholds of improvement (eg, ≥3- and ≥4-point reductions in NRS, near resolution of itch [NRS ≤1]) in patients with NRS ≥4 or NRS ≥7 (severe itch) at baseline. Development of pruritus in patients without itch (NRS = 0) at baseline and safety by subgroup of baseline NRS (≥4 or <4) were also evaluated.
Results: At baseline, 72 of 193 enrolled patients had an NRS ≥4, with 49 randomized to seladelpar and 23 to placebo; 16 patients receiving seladelpar and 12 receiving placebo had NRS ≥7. Among patients with NRS ≥4 at baseline, seladelpar reduced the mean itch intensity from moderate to mild from month 3 through 12, whereas the mean itch intensity for placebo remained moderate (Figure, A). For patients with baseline NRS ≥4, 46.9% of patients on seladelpar had a ≥3-point NRS decrease vs 21.7% on placebo at month 12; a ≥4-point NRS decrease was achieved by 30.6% of patients receiving seladelpar vs 8.7% on placebo (Figure, B). A higher proportion of patients with baseline NRS ≥4 (26.5%) and NRS ≥7 (18.8%) on seladelpar experienced near resolution of itch at month 12 vs 0% of patients on placebo. In patients without itch at baseline, 26.7% (4/15) of patients on placebo reported pruritus at month 12 vs 0% (0/30) of patients on seladelpar. Adverse events were reported in 88.9% and 84.3% of patients with baseline NRS ≥4 and NRS <4, respectively, with similar proportions across treatment arms.
Conclusion: Seladelpar reduced pruritus severity in patients with PBC with a durable effect over time and even led to near resolution of itch in some patients, an effect not observed with placebo. Seladelpar mitigated new onset of itch in patients without pruritus and was overall safe and well tolerated, regardless of baseline itch.

(A) Mean Pruritus NRS Over Time and (B) Declines in NRS[a] in Patients With PBC With Moderate to Severe Pruritus (NRS ≥4) in the RESPONSE Trial



[a]Patients with missing data at the specific time point were considered nonresponders.

NRS, numerical rating scale; PBC, primary biliary cholangitis.

RECURRENT FEVER AND SEROSITIS IN A YOUNG ADULT: UNVEILING A HIDDEN INFLAMMATORY DISORDER

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Introduction: Autoinflammatory diseases are characterized by recurrent episodes of systemic inflammation in the absence of high-titer autoantibodies or antigen-specific T cells. They are primarily caused by dysregulation of the innate immune system, often due to genetic mutations affecting inflammatory pathways. Among these, Adult-onset Still's disease (AOSD) stands out as a rare but significant systemic autoinflammatory condition, typically marked by high spiking fevers, evanescent salmon-colored rash, arthralgia/arthritis and elevated inflammatory markers. Although its etiology remains unclear, both genetic and environmental factors may contribute to its pathogenesis. Diagnosis is clinical and made by excluding infectious, neoplastic and autoimmune causes, with the Yamaguchi criteria being the most widely used. Early recognition is crucial, as targeted therapies can effectively control disease activity and prevent complications.
Case presentation: We report the case of a 34-year-old man with recurrent fever and pleuropericarditis. He was recently admitted to the Cardiology Unit for fever, dyspnea and chest pain due to pleuropericarditis. Symptoms and pleuropericardial effusions resolved following antibiotic and anti-inflammatory treatment (ibuprofen, colchicine and corticosteroids). He was discharged in January 2025 with a corticosteroid taper. At follow-up, ultrasound showed no pleuropericardial effusion, and inflammatory markers had normalized, despite liver enzymes (ALT 152 U/L) being elevated. Due to corticosteroid-induced ocular hypertension, treatment was fully discontinued. Shortly after, the patient experienced a new onset of fever, peaking at 39 °C for about 14 days, exertional dyspnea, mild retrosternal discomfort, and sore throat. He was admitted to our Internal Medicine Unit in February 2025. On admission, electrocardiography showed diffuse, concave ST-segment elevation, suggestive of pericarditis. Ultrasound confirmed pericardium thickening with mild pericardial effusion and bilateral pleural effusion, more pronounced on the left.The following therapy was started: Ibuprofen 600 mg BID, Colchicine 0.5 mg BID, Pantoprazole 40 mg IV daily. Corticosteroids were withheld pending further diagnostic workup for possible autoimmune or autoinflammatory disease.Blood tests showed elevated inflammatory markers (WBC 14,600/μL, CRP 44.7 mg/dL, Ferritin 2149 ng/mL). ESR was normal (27 mm) as well as Procalcitonin.Infectious workup – including serologies for C. pneumoniae, M. pneumoniae, TORCH panel, HIV, Quantiferon TB, and blood/urine cultures – was negative.Radiological investigations showed no signs of neoplasia.Autoimmune screening (ANA, ENA, RF, anti-CCP, IgG4, fecal calprotectin, HLA-B27) was also negative.Due to strong clinical suspicion of an autoinflammatory condition, additional tests were performed: Serum Amyloid A was markedly elevated (3050 mg/L, normal <0.6), IL-6 was elevated (189.9 pg/mL, normal <6.4), IL-1 was within normal range (8.5 pg/mL), although measured 5 days post-collection, raising concerns of sample degradation.Autoinflammatory diseases may result from polygenic or monogenic mutations. Among the latter, Familial Mediterranean Fever (FMF) is well known for recurrent fever and polyserositis. Israeli criteria can guide diagnosis, but genetic testing remains the gold standard. Therefore, a blood sample was sent to external laboratories for MEFV gene mutation analysis, which yielded a negative result.Based on these findings, high-dose corticosteroids were started (Methylprednisolone 40 mg IV BID) with increased colchicine dosage. The patient showed a good clinical response, with resolution of fever and pleuropericardial effusions. Steroids were tapered to a maintenance dose of Prednisone 25 mg 1+1/2 tablets daily.
Discussion and conclusion: Based on exclusion of infectious, autoimmune, and neoplastic causes, a diagnosis of AOSD was considered. Although FMF was initially suspected due to the recurrent fever and serositis, genetic testing for MEFV mutations returned negative. There is currently no definitive diagnostic test for AOSD, but various diagnostic criteria are available. Yamaguchi criteria are the most widely used and sensitive. In this case, five criteria were met, including two major (fever ≥39 °C lasting ≥1 week; leukocytosis > 10,000/μL with > 80% neutrophils) and three minor (sore throat, elevated liver enzymes, negative ANA and RF).The recurrent, steroid-responsive pleuropericarditis, in the absence of other identifiable causes, further supported the diagnosis. A referral to the Rheumatology Unit was arranged. On March 20, 2025, the diagnosis of AOSD was confirmed, and treatment with Anakinra was started, with scheduled follow-up.This case highlights the importance of a thorough differential diagnosis in patients presenting with recurrent fever and serositis. Even in the absence of full clinical picture (e.g., rash, arthritis, lymphadenopathy), AOSD should be considered, as early treatment can significantly improve outcomes and quality of life.

A FOUR-WEEK TREATMENT WITH DAPAGLIFLOZIN REDUCES INSULIN-STIMULATED RENAL GLUCOSE UPTAKE

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Introduction: AND AIMS: Treatment with sodium-glucose cotransportes-2 inhibitors (SGLT-2i) has been shown to significantly reduce the risk of both cardiovascular and renal outcomes in type 2 diabetes (T2D). Recent findings indicate that the human renal cortex is an insulin-sensitive tissue. In obese individuals, both during fasting and hyperinsulinemic stimulation, the kidney exhibits lower 18Fluorodeoxyglucose ([18F]-FDG) uptake rates compared to lean individuals, possibly due to insulin resistance. This study aims to evaluate changes in renal [18F]-FDG uptake in T2D patients following short-term treatment with dapagliflozin and to assess the long-term effects on kidney function after a four-year follow-up.
Methods: In our DAPAHeart Trial, a single-center, four-week, prospective, double-blind, controlled study, we enrolled ten T2D patients with stable coronary artery disease and preserved glomerular filtration rates (eGFR >60 ml/min/1.73m2). Participants were randomly assigned in a 1:1 ratio to receive either dapagliflozin (10 mg daily) or a placebo alongside their standard treatment. Position emission tomography (PET) scans using [18F]-FDG were performed during a hyperinsulinemic-euglycemic clamp (HEC) to measure regional FDG uptake before and after the four- week treatment with SGLT-2i. After the trial, the placebo group initiated dapagliflozin therapy, and both groups were followed for four years.
Results: After the four-week treatment, the SGLT-2i group showed a significant reduction in renal standardized uptake value (SUV) expressed as peak activity concentrations (SUVpeak; p=0.045) compared to the placebo group, with trends towards reductions in SUVmax and SUVmean. Additionally, long-term follow-up data revealed that four years of dapagliflozin treatment was associated with stable eGFR (pre-treatment: 81.4 ± 6.4 ml/min; post-treatment: 76.2 ± 6 ml/min; p=0.4).
Conclusions: Short-term treatment with dapagliflozin is associated with a reduction in renal SUVpeak, indicating decreased glucose uptake during an insulin-stimulated state (hyperinsulinemic euglycaemic clamp). While the causes of this reduction require further investigation, it is suggested that SGLT-2 inhibition decreases tubular energy requirements and glucose uptake, contributing to kidney function preservation, as confirmed by the four-year follow-up data on eGFR.

AUTOIMMUNE MYOSITIS IN A PATIENT WITH PULMONARY NEOPLASIA: A CASE REPORT

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Paraneoplastic syndromes are often underrecognized in the early stages of cancer. Among these, immune-mediated myositis represents a rare but serious complication, especially when overlapping with advanced malignancies.
Case description: A 67-year-old male patient presented to the Emergency Department (ED) with a three-month history of worsening chest and lower limbs pain leading to a gradual reduction in motor autonomy up to bed rest. The patient's history was remarkable for a cerebral haemorrhage in 1992 with residual left hemiparesis and the detection, three months prior, of a pulmonary lesion of likely neoplastic origin.
Upon laboratory investigation, hyponatremia, a normal renal function, elevated transaminases, normal troponin and a significant rise in creatine kinase [CPK; 31.000 U/L (n.v. <190 U/L)] and lactate dehydrogenase [LDH; 1.162 U/L (n.v. <246 U/L)] were noted. ECG monitoring was negative for cardiac ischemic events. A chest CT with contrast was performed because of an elevated D-dimer, revealing a possible subsegmental pulmonary embolism in the left lower lobe, a pericardial effusion of 17 mm and pulmonary lesions and lym-

phadenopathies of already known likely malignant origin. Transthoracic echocardiography confirmed a moderate pericardial effusion with initial hemodynamic involvement.
An antithrombotic prophylaxis with enoxaparin was started as well as treatment for acute pericarditis (non-steroidal anti-inflammatory drugs and colchicine). Rhabdomyolysis remained of unclear origin. A more detailed medical history revealed that the patient had not experienced any falls or trauma, and he was not on any medications associated with muscle toxicity. Intravenous fluids were initiated. The persistence of pain in the lower limbs, associated with the pulmonary lesions of likely malignant origin, prompted the hypothesis of paraneoplastic muscle damage. Thus, an electromyography was performed showing signs of severe acute myositis. Systemic high-dose corticosteroid therapy (methylprednisolone 1 gram daily for three consecutive days) was initiated followed by maintenance high-dose prednisone (1 mg/kg/day). In the next days, CPK reduction and clinical improvement (less pain and gradual recovery) were observed. Moreover, an MRI of the lower limbs was performed, revealing signs of acute muscle injury (widespread muscle oedema and fat atrophy with oedematous infiltration of multiple muscle bellies). To further investigate the aetiology of the myositis, viral and autoimmune serologies were performed: no infectious causes were found, whereas the autoimmune panel was remarkable for a positive ANA (titre 1:640, granular pattern) and anti-Ro52 antibodies, whereas the anti-ENA panel for autoimmune myositis was negative. Follow-up transthoracic echocardiography showed a reduction in the pericardial effusion with resolution of the signs of hemodynamic compromise. The patient was discharged in good general condition, with instructions for a gradual prednisone taper. The pulmonary lesion was histologically identified as a mucinous adenocarcinoma with overexpression of PD-L1. The staging investigations revealed hilar, subcarinal, and mediastinal lymphadenopathy, along with metastases to the left adrenal gland and the left ischiopubic branch, indicating stage IVc cancer. At a one-month follow-up, the patient was in good general condition with complete resolution of myositis-related symptoms. The oncology team indicated the start of monotherapy with pembrolizumab after the taper of corticosteroid therapy.
However, the patient died a few days later due to septic shock originating from the respiratory tract. A chest CT scan demonstrated extensive ground-glass opacities with a crazy paving pattern. The previously identified pulmonary lesion caused complete obstruction of the right middle and lower lobes. Additionally, contralateral pulmonary lesions suspicious for secondary involvement were observed.
Conclusions: We have described the case of a patient presenting with severe rhabdomyolysis of unclear origin, a common cause of hospitalization in Internal Medicine wards. In approximately 10% of cases, such presentations may be attributed to myositis, either of autoimmune or paraneoplastic nature1. Lung cancer may cause many paraneoplastic syndromes, including immune-mediated myositis2. This clinical case prompts two key reflections. Firstly, the knowledge of an active cancer mass may facilitate the recognition of a paraneoplastic syndrome and allow for the early initiation of treatment. In the case we presented, treatment started even before the histologic confirmation of cancer. Secondly, this case illustrates the difficult decision of starting immunotherapy in patients with immune-related paraneoplastic syndromes, weighing the risk of cancer progression without treatment against the possibility that immunotherapy may trigger or worsen immune complications.
References: 1doi:10.1097/01.md.0000188565.48918.41
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ANAPLASTIC MYELOMA WITH PANCREATIC LESIONS – CASE REPORT

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Presentation: We present the case of a 75-year-old man with a history of recurrent pulmonary embolism, dyslipidemia, and IgA kappa monoclonal gammopathy of undetermined significance, first diagnosed two years prior (serum free light chain kappa/lambda ratio: 5.47; IgA kappa level approximately fourfold above normal). The patient was being evaluated at an external facility for suspected multiple myeloma due to severe bone pain localized to the pelvic region and iliac crests, though CT imaging revealed no lytic lesions. At the time of admission, results from a bone marrow biopsy and PET scan were pending.
The patient presented to the emergency department (ED) for progressive functional decline and altered mental status. Days prior, an elastomeric infusion pump (morphine 40 mg, artrosilene 160 mg, dexamethasone 8 mg) was initiated for refractory pain, after which he developed agitation, aggression, and confusion. Abdominal ultrasound in the ED identified a heterogeneous hypoechoic pancreatic tail mass (63 × 51 mm) and a hyperechoic hepatic lesion. Severe anemia requiring blood transfusion was seen as well.
Management: During hospitalization, PET imaging demonstrated FDG-avid lesions in skeletal muscle, bone, peritoneum, pancreas, and lymph nodes. Bone marrow biopsy, despite extensive necrosis, suggested immature/anaplastic multiple myeloma (MM). Being anaplastic MM an extremely rare entity, multidisciplinary review prompted for endoscopic ultrasound-guided pancreatic biopsy for suspected multiple primary malignancy, i.e. solid pancreatic tumor and MM. The pancreatic biopsy however confirmed the presence anaplastic myeloma via CD138 positivity and kappa light chain restriction. Post-diagnostic CT revealed 74 × 53 mm (Figure 1) pancreatic mass encasing mesenteric vessels, alongside extramedullary lesions in the left thoracic wall (with rib fractures), right scapula/deltoid (bone erosion), retrocaval/iliopsoas soft tissue, and a large right gluteal/iliac lesion eroding pelvic bones. Vertebral collapse at D4 caused spinal cord compression, with widespread lytic bone destruction. The diagnosis of symptomatic IgA kappa MM (ISS III-A) with extramedullary involvement and transfusion-dependent anemia was established.
Treatment: After discussing the poor prognosis with the patient and caregivers, a reduced-intensity regimen of bortezomib (dose-adjusted for thrombocytopenia), lenalidomide (reduced for thromboembolic risk), and dexamethasone (attenuated for age) was initiated. Three days post-first cycle, the patient developed fever and respiratory distress. Chest CT (Figure 2) showed peribronchovascular ground-glass opacities, but was inconclusive for infectious pneumonia, and differentials included bortezomib-induced pneumonitis versus Pneumocystis jiroveci pneumonia (PJP). Blood cultures and bronchoalveolar lavage were negative. Given the diagnostic uncertainty and concern for drug-related lung injury, empiric therapy with high-dose steroids (1 mg/kg) and IV Bactrim was was initiated, leading to clinical improvement.
Despite pulmonary complications, chemotherapy was resumed after a 21-day antimicrobial course, driven by radiologic evidence of treatment response (regression of a left thoracic wall lesion) and the aggressive biology of anaplastic myeloma. Post-discharge, the patient maintained ambulation with a walker and reported decent quality of life for two months before succumbing to likely disease progression or treatment-related complications three months post-diagnosis.
Conclusions: Anaplastic myeloma is a rare, aggressive malignancy with only 52 documented cases in the last four decades worldwide. Its extramedullary spread mimics other malignancies, necessitating histopathologic confirmation. Median survival is 6–12 months with therapy and <3–6 months untreated, worsening to <6–9 months with visceral involvement due to chemoresistance and infections (1,2), as seen in our patient's 3-month survival despite transient response.
This case highlights the therapeutic futility of anaplastic MM with extramedullary dissemination, mainly in an elderly patient. Multidisciplinary efforts must prioritize quality of life, particularly in balancing analgesia with iatrogenic risks (e.g., opioid-induced delirium) and providing the most appropriate and feasible first-line treatment. A patient-centered approach, integrating early palliative care and frank prognostic discussions, is essential to navigate the challenges posed by this relentlessly progressive disease, which still represents an unmet clinical need.
"High-risk multiple myeloma: A classification of the most aggressive disease"
"Extramedullary pancreatic involvement in multiple myeloma: A systematic review of clinical features and outcomes"

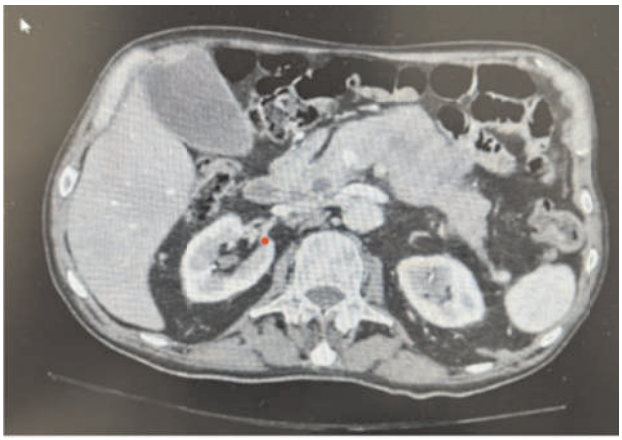

Figure 1 Pancreatic MM lesion

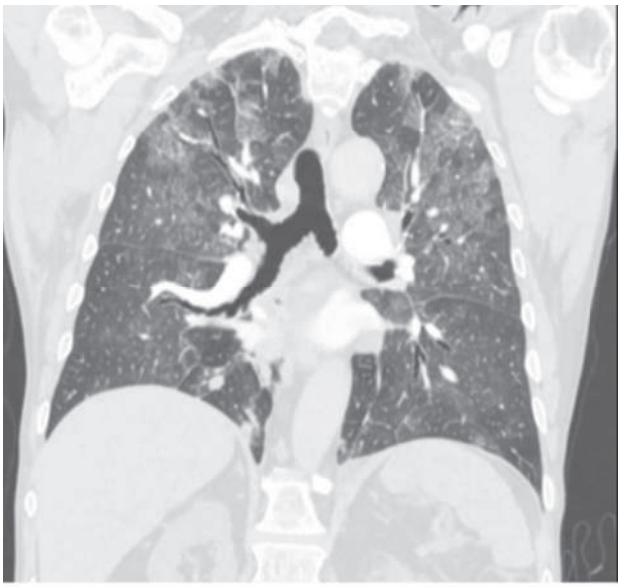

Figure 2 Chest CT (after 1st cycle of treatment)

A CHANGE IN POINT OF VIEW: THE USE OF IDDA 2.1 IN INBORN ERRORS OF IMMUNITY. A SINGLE-CENTER EXPERIENCE

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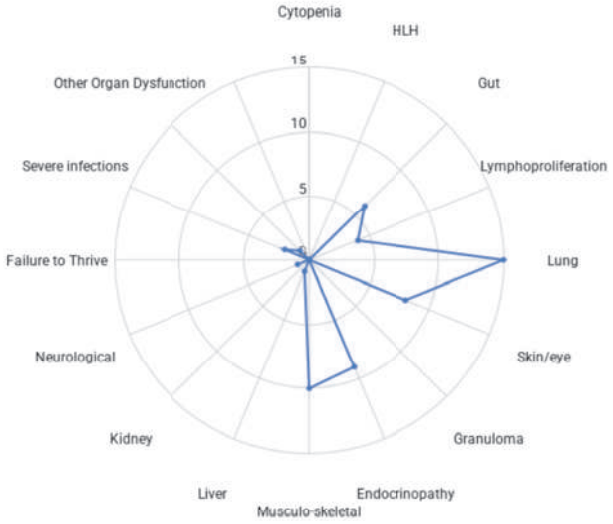
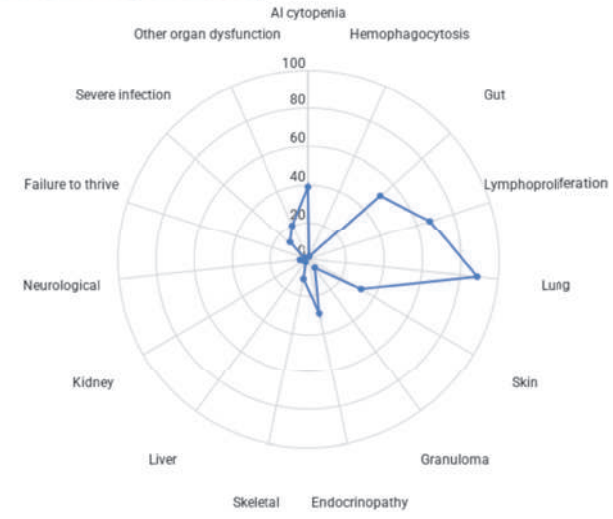
Introduction: Inborn errors of immunity (IEIs), as defined by the International Union of Immunological Societies Expert Committee (IUIS), are a broad group of diseases caused by damaging germline variants in single genes. Clinical presentations are wide-ranged, spacing from susceptibility to infections to immune dysregulation, such as autoimmunity and allergy, as well as bone marrow failure and/or malignancy. The aim of this study is to analyze the prevalence of immune disregulatory manifestations in different types of IEIs.
Methods: This retrospective, monocentric, observational study included patients with IEIs that have had an immunological follow-up at the Ca' Foncello Hospital in Treviso for at least 1 year. For every patient, we calculated IDDA 2.1 score at the last follow-up visit; IDDA 2.1 is a tool devised by the European Society of Immune Deficiencies (ESID) to quantify the degree of immune dysregulation in patients with IEIs, as well as the patterns of distributions; this is done by giving a quantitative score to each organ involvement, as well as quantifying (in percentage) hospitalisation time and performance score; results were then turned into qualitative data and inserted in a radar plot to better show patterns of distribution of organ involvement in different IEIs.Quantitative results are shown as median with IQR Continuous variables were analyzed through Mann Whitney test.
Results: Our cohort included 252 patients, 119 of whom were female. The median age was 53 years old (IQR 25). The cohort included the following IEIs: Common variable immune deficiency (CVID, n=151), selective IgG deficiency (N=37), selective IgM deficiency (n=3), Unclassified Antibody deficiency (UAD n=29); X linked agammaglobulinemia (XLA, n=6), Digeorge Syndrome (DGS, n=6), Good Syndrome, (GS n=4), Hyper-IgE syndrome (HIES n=3), Kabuki syndrome (KS n=2), STAT3 gain of function (STAT3GOF n=2), STAT1 gain of function (STAT1GOF n=1) Autoimmune lymphoproliferative-like syndrome (ALPS-like n=1), autoimmune polyendocrinopathy candidiasis ectodermal dystrophy (APECED, n=1), Immune dysregulation polyendocrinopathy enteropathy, X-linked (IPEX, n=1), Mendelian susceptibility to mycobacterial diseases (MSMD, n=1). Of these, 161 patients were treated with immunoglobulin replacement therapy. Overall, the median IDDA 2.1 score was 36 (IQR 42). Median IDDA score for CVID was 48 (IQR 36), selective IgG deficiency patients had a median score of 24 (IQR 12), IgM deficiency patients had a median score of 12 (IQR 9); UAD patients had a median IDDA score of 21 (IQR 12). Patients affected by XLA had a median IDDA score of 48 (IQR 13); HIES patients had a median score of 78 (IQR 6); patients with DGS had a median score of 66 (IQR 35), while patients with GS had a median score of 51 (IQR 13). Patients with STAT3GOF had a median score of 66 (IQR 11), while patients with KS had a median score of 57 (IQR 39). The ALPS-like patient had a score of 30; the APECED patient had a score of 102; the IPEX patient had a score of 96; the MSMD patient had a score of 162, the STAT1 GOF patient had a score of 72. 64% of patients (n=161) were receiving Immunoglobulin replacement therapy (IgRT) Overall, 14% (n=32) presented with severe infections (defined as requiring hospitalization); 47% presented with chronic or recurring infections (n=104); 16.2% (n=41) presented autoimmune cytopenia; 24.2% (n=61) of patients presented GI involvement; 18% (n=46) presented with skin/eye manifestations; 17% (n=43) presented with autoimmune endocrinopathy; 29.7% (n=75) presented lymphoproliferation or splenomegaly. Patients affected by known genetic-based IEIs (n=24) had higher IDDA 2.1 values compared to the rest (median 69 IQR 42 vs median 36 IQR 36, p <0.001). When considering patients with primary antibody deficiency without known genetic basis, namely selective IgG, IgM deficiency and UAD (total n= 72) and CVID; the latter group presented a significantly higher median IDDA score (median 48 IQR 36 vs 18 IQR 24, p<0.001).
Conclusions: As seen in recent literature (first and foremost the new IUIS 2024 classification), it's becoming clearer and clearer that inborn errors of immunity are broad clinical entities in which susceptibility to infection is not necessarily the predominant clinical feature; organ-specific and hematological signs of immune dysregulation (such as atopy or autoimmune cytopenia) are often the sole and presenting clinical sign. It is important to highlight that infection was evaluated during ongoing IgRT. Compared to other primary antibody deficiencies, CVID patients had a significantly higher burden of immune dysregulation, determined not only by the infection but also by autoimmune cytopenia, lymphoproliferation and enteropathy; However, the prognostic value and clinical utility of IDDA 2.1 score in CVID is still unknown and needs further investigation. Finally, it's clear that understanding the clinical variability of IEIs is key in suspecting them, even in the absence of an infectious burden.

IDDA 2.1 IN SELECTIVE IGG, IGM DEFICIENCY AND UAD (AT FOLLOW-UP)



IDDA 2.1 IN CVID (AT FOLLOW-UP)



MINERALOCORTICOID RECEPTOR ANTAGONISTS IN HEART FAILURE WITH MILDLY REDUCED AND PRESERVED EJECTION FRACTION: AN UPDATED SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CLINICAL TRIALS

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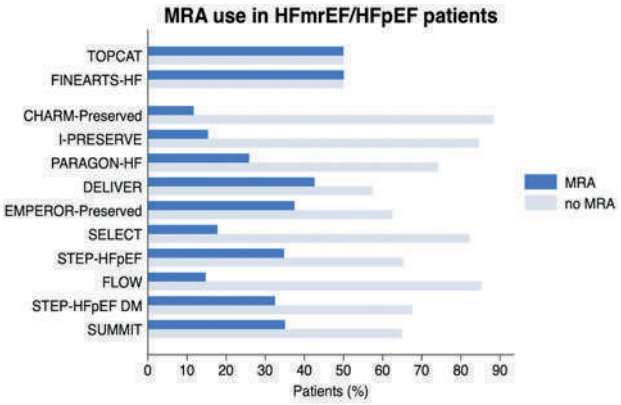
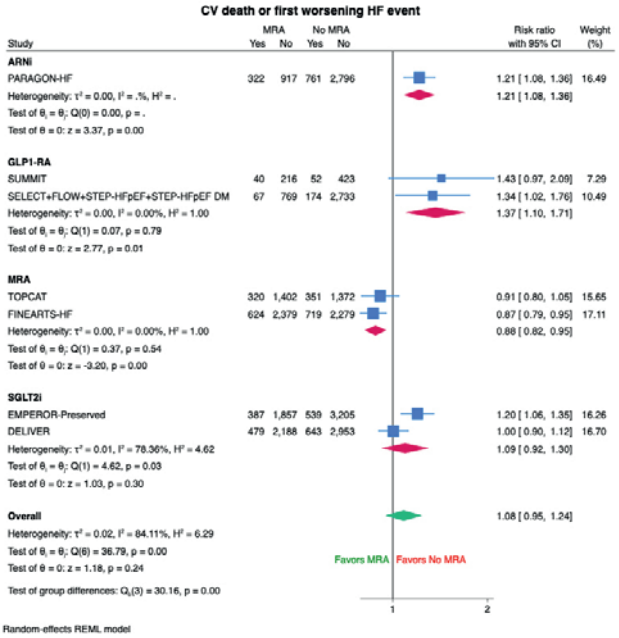
Background: Finerenone, a non-steroidal mineralocorticoid receptor antagonist (MRA), has shown to reduce morbidity and cardiovascular (CV) mortality in heart failure with mildly reduced (HFmrEF) and preserved (HFpEF) ejection fraction, while the benefit of steroidal MRAs in HFmrEF and HFpEF is uncertain.Purpose. To investigate the use of MRAs among patients with HFmrEF/HFpEF in randomized clinical trials (RCTs) and to explore the association between MRA use and outcomes.
Methods: We performed a systematic-review and meta-analysis of RCTs including patients with chronic HFmrEF/HFpEF and testing MRA vs. placebo or reporting baseline characteristics and events in MRA users vs. non-users. Primary outcome was a composite of CV mortality and first-event of worsening heart failure (HF). Secondary outcomes were the single components of the primary outcome and all-cause death. Risk ratios (RR) with 95% confidence interval (CI) were calculated by using a random-effects model. Sources of heterogeneity were explored by leave-one-out and subgroup analyses, as well as by meta-regression models.
Results: A total of 38,849 patients from 13 RCTs were included. Background therapy with MRA was <50% in patients with HFmrEF/HFpEF (Figure 1). In 30,967 patients from 7 trials, RR (95% CI) for the primary outcome was 1.08 (0.95-1.24) in MRAs users vs. non-users, with considerable heterogeneity (Figure 2). The association remained neutral with a leave-one-out approach. In trials randomizing MRA vs. placebo, the RR (95% CI) for the primary outcome was 0.88 (0.82-0.95). At meta-regression, use of sodium-glucose cotransporter 2 inhibitors (SGLT2i), mean left ventricular ejection fraction (LVEF) and body mass index (BMI) were not significantly associated with the risk of primary outcome (P=0.27, 0.17 and 0.51, respectively). An increased risk of primary outcome was associated with higher NT-proBNP values (P=0.02), higher NYHA class (P<0.001) and higher systolic blood pressure at baseline (P<0.001) in patients using MRAs vs. patients not using MRAs.
Conclusions: Non-steroidal MRAs are effective in HFmrEF/HFpEF. Further studies are needed to assess the therapeutic effects of MRAs across multiple phenotypes and a wide spectrum of disease severity.





PILOT STUDY: DIFFERENCES IN THE PLASMA LIPIDOME BETWEEN PATIENTS WITH POST-HCV AND METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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Background: Chronic Hepatitis C (CHC) is a leading cause of end-stage liver disease and hepatocellular carcinoma (HCC) whose risk is worsened by obesity, insulin resistance (IR) and hepatic steatosis. Direct-acting antivirals (DAA) transformed the natural history of CHC: they effectively eradicate the virus, however they may also lead to weight gain potentially worsening hepatic steatosis and reducing the protection against hepatic outcomes. It is currently unknown if processes leading to post-HCV steatotic liver disease (SLD) overlap with those characterising metabolic dysfunction-associated steatotic liver disease (MASLD). Furthermore, it has been suggested that peripheral IR in post-HCV SLD affects skeletal muscle more than adipose tissue, potentially affecting the lipidomic signature and cardiometabolic outcomes of this specific SLD form. To learn more about post-HCV pathophysiology, in this pilot study, we analysed the plasma lipidomic signatures of post-HCV patients and compared them to sex-matched MASLD patients and healthy controls.
Methods: This analysis included 22 male SLD patients (7 post-HCV SLD, 15 patients with MASLD) and 6 sex-matched healthy controls (CTRL) recruited at the Clinica Medica Frugoni (Policlinico di Bari). We assessed plasma biochemistry, body composition, and imaging. Untargeted plasma lipidomic analysis was performed using state-of-the-art liquid chromatography–mass spectrometry.
Results: Patients with SLD showed higher BMI compared to CTRLs, with no significant differences among SLD groups. MASLD patients featured a significant increase in Fat Mass percentage (FM%), whereas body composition of post-HCV SLD patients did not differ from healthy controls. These differences in body composition among SLD groups reflect insulin resistance (HOMA-IR trended to increase in MASLD compared to post-HCV SLD), circulating liver enzymes, and hepatic fat content (predicted with the non-invasive score Fatty Liver Index). Of interest, although the clinical lipid profile was comparable across all groups, the whole plasma lipidomic analysis was more sensitive in detecting disease-specific lipid signatures. Specifically, post-HCV patients

displayed increased levels of absolute circulating polyunsaturated (PUFA) triglycerides (e.g. TG 56:4; TG 56:5; TG 58:4; TG58.5) compared to CTRL and MASLD. In contrast, saturated and monounsaturated TGs (SFA/MUFA-TGs), mainly De Novo Lipogenesis (DNL) products, did not differ among SLD groups and correlated positively with BMI and HOMA-IR, as expected.
Conclusions: This preliminary study highlights potential biological differences among SLD patients based on aetiology. Post-HCV SLD patients may have a more favourable body composition than those with MASLD, thus being potentially protected from hepatic lipotoxicity. Fasting circulating TGs mainly reflect the composition of the hepatic lipidome: our data, while confirming that hepatic DNL in SLD is primarily driven by obesity and IR, also suggest that PUFA-TGs may have a protective role against liver damage in post-HCV SLD patients. These preliminary data strongly support our goal to perform a more detailed analysis of the separated lipoproteins to gain biological insights into the pathophysiology of post-HCV hepatic steatosis.

PERICARDIAL DISEASE IN THE OVER-65 POPULATION: FOCUS ON PERICARDITIS AND ISOLATED PERICARDIAL EFFUSION

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Introduction: Scientific evidence on pericardial diseases is limited, particularly in the geriatric population. To contribute further data to the existing literature, we conducted an observational study collecting clinical, laboratory, and treatment-related characteristics of patients diagnosed with pericarditis according to the 2015 ESC criteria (idiopathic, post-cardiac injury, inflammatory/autoinflammatory, para-infectious) and those with isolated pericardial effusion.
Materials and methods: We included a cohort of 108 patients evaluated between 2020 and 2024 at the "A. Gemelli" University Hospital "CeMI Pericarditis Outpatient Clinic". We excluded cases of purulent pericarditis, active autoimmune diseases, and active malignancies. Patients were divided into three groups:1) Pericarditis with associated pericardial effusion (76 patients); 2) Pericarditis without pericardial effusion (11 patients); 3) Isolated pericardial effusion (21 patients). At the initial visit, we collected the following data: age, sex, BMI, type and etiology of pericarditis, clinical presentation, presence and severity of pericardial effusion (<10 mm, 10–20 mm, >20 mm), ECG changes at onset, presence of cardiac tamponade, need for pericardiocentesis, presence of pleural effusion, comorbidities, albumin, C-reactive protein (CRP) and creatinine levels, and medical treatment prescribed.
Results: The features of the study group are shown in Table 1. The isolated pericardial effusion group consisted exclusively of patients ≥65 y.o., while the "dry" pericarditis group included only patients <65 y.o. Female sex was predominant across all groups. No significant differences were observed in pericarditis etiology, with recurrent idiopathic pericarditis being the most common form. Comorbidities were more frequent in patients ≥65 y.o., with a median of five comorbidities in those with isolated effusion compared to four in their age-matched counterparts with pericarditis. Among patients ≥65 y.o., hypertension and hypothyroidism were significantly more prevalent in the isolated effusion group. As expected, chest pain was more frequent in patients <65 y.o. and in those with pericarditis. Fever occurred regardless of age, while palpitations were reported in 27% of cases, mostly in younger patients (<65 y.o.). Contrary to recent literature, no significant age-related differences in dyspnea at onset were observed, although it tended to be more frequent in older adults. Dyspnea was the predominant symptom in patients ≥65 y.o. with isolated effusion compared to those with pericarditis, with a statistically significant difference (p = 0.0057). Patients ≥65 y.o. were at higher risk of major complications despite a less symptomatic presentation: they had moderate-to-severe pericardial effusion (regardless of diagnosis), atrial fibrillation, tamponade or pre-tamponade onset, and required pericardiocentesis more often. They also had a significantly higher prevalence of pleural effusion associated with pericarditis compared to both younger patients (p<0.0001) and their age-matched peers with isolated effusion (p=0.0083). Interestingly, patients ≥65 y.o. with isolated effusion showed lower creatinine levels, higher BMI, and higher albumin levels than age-matched patients with pericarditis, despite having more comorbidities. In patients <65 y.o., no significant correlation was found between the severity of the effusion and the levels of CRP (p=0.25), although a tendency for CRP to increase with the intensification of the effusion was observed. On the contrary, in patients aged ≥65 y.o. a significant difference in CRP levels was observed (p=0.047): these were higher in mild effusions (median 176.6 mg/l; IIQ 91.4) compared to moderate (median 18.1 mg/l; IIQ 107.3) and severe (median 22.2 mg/l; IIQ 96.3) ones, highlighting a behavior opposite to that of young people. However it should be noted that this analysis concerns all subjects aged ≥ 65 years, without distinguishing between isolated effusion and effusion with pericarditis. NSAIDs were less frequently prescribed in elderly patients, while corticosteroids and colchicine were used similarly across all age groups. Anakinra was prescribed mainly in younger patients and in 42.2% of patients ≥65 years with pericarditis who had contraindications to NSAIDs and corticosteroids; follow-up is ongoing in this group.
Conclusions: The study highlights that pericardial diseases affect women more frequently and that there are no significant etiological differences in pericarditis among the analyzed groups. In patients aged ≥65 years, pericarditis tends to present with less evident symptoms but more severe effusions and greater pleural involvement. Advanced age and comorbidities influence clinical presentation and management, increase the risk of complications, and make adherence to guideline-based therapeutic algorithms more challenging. Recognizing these differences is crucial to optimize therapeutic approaches and improve clinical outcomes in patients with pericardial disease.

Features	Total (n. 108)	<65 (n. 53)	≥65 (n. 55)	P value
Average age (years)	59.1 ± 21.2	40.2 ± 12.8	77.3 ± 6.8	
Sex (M/F)	36/72	17/36	19/36	n.s.
Clinical Presentation				
Chest pain	78	48 (62%)	30 (38%)	<0.001
Palpitations	30	23 (77%)	7 (23%)	<0.001
Sinus Tachycardia	14	11 (78%)	3(22%)	<0.001
Atrial Fibrillation	13	3 (23%)	10 (77%)	<0.001
Dyspnea	60	26	34	n.s.
Fever	40	22	18	n.s.
Comorbidities				
Heart Failure	26	1	25	<0.001
Atrial Hypertension	46	6	40	<0.001
Diabetes Mellitus	18	3	15	<0.001
Renal Insufficiency	24	1	23	<0.001
Hypotyroidism	16	4	12	<0.001
Autoimmune diseases	16	6	10	n.s.
Anemia	22	3	19	<0.001
Atrial Fibrillation	27	2	25	<0.001
COPD	16	1	15	<0.001
Severity grade of effusion				
Pericardial effusion <10mm	31	22 (71%)	9 (29%)	0.0034
Pericardial effusion 10-20mm	26	9 (35%)	17 (65%)	0.099
Pericardial effusion >20mm	32	8 (25%)	24 (75%)	0.0010
Tamponade or pre-tamponade	17	3 (18%)	14 (82%)	0.0052
Pleural effusion	40	13 (33%)	27 (67%)	<0.001
Laboratory parameters				
C reactive protein (mg/L)	79.6 ± 90.5	69.4 ± 101	93.7 ± 73.3	n.s.
Treatment				
NSAIDs	91	38 (58%)	53 (42%)	n.s.
Colchicine	100	51 (51%)	51 (49%)	n.s.
Corticosteroids	56	28 (50%)	28 (50%)	n.s.
Anakinra	37	22 (60%)	15 (40%)	n.s.
Percardiocentesis	14	1 (7%)	13 (93%)	<0.001

Table 1

DIAGNOSTIC ACCURACY OF FECAL CALPROTECTIN IN DISCRIMINATING ORGANIC-INFLAMMATORY GASTROINTESTINAL DISEASES AND FUNCTIONAL GASTROINTESTINAL DISORDERS IN OLDER PATIENTS

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La calprotectina fecale (CF) è un marcatore ampiamente riconosciuto dell'infiammazione neutrofilica intestinale e rappresenta uno strumento affidabile sia per distinguere la malattia infiammatoria cronica intestinale (MICI) dalla sindrome dell'intestino irritabile (SII), sia per il monitoraggio clinico e terapeutico delle MICI grazie alla sua stretta correlazione con il processo di guarigione della mucosa intestinale. Inoltre, sebbene la maggior parte delle evidenze si concentri sul ruolo della CF nella diagnosi e gestione delle MICI, livelli leggermente elevati di CF sono stati osservati anche in pazienti con diverse condizioni infiammatorie che interessano il tratto gastrointestinale inferiore. L'età avanzata è stata identificata come un potenziale fattore che influenza i risultati del test della CF e la sua accuratezza diagnostica; tuttavia, ad oggi, nessuno studio si è specificamente concentrato su questo aspetto. Il nostro studio si propone pertanto di indagare eventuali differenze nell'accuratezza diagnostica della calprotectina fecale tra soggetti giovani e anziani nel distinguere tra patologie gastrointestinali organico-infiammatorie e disturbi gastrointestinali funzionali.
È stato condotto uno studio retrospettivo monocentrico presso un centro di cura terziario (Fondazione Policlinico Gemelli, Roma, Italia). I pazienti sono stati selezionati da un Registro della Calprotectina Fecale gestito dal nostro Dipartimento di Biochimica; i dati sono stati raccolti retrospettivamente attraverso la consultazione delle cartelle cliniche elettroniche, comprendenti tutti gli esami endoscopici e radiologici, le visite ambulatoriali e i ricoveri ospedalieri, con un periodo di osservazione minimo di un anno. I dati raccolti hanno incluso età, sesso, valore di calprotectina fecale, data del campione e presenza di comorbidità valutata mediante l'Indice di Comorbidità di Charlson. L'indicazione all'esecuzione del test di calprotectina fecale è stata definita come sintomo gastrointestinale primario o come parte del follow-up regolare in pazienti con MICI (in fase attiva o in remissione di malattia). Le diagnosi finali, formulate sulla base di tutta la documentazione disponibile, sono state suddivise in "malattie gastrointestinali organico-infiammatorie" (ulteriormente distinte in MICI attiva e altre condizioni organico-infiammatorie quali cancro del colon-retto, colite infettiva, diverticolite e infiammazione severa del tratto gastrointestinale superiore) e "disturbi gastrointestinali funzionali" (definiti dai criteri di Roma IV e confermati da risultati endoscopici/radiologici normali e assenza di patologia organica dopo un follow-up di 12 mesi). Sono stati esclusi i casi con dati insufficienti riguardo al motivo dell'esecuzione del test di CF o alla diagnosi finale.
La coorte finale del nostro studio era composta da 745 pazienti, di cui 316 (42,4%) di sesso maschile e 429 (57,6%) di sesso femminile. All'interno di questa coorte, 573 individui (76,9%) avevano un'età inferiore a 65 anni, mentre 172 (23,1%) avevano 65 anni o più. I pazienti anziani hanno mostrato livelli di calprotectina fecale significativamente più elevati rispetto ai soggetti più giovani: 72 (25–260) µg/g versus 47 (25–165) µg/g ($p < 0.01$). I soggetti più giovani erano più frequentemente affetti da MICI, mentre il cancro del colon-retto e i polipi ad alto rischio, la colite infettiva e la malattia diverticolare rappresentavano i riscontri più comuni nel sottogruppo di pazienti più anziani con malattie gastrointestinali organico-infiammatorie ($p < 0.01$ per tutti i confronti). Tuttavia, la soglia ottimale stimata di calprotectina fecale per distinguere tra malattie gastrointestinali organico-infiammatorie e disturbi gastrointestinali funzionali è risultata piuttosto simile tra i due gruppi (109 µg/g per il sottogruppo più giovane e 98 µg/g per il sottogruppo più anziano), mantenendo una specificità molto elevata.
In conclusione, il nostro studio mostra come la calprotectina fecale si confermi un test altamente specifico di infiammazione intestinale anche nei pazienti anziani, con soglie di positività comparabili a quelle dei soggetti giovani. Un vantaggio clinico cruciale della calprotectina fecale emerge nell'identificazione di pazienti adulti che necessitano di accertamenti invasivi, come le endoscopie, per indagare un'eventuale infiammazione intestinale; questa informazione è particolarmente preziosa negli anziani, per i quali la colonscopia rappresenta un esame invasivo con un profilo di rischio di complicanze più elevato rispetto ai pazienti più giovani. È importante rimarcare, tuttavia, che la calprotectina fecale non è indicata per lo screening del carcinoma colorettale. Invece, in assenza di sintomi allarmanti, suggeriamo che il suo dosaggio possa essere utile, specialmente nella popolazione anziana, per escludere patologie gastrointestinali organico-infiammatorie, mantenendo un'elevata specificità, anche utilizzando soglie di valori simili a quelle dei soggetti più giovani.

CONTROLLED ATTENUATION PARAMETER DOES NOT PREDICT LONG-TERM OUTCOMES AFTER DAA-INDUCED HCV CLEARANCE: THE ROLE OF BASELINE LIVER STIFFNESS

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Rationale. Steatotic liver disease (SLD) is a common comorbidity in patients with HCV infection, arising from a combination of viral and host-related factors. However, the extent to which SLD—defined by a Controlled Attenuation Parameter (CAP) ≥288 dB/m—prior to antiviral treatment influences long-term hepatic and extra-hepatic outcomes after successful HCV eradication remains unclear.
Methods: The study included a consecutive cohort of 237 patients (119 males, 50%) recruited from two liver clinics in Italy and Spain. All participants had achieved sustained virologic response (SVR) following treatment with direct-acting antivirals (DAAs) for chronic hepatitis C (53% were HCV genotype 1). Liver stiffness and CAP were assessed via vibration-controlled transient elastography (VCTE) within six months of initiating antiviral therapy. Five years after completing treatment, patients were recalled for clinical and instrumental follow-up. The primary endpoint was a composite of liver-related events (including decompensation and hepatocellular carcinoma \[HCC]), major adverse cardiovascular events (MACE), or all-cause mortality, stratified by the presence or absence of SLD at baseline.
Results: Thirty-seven patients (16%) met the criteria for SLD based on baseline CAP measurements (median 309 dB/m, IQR 298–330), compared to 200 patients without SLD (median 221 dB/m, IQR 201–248). During follow-up, 18 patients (8%) died, including 4 deaths from liver-related causes. The composite primary endpoint was reached by 32 patients (13%), including 15 MACE, 4 cases of liver decompensation, and 4 HCC. Baseline SLD status was not associated with increased risk of the primary endpoint. Among surviving patients, CAP values remained stable between baseline and follow-up ($p = 0.390$), whereas liver stiffness significantly declined (median reduction of 1.5 kPa; IQR 3.0–0.2, $p <0.001$). Both CAP and liver stiffness values at follow-up were strongly correlated with baseline values ($p <0.0001$). No significant associations with the primary endpoint were found for sex, body mass index (BMI), alcohol or tobacco use, diabetes, hypertension, or dyslipidemia at the time of antiviral therapy. CAP values at baseline did not differ between patients who did and did not reach the primary endpoint (median 229 dB/m, IQR 202–274 vs. 228 dB/m, IQR 205–269; $p = 0.773$). However, liver stiffness was significantly higher in those who experienced adverse outcomes (median 8.9 kPa, IQR 6.1–18.8 vs. 6.3 kPa, IQR 5.1–8.4; $p <0.001$). In multivariate logistic regression, baseline liver stiffness (Odds Ratio \[OR] 1.09; 95% CI 1.03–1.13; $p <0.001$) and BMI (OR 0.88; 95% CI 0.78–0.98; $p = 0.019$) were independent predictors of the primary outcome. A liver stiffness value ≥20 kPa was 95% specific—but only 25% sensitive—for predicting adverse outcomes.
Conclusions: In patients who achieve HCV eradication, long-term complications are primarily extra-hepatic. Baseline liver stiffness—not CAP—is the strongest predictor of these outcomes.

HYPERTRIGLYCERIDEMIA-INDUCED PANCREATITIS: A CASE REPORT

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Background: Acute pancreatitis induced by severe hypertriglyceridemia, associated with diabetic ketoacidosis (DKA), represents a rare but serious clinical condition with a significantly elevated mortality rate. DKA can act as a triggering factor for severe hypertriglyceridemia through insulin resistance and insulin deficiency-mediated lipolysis, leading to a further increase in blood triglyceride levels. Hypertriglyceridemia accounts for 2%-4% of acute pancreatitis cases. Triglyceride (TG) levels exceeding 1,000 mg/dL are more strongly associated with the development of acute pancreatitis. The combination of DKA, hypertriglyceridemia, and acute pancreatitis is rare but associated with worse clinical outcomes. A study involving over 2.8 million patients found that those presenting with this triad had significantly higher in-hospital mortality (adjusted odds ratio [aOR] 2.8), higher incidence of acute kidney injury (aOR 4.1), systemic inflammatory response syndrome (aOR 4.9), and

shock (aOR 4.3), compared to patients with acute pancreatitis alone. The present clinical case explores the diagnostic and therapeutic course of a patient with this rare but critical pathological association.
Case: A 30-year-old male with a family history of dyslipidemia presented to the emergency department with chest stabbing pain exacerbated by palpation. His pain had a band-like distribution, radiating to the hypochondria. He also reported a single episode of vomiting. He denied palpitations, dyspnea, or syncope. Emergency evaluation revealed elevated inflammatory markers WBC up to 17,000/µL (normal: ~4,000–10,000/µL); C-Reactive Protein up to 339 mg/L (normal: <5 mg/L); elevated lipase 1,400U/L (normal: ~10–140 U/L, severe hypertriglyceridemia up to 8,800 mg/dL (normal: <150 mg/dL), total cholesterol 1,386 mg/dL(normal: <200 mg/dL), and normal renal and liver function. An abdominal CT scan showed findings consistent with edematous pancreatitis. The patient subsequently underwent two sessions of plasma exchange (PEX) according to ASFA 2023 guidelines (indication: TG <1,000 mg/dL). After PEX, TG levels were reduced to 400 mg/dL, and pharmacologic treatment with a fibrate, omega-3, and a statin was started. Concurrently, the patient developed diabetic ketoacidosis in the context of newly diagnosed diabetes mellitus, prompting insulin pump therapy. C-peptide and specific autoantibody testing did not support a diagnosis of type 1 diabetes. During hospitalization, a follow-up CT scan showed damage progression with abdominal fluid collection extending to the left iliac fossa. The case was discussed with surgeons, who did not recommend surgical intervention. Further discussion with endocrinologists and lipid disorder specialists led to the suspicion of multifactorial hyperlipidemia unmasked by glycemic decompensation in newly diagnosed diabetes mellitus. Lipid-lowering therapy with ezetimibe was confirmed.
Discussion: Simultaneous acute pancreatitis, severe hypertriglyceridemia, and diabetic ketoacidosis (DKA) represents a rare clinical entity, associated with a significantly worse prognosis compared to acute pancreatitis alone. This case highlights the importance of considering the pathogenic interplay between DKA and hypertriglyceridemia, where insulin deficiency and resistance contribute to a massive increase in TG, promoting the onset of pancreatitis. It is well documented that TG levels >1,000 mg/dL, and especially >2,000 mg/dL, constitute a significant risk factor for acute pancreatitis. This patient presented with exceptionally high values (TG >8,800 mg/dL), placing him at very high risk for systemic complications, as indeed emerged during his clinical course.Early treatment with plasma exchange (PEX), in accordance with ASFA guidelines, proved effective in rapidly reducing TG levels, allowing the transition to conventional pharmacologic therapy. This therapeutic approach likely limited the extent of pancreatic damage and prevented potentially fatal complications. The subsequent diagnosis of new-onset diabetes mellitus in the absence of autoantibodies but with preserved C-peptide levels pointed toward a form of type 2 diabetes with ketoacidosis at onset, often observed in young patients with marked β-cell dysfunction of multifactorial origin.
Conclusion: The triad of diabetic ketoacidosis, severe hypertriglyceridemia, and acute pancreatitis represents a rare but formidable metabolic emergency, whose management requires prompt recognition and targeted, multidisciplinary therapeutic intervention. This case emphasizes how early use of plasma exchange, in combination with appropriate insulin and lipid-lowering therapy, can lead to rapid clinical and metabolic stabilization, improving patient outcomes. It is essential to maintain a high index of suspicion in cases of abdominal pain associated with marked hypertriglyceridemia and glycemic alterations to prevent the severe systemic complications linked to this condition. An integrated approach involving internists, endocrinologists, lipid specialists, and interventional radiologists is crucial for effective and personalized management.

ASSESSMENT OF NUTRITIONAL STATUS AND EATING HABITS IN OLDER HOSPITALIZED PATIENTS IN THE FRAME OF THE REPOSI REGISTER

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Background: A healthy and balanced diet plays a crucial role in ensuring good health for subjects at all ages. In particular, adherence to the Mediterranean Diet (rich in plant-based foods, low in red and processed meat and saturated fats) brings numerous health benefits, such as to reduced risk of non-communicable diseases (cardiovascular diseases, diabetes and some types of cancer), to preserve cognitive functions, finally ensuring healthy aging [1-2]. In particular, a series of physiological changes may occur in older subjects, such as, for example, the progressive reduction of basal metabolism, alteration of taste and smell, trouble in chewing and swallowing, slowing of intestinal activity and reduction of absorption at intestinal level, poor appetite and thirst which can lead to a change in eating habits and to a progressive imbalance of nutrients and serious deficiencies of minerals and vitamins, i.e. malnutrition. Malnutrition (especially protein-energy undernutrition) is one of the most typical conditions that negatively affects the health and wellbeing of these patients. This condition leads to a reduction in immune response, facilitates the onset of complications, reduces muscle mass and strength (i.e. sarcopenia), worsens physical performance and limits the activities of daily living, and increases the risk of fractures and bedsores. Nevertheless, this condition has long been unrecognized as a health risk and often overlooked. Various studies have shown that up to 60/70% of malnutrition cases are not diagnosed at hospital admission.
Aim: Based on this background and considering the rapid world population aging, with people aged over 60 expected to reach 2 billion by 2050, we proposed to start an investigation in the context of the REPOSI register, that will allow to evaluate the nutritional profile and eating habits of hospitalized older patients in order to assess possible associations with different clinical outcomes.
Methods: The REPOSI register, launched in 2008, is a collaborative study between the Italian Society of Internal Medicine (SIMI), the IRCCS Foundation Cà Granda Ospedale Maggiore Policlinico di Milano and the Mario Negri Institute for Pharmacological Research IRCCS, with the aim of activating a network of internal medicine and geriatric wards throughout Italy, for the recruitment, the monitoring and the study of hospitalized older patients aged 65 years or more. The final goal was to investigate the prevalence of multimorbidity, polypharmacy and their clinical determinants and outcomes. To date, the register collected data for about 11,000 patients within 105 active recruiting wards.
In order to evaluate the patient's eating habits, a semi-quantitative food frequency questionnaire (FFQ) was included in the case report form, which requires indicating the frequency of consumption and the portion usually consumed of about 60 foods and recipes typically included in the Italian diet, grouped into 7 chapters (first course and cereals, second course – meat, fish, cheese and eggs, vegetables and legumes, fruits, milk and dairy products, bread and backed products, sweets and snacks). The use of seasonings and salt consumption were also investigated. The proposed FFQ is an adaptation of a medium-short questionnaire validated in an Italian adult and elderly population, with the addition of some specific items [3-5]. Several figures of dishes have been added to the questionnaire to facilitate the recognition of portions and facilitate self-compilation. A section related to the evaluation of the nutritional status of the subject to allow a possible diagnosis of malnutrition has also been added. These questions, with other information collected in the case report form (CRF), will allow us to fill up the Mini Nutritional Assessment (MNA), a validated and most used tool in geriatrics for the assessment of malnutrition [6].
Preliminary results: To date, out 67 the active recruiting centers, 38 have started to enter data on the patient's eating habits. All in all, we collected data for 176 subjects: 99 were males (56.3%) with a mean age of 80 years (std.dev. 7.9). Out of 152 patients assessable, 13 (8.6%) were underweight (BMI < 20), and 63 (41.7%) were normal weight. Near 28% of patients reported unintentional weight loss, and more than 40% a loss of appetite within the last months.
Conclusion: During the congress, we will show the design of this new collection of data on nutritional status and dietary habits and in the frame of the REPOSI register and the preliminary results updated to date.

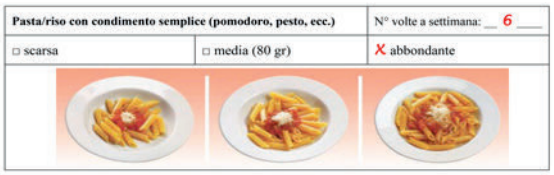

Figure 1. Graphical example of a question included in the case report form on patients' eating habits
The example indicates that the consumption of pasta or rice with simple sauce (tomato, pesto, ...) is 6 servings per week and that the portion usually consumed is large (about 110 g)

A CASE OF PNEUMOMEDIASTINUM

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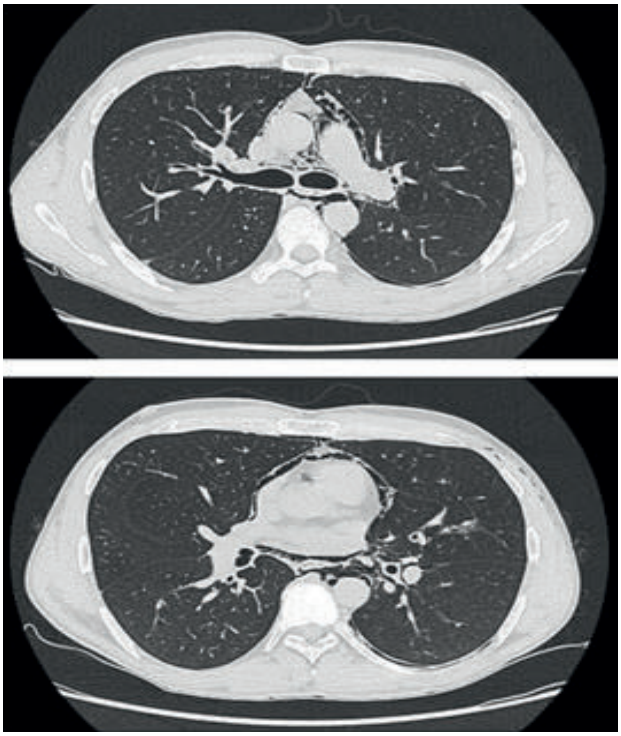
We present the case of a 37-year-old Italian male patient who came to the attention of our Emergency Department (ED) for subcutaneous emphysema on the left side of the neck and retrosternal pain since the morning. He also reported pharyngodynia and rhinitis in the previous days, persistent cough the previous day and fever since the same day. His medical history included

asthma and tobacco and marijuana smoking.
In the ED he was eupneic and had normal vital signs. The electrocardiogram showed sinus rhythm 80 bpm. Arterial blood gas analysis revealed good respiratory exchanges in ambient air (pO2 86 mmHg, pCO2 35 mmHg). Blood tests showed leukocytosis and mild elevation of CRP (WBC 16.000/mm3, CRP 1,4 mg/dL) and normal troponin. SARS COV-2 antigen swab was negative. Chest X-ray showed subcutaneous emphysema on the left in the supraclavicular and latero-cervical areas. Chest CT scan confirmed the presence of a large amount of pneumomediastinum and subcutaneous emphysema along the thickness of the left chest wall in the subpectoral area, in the axillary cavity, in the thickness of the intercostal muscles and paravertebral lodges and at the root of the neck, furthermore it showed the presence of pulmonary interstitial emphysema along the bronchovascular structures and in subpleural along the profiles of the left lower lobe.
The patient refused hospitalization and signed a voluntary discharge.
Pneumomediastinum mainly affects young males with respiratory pathologies. The mechanism involves an increase in intra-alveolar pressure, which causes the rupture of the alveoli.
Among the risk factors and triggers there are: tobacco smoke, inhalation of drugs including marijuana, lung diseases such as asthma, coughing fits.
In most cases it resolves spontaneously, thanks to the slow reabsorption of air in the cavity.
Oxygen therapy can be useful.
In the case of extensive subcutaneous emphysema, surgical decompression can be performed, while if there is an associated pneumothorax, the positioning of a chest drain may be necessary.



A SPECIAL CASE OF ISCHAEMIC STROKE: THE CAROTID WEB

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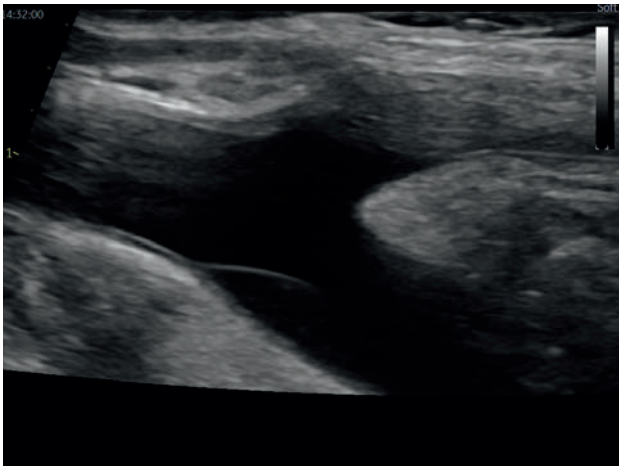
Background: A carotid web (CaWeb) is a rare, atypical variant of fibromuscular dysplasia (FMD) characterized by a fibrous intimal flap originating from the wall of the carotid bulb and projecting into the arterial lumen. This anatomical entity can cause altered blood flow and stasis thereby promoting thrombogenesis. Latest reports and observational studies documented strong associations between CaWebs and recurrent TIA or severe strokes of unknown etiology, especially in proximal anterior arterial–arterial embolic stroke, with a prevalence between young woman with few traditional cardiovascular risk factors. The noninvasive gold standard imaging technique for CaWeb diagnosis is currently computed tomography angiography (CTA) followed by duplex ultrasound (DUS) and magnetic resonance angiography (MRA). Before 2021 there aren't established guidelines on the management of symptomatic patients with CaWebs, although the current consensus to the medical treatment is still discordant and involves on one hand pharmacological treatment with mono or dual-antiplatelet therapy and in the other hand surgical treatment with carotid stenting or carotid endoarterectomy (CEA), in patient's refractory to medical management.
Case description: A 63-year-old woman with history of hypertension and a previous right atrial myxoma treated 2-years prior with mass removal surgery, shows up at the hospital for sudden symptoms of left facial paresthesia, right retrobulbar pain, clumsiness in the upper limbs and confusion. The CT cranial scan showed an ischemic right area cortico-subcortical temporo-parietal. The following CT angiography and MRI confirmed an occlusion of the right middle cerebral artery's M2 branch. As a collateral finding on CT angiogram, an opacification defect was reported at right carotid bulbs, suspicious for CaWeb. The ischemic event was classified as minor stroke (NHISS=3) therefore dual antiplatelet therapy was started. In view of the angiographic finding, a duplex ultrasound of supre-aortic trunks was performed, which confirmed the presence of a thin septum attached to the posterior wall of the right carotid bulb whose projecting towards the lumen, compatible with carotid web and potentially be the etiology of the event. Meanwhile, other causes of stroke were ruled out by transcranial echocolordoppler which excluded the possibility of a patent foramen ovale (PFO) and an extensive electrocardiographic study excluded arrhythmic events. Lastly a transthoracic echocardiogram and the subsequent transesophageal echocolordoppler were performed, which reported the presence of mobile material at the left atrial appendage, of doubtful interpretation between myxoma recurrence or thrombotic material adhered to the Teflon residues left from the myxoma operation, positioned to repair a wound that had arisen as a complication of the procedure. Given the new findings, and since a cardio-embolic stroke could not be ruled out at that point, warfarin therapy was promptly undertaken, and the patient was transferred to a surgical setting for subsequent removal of the mass and histological examination of it.
Discussions: This clinical case confronted us with two possible causes of large-vessel ischemic stroke, both of which were possible, but which were ultimately given as large-vessel cardio-embolic stroke, considering the higher probability associated to it. However, the possibility of an event related to CaWeb, even if rare, shouldn't completely be ruled out since it accounts for about 13% of cryptogenic stroke in young patients, with a 2-year recurrence rate of 20% especially in patients with specific anatomical features of the CaWeb. Carotid webs are not so rare and should always be excluded in all cases of cryptogenic ischemic events, especially in young female patients without other relevant risk factors, even if diagnosis of CaWeb remains one of exclusion in the absence of other more frequent causes of stroke.



LEAN SUBJECTS CONSUME MORE EXTRA-VIRGIN OLIVE OIL THAN ABDOMINAL OBESE: INSIGHTS FROM THE CHRONO MED DIET SCORE COHORT

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Background: Abdominal obesity is a significant global health challenge, acting as a key driver for metabolic syndrome, cardiovascular disease, type 2 diabetes and cancer (1). Lifestyle interventions, particularly dietary changes, are paramount. The Mediterranean Diet (MedDiet), recognized for its health

benefits, features Extra-Virgin Olive Oil (EVOO) as its principal fat source, providing abundant monounsaturated fatty acids and bioactive polyphenols. We previously validated the Chrono Med Diet Score (CMDS), integrating dietary quality with chrono-nutritional principles, and linked it to abdominal adiposity and cardiometabolic risk (2,3). While EVOO is crucial to the MedDiet, its specific contribution—whether its benefits are solely mediated through overall diet quality or if it exerts independent effects—remains incompletely understood. We aimed to dissect this relationship by investigating associations between habitual EVOO intake frequency, CMDS adherence, and key anthropometric measures, explicitly testing the role of EVOO as both a mediator and a standalone factor influencing WC and assessing its link to abdominal obesity risk in a large population sample.

Methods: We analyzed data from 16,273 adults (46.5% male; 94.1% European origin) who completed the CMDS-based survey (www.chronomeddiet.org) since April 2023. Anonymous, self-reported data included age, sex, height, weight, waist circumference (WC), and dietary/lifestyle parameters comprising the CMDS. Body Mass Index (BMI) was then automatically calculated based on patient's' inputs. Habitual EVOO intake was assessed based on the frequency of consuming ~2 tablespoons (25g)/day and categorized as: sporadic (<3 days/week), frequent (≥3 but <6 days/week), or regular (≥6 days/week). Abdominal obesity was defined using the IDF 2006 criteria specific for Europids. Statistical analyses included Student's t-tests, ANOVA with Bonferroni post-hoc tests, mediation analysis, and multivariable logistic regression to estimate Odds Ratios (OR).

Results: Baseline characteristics showed significant sex differences in age, BMI, WC, and CMDS scores. Stratifying by EVOO intake revealed that the regular group, despite being significantly older (55.9±8.1) than sporadic (53.9±7.1) and frequent (54.1±7.7) groups (p=0.0019), exhibited significantly more favorable anthropometrics. Compared to sporadic intake, regular intake was associated with significantly lower mean BMI (24.7±3.0 vs 26.6±2.9, p<0.001) and mean WC (89.1±6.7 vs 99.4±9.1, p<0.0001). Nonetheless, regular intake was also linked to significantly higher CMDS adherence (13.9±2.1 vs. 7.5±2.1 sporadic, p<0.0001). These findings remained highly significant when analyzed separately for males (p<0.0001) and females (p<0.0001). The mediation analysis (Table 1) demonstrated a significant indirect effect of EVOO on WC operating through CMDS (β= -0.83, p<0.0001), which accounted for 61.98% of the total association. Crucially, a significant direct effect of EVOO intake on lower WC persisted after controlling for CMDS (β= -0.59, p<0.0001), indicating a standalone association. Multivariable logistic regression showed that, compared to Regular intake, non-regular (sporadic + frequent combined) olive oil consumption was associated with substantially higher odds of having abdominal obesity (OR 5.1, 95% CI: 3.3–6.8, p<0.0001).

Clinical variable	EVOO Sporadic Intake	EVOO Frequent Intake	EVOO Regular Intake	p-value
N (M:F)	3,871 (2,112M:1,759F)	7,791 (3,810M:3,981F)	4,611 (1,639M:2,972F)	
Age (years)				
Mean	53.9±7.1[c]	54.1±7.7[c]	55.9±8.1[a,b]	0.0019**
Males	55.1±7.2[c]	53.1±5.9[c]	56.8±8.9[a,b]	0.0381*
Females	52.4±8.4	54.6±6.5	54.9±7.3	0.0822
BMI (Kg/m²)				
Mean	26.6±2.9[c]	25.9±2.1[c]	24.7±3.0[a,b]	0.0081**
Males	26.9±2.1[b,c]	26.0±2.5 [a,c]	25.0±2.1[a,b]	0.0029**
Females	26.1±2.8[b,c]	25.5±2.7[a,c]	24.2±2.7[a,b]	0.0001***
WC (cm)				
Mean	99.4±9.1[b,c]	96.5±8.3[a,c]	89.1±6.7[a,b]	0.0001***
Males	103.1±7.8[b,c]	99.4±9.3[a,c]	93.0±3.1[a,b]	<0.0001***
Females	94.3±6.3[b,c]	89.4±7.3[a,c]	84.2±5.5[a,b]	<0.0001***

Conclusion: In this substantial cohort, regular EVOO consumption is significantly associated with improved anthropometric indices and greater adherence to a healthy chrono-Mediterranean dietary pattern. The study supports a dual role for EVOO in metabolic health: it acts as a significant mediator, explaining a large part of the beneficial association between MedDiet and WC, while also demonstrating a significant, independent beneficial association with abdominal obesity itself. Indeed, non-regular EVOO intake represents a significant risk factor for abdominal adiposity, independent of overall diet quality of adherence.

References:

1. Crudele L, Piccinin E, Moschetta A. Visceral Adiposity and Cancer: Role in Pathogenesis and Prognosis. Nutrients. 2021 Jun 19;13(6):2101.
2. De Matteis C, Crudele L, Battaglia S, Loconte T, Rotondo A, Ferrulli R, et al. Identification of a Novel Score for Adherence to the Mediterranean Diet That Is Inversely Associated with Visceral Adiposity and Cardiovascular Risk: The Chrono Med Diet Score (CMDS). Nutrients. 2023 Apr 15;15(8):1910.
3. De Matteis C, Crudele L, Gadaleta RM, Di Buduo E, Novielli F, Petruzzelli S, et al. Low Adherence to Mediterranean Diet Characterizes Metabolic Patients with Gastrointestinal Cancer. Nutrients. 2024 Feb 24;16(5):630.

ALLOPURINOL-INDUCED TOXIC EPIDERMAL NECROLYSIS IN AN ELDERLY PATIENT: A DIAGNOSTIC CHALLENGE

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Background: Toxic epidermal necrolysis (TEN) is a severe cutaneous adverse reaction characterized by consisting of necrosis and detachment of at least 30% of the total body surface area [1]. It is most commonly triggered by medications, particularly in patients with risk factors such as malignancy or autoimmune diseases [2]. In elderly patients, the diagnosis of TEN is often more challenging due to the presence of multiple confounding factors, and the prognosis tends to be worse compared to younger individuals [3]

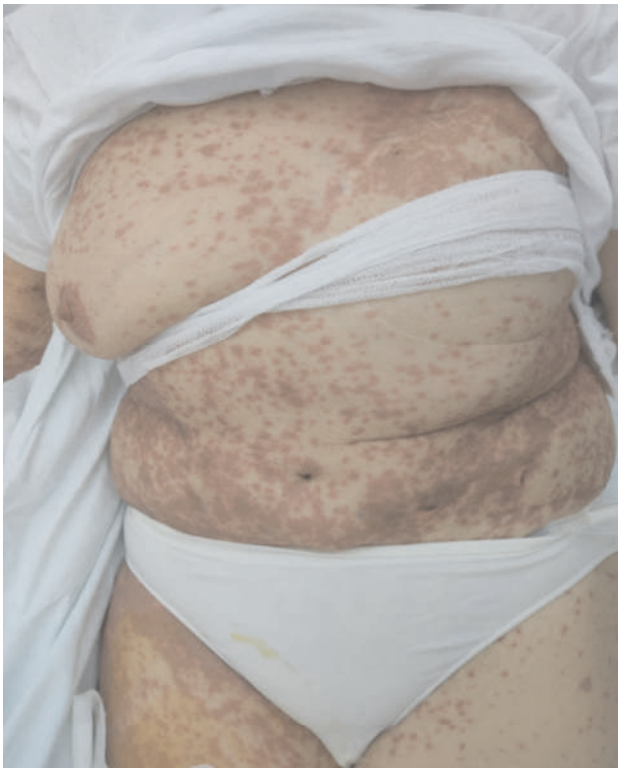
Case presentation: An 82-year-old woman with past history of chronic ischemic cardiopathy, hypertension, left breast cancer (treated with ipsilateral mastectomy followed by chemotherapy) was admitted to our care. Her chronic medication included lysine acetylsalicylate, bisoprolol, delapril and indapamide. She came to our observation when, during a rehabilitation cycle occuring after fractures of the right femur and distal humerus, reporting the onset of fever, keratoconjunctivitis and erythematous-papular lesions that initially appeared on the abdomen and subsequentially across the body. The patient denied any pruritus. Initial laboratory tests showed mild anemia (Hb 10.8 gr/dl), normal white blood cell count, elevated C-reactive protein (142.8 mg/L) and negative procalcitonin. Suspecting idiopathic purpuric vasculitis, treatment with prednisone (12.5 mg bid, prescribed in the emergency department) was initiated. A subsequent physical examination performed two days later revealed, in addition red macules and bilateral filamentous keratoconjunctivitis, the presence of bollous lesions on the thorax, buttocks, and thighs, with areas of skin detachment and oral erosions.

A more detailed history revealed that approximately two weeks prior to admission, the patient had been prescribed allopurinol for newly diagnosed hyperuricemia. Toxic epidermal necrolysis secondary to allopurinol was suspected, and corticosteroid therapy was escalated to methylprednisolone 40 mg bid. Intravenous fluid were administrated. Due to persistent fever, piperacillin/tazobactam and fluconazole were started. An incisional biopsy was performed and showed "features of vacuolar degeneration of the basal layer of the epidermis", findings compatible with TEN. A plastic surgical consultation recommended wound care with petrolatum gauze, sterile dressing, and transfer to a specialized Burn Center for further management. The SCORTEN score for mortality risk was 3 characterized by an associated mortality rate of 35.3%. For ocular hyperemia and filamentous keratitis, an antibiotic ointment and lubricating eyes drops were prescribed. During hospitalization, the clinical course was complicated by the onset of fever and the isolation of Candida spp. in blood cultures, which led to the replacement of fluconazole with caspofungin highlighting the frequent occurrence of infectious complications in TEN patients. After few days later, the patient was transferred to the Burn Center.

Conclusion: Toxic epidermal necrolysis remains a rare but life-threatening condition, particularly in elderly and comorbid patients, where diagnosis can be delayed due to atypical presentations and confounding factors. This case highlights the importance of a thorough drug history and a high index of suspicion when facing rapidly evolving skin lesions. Early recognition and appropriate management including prompt discontinuation of the offending drug and supportive care are crucial to reduce mortality and prevent severe complications. Reporting such cases reinforces clinical awareness and may help avoid diagnostic delays in similarly complex scenarios.

References

1) Hasegawa A, Abe R. Recent advances in managing and understanding Stevens-Johnson syndrome and toxic epidermal necrolysis. F1000Res. 2020 Jun 16;9:F1000 Faculty Rev-612. doi: 10.12688/f1000research.24748.1. PMID: 32595945; PMCID: PMC7308994.
2) Noe MH, Micheletti RG. Diagnosis and management of Stevens-Johnson syndrome/toxic epidermal necrolysis. Clin Dermatol. 2020 Nov-Dec;38(6):607-612. doi: 10.1016/j.clindermatol.2020.06.016. Epub 2020 Jun 30. PMID: 33341195.
3) Honari S, Gibran NS, Heimbach DM, Gibbons J, Pharmd, Cain V, Engrav LH. Toxic epidermal necrolysis (TEN) in elderly patients. J Burn Care Rehabil. 2001 Mar-Apr;22(2):132-5. doi: 10.1097/00004630-200103000-00009. PMID: 11302601.



IgG4 RELATED AUTOIMMUNE PANCREATITIS: THE GREAT SIMULATOR. THE IMPORTANCE OF MULTIDISCIPLINARY DISCUSSION.

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Introduction: Autoimmune pancreatitis (AIP) is the specific type of chronic pancreatitis with an autoimmune background. Two subtypes of AIP have been identified so far: the "lymphoplasmacytic" type 1 variant and the "neutrophilic" type 2 variant. Type 1 represents the most common manifestation of IgG4-related disease, a fibro-inflammatory disorder characterized by elevated IgG4 levels in the serum and affected tissues; type 2 is a pancreas-specific disorder not associated with IgG4. The clinical presentation of type 1 and type 2 AIP is often undistinguishable and depends on the distribution and extent of the pancreatic gland involvement. AIP involving the pancreatic head or the entire gland, for instance, may lead to obstructive jaundice and abdominal pain, whereas involvement of the uncinate process may be incidentally discovered. Additional manifestations may include signs and symptoms of endocrine and exocrine pancreatic insufficiency, such as steatorrhea, postprandial bloating, increased stool frequency, and weight loss. Notably, type 1 AIP more commonly presents insidiously with a relapsing remitting course that ultimately leads to chronic pancreatitis. On the other hand, the onset of type 2 AIP is typically acute, yet without local or systemic complications The diagnosis of AIP is built upon clinical, laboratory, histological, and radiological features. Glucorticoids represent first-line therapy: prednisone starting dose ranges between 0.6 and 0.8 mg/kg for 2–4 weeks; GCs are then tapered by 5 mg every 2 weeks and discontinued after 3–6 months. Maintenance treatment is often employed in type 1 AIP because of the higher relapse rate compared to type 2 AIP. For patients who do not respond to glucorticoids, other immunomodulators (as azathioprine, mycophenolate mofetil, methotrexate, leflunomide, tacrolimus, ciclosporin A) or rituximab are an alternative.
Clinical case: A 70-years old woman was admitted to our hospital for confusional state and general decline; she also presented weight loss in the last month. Medical history was not reported. In the ER vital signs were regular, on examination the patient appeared alert, severely disoriented and malnourished; the physical examination did not show any pathological elements. A chest x-ray was normal; a cerebral CT showed liquoral spaces enlargement as atrophic signs on parietal zone and sylvian fissure; blood tests revealed mild anemia, no significant elevation of inflammation markers, normal liver and renal function. Upon admission, tests were conducted to investigate weight loss. Low levels of phosphorus, vitamin B12 and folic acid testified for malnourishment, oncomarkers were normal, IgA and IgG4 increased. Abdominal ultrasonography showed hypoechoic area with expansive and infiltrative aspect in body-tail pancreatic passage. A thorax-abdominal CT revealed acute pancreatitis, however radiological sign was not supported by the clinical presentation and by blood tests with normal levels of amylase and lipase. Magnetic risonance imaging confirmed solid and expansive lesion of 5 cm x 3 cm in body-tail pancreatic passage with characteristics compatible with primitive dysproliferative nature that caused infiltration of stomach lesser curvature. Esophagogastroduodenoscopy revealed ulcerated lesion of the gastric fundus suspected for heteroplasia, submitted to biopsy. Istologic examination showed inflammatory infiltrate with a rich lymphoplasmacytic and granulocytic eosinophilic component, edema and hyperemia; no atypical epithelial cells. The presence of IgG4 elements (about 12% of IgG plasmacells) suggests an autoimmune disease. Corticosteroid therapy was initiated with oral prednisone 1mg/kg/day for four weeks, followed by a gradual tapering until complete withdrawal of the drug. Her follow-up MRI, repeated after six weeks following the first one, revealed complete resolution of radiological sign with normal pancreatic parenchyma and no evidence of focal mass or lesion or progression; which was in favor of IgG4-related AIP.
Discussion and conclusion: This case report highlights how IgG4-related AIP can present itself with misleading pictures by simulating a neoplasm and how crucial collaboration is between clinician, radiologist and pathologist. Multidisciplinary dialogue is confirmed as a key element to avoid misdiagnosis and unnecessary invasive treatments.
References:
1. Lanzillotta M, et al. Update on Autoimmune Pancreatitis and IgG4-Related Disease. United European Gastroenterol J. 2025 Feb
2. Muhi A, et al. Mass-forming autoimmune pancreatitis and pancreatic carcinoma: differential diagnosis on the basis of computed tomography and magnetic resonance cholangiopancreatography, and diffusion-weighted imaging findings. J Magn Reson Imaging. 2012 Apr.

MUSCLE MASS ASSESSED BY RECTUS FEMORIS ULTRASOUND PREDICTS CLINICAL OUTCOMES IN CIRRHOSIS: A STEP BEYOND THE "BLACK-AND-WHITE" CLASSIFICATION OF SARCOPENIA

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Background: and aims: Sarcopenia is common in patients with cirrhosis and is strongly linked to adverse clinical outcomes. Traditionally, sarcopenia is viewed as a binary condition - either present or absent. However, the degree of muscle loss may significantly influence clinical outcomes, highlighting the need to consider muscle mass as a continuous variable rather than a dichotomous one. Despite this, few studies have yet evaluated muscle loss in a linear context. The

ultrasound measurement of rectus femoris cross-sectional area (RF-CSA) has demonstrated excellent accuracy in assessing sarcopenia in patients with cirrhosis. This study aimed to evaluate: (a) the prognostic significance of the RF-CSA in patients with cirrhosis hospitalized for an acute decompensation (AD) of the disease.
Methods: Thigh ultrasound was performed at bedside in 203 consecutive patients hospitalized for an AD of cirrhosis. RF-CSA was measured at two-thirds of the distance from the anterior superior iliac spine to the superior patellar border; three measurements were collected, and the mean value was calculated. RF-CSA was considered as a continuous variable. Patients were followed up until death, liver transplant or 90 days and data about complications during hospitalization and mortality were recorded.
Results: Among hospitalized patients (mean age: 64 ± 10 years, median MELD 17), median RF-CSA was 3.09 cm2. During hospitalization, 32 patients (16%) died. RF-CSA was significantly lower in patients who died compared to survivors (2.64 cm2 vs 3.20 cm2; p=0.005). In multivariable analysis (adjusted for age, gender, MELD and infections) RF-CSA was an independent predictor of 90-day mortality (sHR 0.57; p=0.006), along with MELD (sHR 1.11; p<0.001). Stratification of RF-CSA in tertiles demonstrated that greater severity of muscle loss was associated with a higher cumulative incidence of 90-day mortality (lower tertile 39% vs intermediate 26% vs higher 12%; p=0.001; Figure A). Additionally, RF-CSA was an independent predictor of in-hospital complications, including sepsis (OR 0.59; p=0.001), shock (OR 0.60; p=0.005), acute kidney injury (OR 0.75; p=0.019) and hepatic encephalopathy (OR 0.78; p=0.023).
Conclusions: Sarcopenia represents a spectrum, with greater muscle loss leading to worse outcomes and higher short- and mid-term mortality. Ultrasound assessment can aid in risk stratification, enabling targeted interventions to slow or prevent muscle loss and potentially improve clinical outcomes.

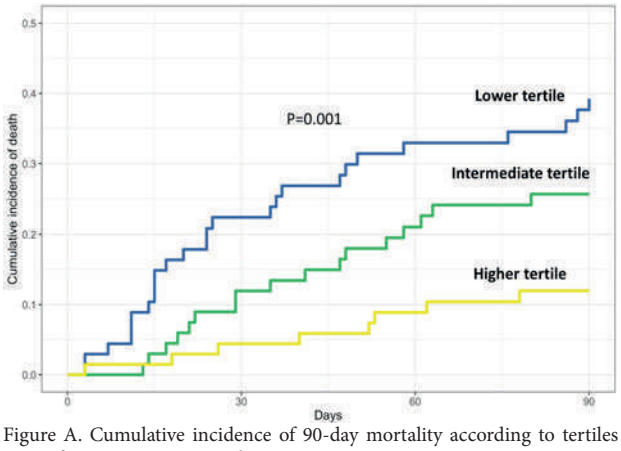

Figure A. Cumulative incidence of 90-day mortality according to tertiles of rectus femoris cross sectional area

AUTOIMMUNE HAEMOLYTIC ANAEMIA IN IGG4 RELATED DISEASE: A CASE REPORT

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IgG4-Related Disease (IgG4-RD) is a syndrome characterized by elevated serum IgG4 levels and tissue infiltration by IgG4-positive plasma cells. In the current literature, six cases are reported to be associated with haemolytic anaemia [1]. Although both IgG4-RD and haemolytic anaemia are related to dysimmune processes, their possible correlation is yet to be determined.
We present the case of a 78-year-old male patient with a known history of IgG4-RD, presenting with haemolytic anaemia. His past medical history included type 2 diabetes, hypertension, dyslipidaemia, and benign prostatic hyperplasia. The initial diagnosis of IgG4-RD was made in 2021 following the detection of pancreatic gland swelling and a serum IgG4 level of 6904 mg/dL. In his clinical history, the manifestations of IgG4-RD primarily involved the pancreas and salivary glands, with minor involvement of the lungs, kidneys, and gastric antrum. These manifestations were treated with steroid therapy (prednisone ranging from 5 to 25 mg) and a single dose of intravenous rituximab (1 g) in June 2023, with therapeutic success.
In January 2025, he was admitted to our department with anaemia (haemoglobin 75 g/L) and elevated inflammatory markers, presenting with asthenia, jaundice (total bilirubin: 1.38 mg/dL), abdominal pain, and undetectable haptoglobin levels. At the moment of hospitalization, he was not undergoing immunosuppressive treatment. Cytomegalovirus and Epstein-Barr Virus DNA sequences were negative, thus, excluding a parainfectious aetiology. The patient underwent an esophagogastroduodenoscopy to exclude gastrointestinal bleeding. A bone marrow biopsy was performed to rule out an underlying lymphoproliferative disorder, revealing instead mild dyshaematopoiesis and hyperplasia. Direct and indirect Coombs tests confirmed the presence of warm antibodies, while cryoagglutinin testing resulted negative. Treatment was initiated with methylprednisolone (0.5 mg/kg/day) and a short course of intravenous immunoglobulin (1 g/kg over two days), alongside haemoactive vitamins and iron supplementation, leading to a steady and gradual reduction of haemolysis markers and a progressive haemoglobin increase.
He was discharged on prednisone (75 mg/day), which was tapered during haemato-immunological follow-ups. Moreover, haemoglobin level at the last follow-up was 102 g/L, showing adequate response to immunosuppressive treatments.
Haemolytic anaemia is not a well-documented manifestation of IgG4-RD. However, in this case, thorough investigations ruled out other causes of anaemia, including infectious triggers and underlying lymphoproliferative disorders. Our patient matches the general features of the six cases reported in literature [Table 1]. Another similarity among these cases was the successful response to immunosuppressive treatment, suggesting an autoimmune aetiology. Furthermore, no other case presenting with this specific co-presentation were found among the other IgG4-RD cases in our Centre cohort.

Case	Age/Gender	Phenotype [3]	Serum IgG4	Course of Treatment
1	52/M	Pancreato-biliary	1920	Steroid + CTX
2	70/M	Pancreato-biliary	2965	Steroid
3	73/M	Pancreato-biliary	1800	Steroid
4	67/M	Systemic	3421	Steroid
5	60's/F	Retroperitoneal	4604	Steroid
6	73/F	Systemic	1889	Steroid
Current Case	78/M	Systemic	6904	Steroid + Rituximab

Population characteristics, cases 1 to 6 from reference [1], classified according to reference [3].

Table 1. Population characteristics, cases 1 to 6 from reference [1], classified according to reference [3]. The subclasses of IgG known to be correlated to autoimmune haemolytic anaemia are IgG1 and partly IgG3, while IgG2 and IgG4 are not yet linked to its pathogenesis [2], serological laboratory analysis of these patients affected by IgG4-RD presenting with active haemolytic anaemia, possibly not undergoing any immunosuppressive treatment, is needed to better address the potential role of IgG4 in this process. Both IgG4-RD and autoimmune haemolytic anaemia are immune-mediated pathologies, with only six cases reporting their association [1]. Further studies are needed to understand the potential role of IgG4-mediated mechanisms in the correlation between these conditions.

[1] IgG4-related Lung Disease Associated with Autoimmune Hemolytic Anemia: A Case Report and a Literature Review. Shingo N, Kazuhiro Y, et al.
[2] First case of IgG4-related sclerosing cholangitis associated with autoimmune hemolytic anemia. Masutani H, Okuwaki K, Kida M, et al.
[3] Clinical phenotypes of IgG4-related disease reflect different prognostic outcomes. Lanzillotta M, Campochiaro C, Mancuso G, Ramirez GA, Capurso G, Dagna L, Della Torre E, et al.

MARKED HYPOTENSION, BLEEDING, AND A HIDDEN ENEMY: A CASE OF AL AMYLOIDOSIS

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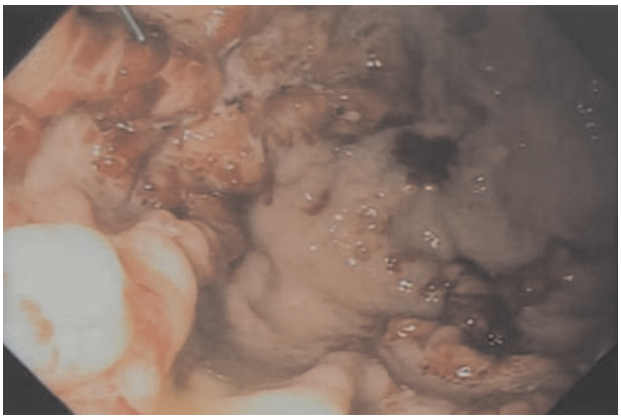
Introduction: AL (light-chain) amyloidosis is a systemic disorder caused by

tissue deposition of misfolded immunoglobulin light chains, typically associated with plasma cell dyscrasias such as multiple myeloma. Clinical manifestations are highly heterogeneous, reflecting the organs involved. [1] Cardiac and gastrointestinal infiltration can mimic more common conditions such as heart failure or malignancy, making early recognition a clinical challenge.
Case presentation: A 72-year-old man with paroxysmal atrial fibrillation, previous percutaneous coronary intervention for acute coronary syndrome, and a history of gastric ulcer presented with weight loss (−8 kg in 3 months), progressive fatigue, exertional dyspnea, and episodes of bright red rectal bleeding. His chronic therapy included amiodarone, apixaban, and pantoprazole. On admission, he showed marked hypotension (85/50 mmHg), bilateral leg edema, and absent breath sounds at the lung bases. Chest X-ray revealed bilateral pleural effusions. ECG showed low QRS voltages; serial troponins were constantly >100 ng/L. NT-proBNP was markedly elevated (8430 pg/mL). Laboratory tests revealed microcytic hypochromic anemia (Hb 9.4 g/dL, MCV 78.3 fL), mild elevation of CA 125 (53.2 U/mL) and beta-2 microglobulin (4.3 mg/L). Serum protein electrophoresis showed a subtle gamma peak with hypogammaglobulinemia. Fecal occult blood test was positive. Colonoscopy was negative, but upper GI endoscopy revealed bluish submucosal gastric lesions and a bleeding ulcer. Biopsies showed Congo Red-positive amyloid deposits. CT scan showed diffuse thickening of the gastric wall. A repeated echocardiogram revealed interventricular septal thickening (>19 mm) and a restrictive filling pattern. Serum free light chain analysis showed markedly increased lambda chains (5779 mg/L) with a suppressed kappa/lambda ratio (0.005). Bone marrow biopsy confirmed a diagnosis of lambda light-chain multiple myeloma. A bone scintigraphy was negative, consistent with AL rather than ATTR amyloidosis.
Conclusion: This case exemplifies the diagnostic complexity of AL amyloidosis and highlights the need for heightened clinical suspicion in cases of unexplained hypotension, anemia, and multiorgan dysfunction. Subtle ECG and echocardiographic findings, protein abnormalities, and gastrointestinal lesions may be the only clues. Congo Red staining remains the histopathological gold standard, while serum free light chains provide a rapid, sensitive diagnostic tool. Early diagnosis is critical to initiate targeted therapy and improve outcomes. Internists must remain vigilant when facing nonspecific systemic presentations, as prompt recognition of AL amyloidosis may change the clinical trajectory and survival of the patient.
Reference: 1) Mauermann ML, Clarke JO, Litchy WJ, Obici L, Lousada I, Gertz MA; Amyloidosis Forum Working Group Participants. Peripheral Nervous, Hepatic, and Gastrointestinal Endpoints for AL Amyloidosis Clinical Trials: Report from the Amyloidosis Forum Multi-organ System Working Group. Adv Ther. 2023 Nov;40(11):4695-4710. doi: 10.1007/s12325-023-02637-4. Epub 2023 Sep 2. PMID: 37658177; PMCID: PMC10567953.



EPIPLOIC APPENDAGITIS MIMICKING DIVERTICULITIS IN A MIDDLE-AGED ASIAN FEMALE: DIAGNOSTIC PITFALLS AND THE CRUCIAL ROLE OF CT IMAGING

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ObjectiveTo report a rare case of epiploic appendagitis in an adult female patient, a condition predominantly affecting males, and to highlight the diagnostic challenges posed by its non-specific clinical presentation.
Case presentation: A 53-year-old Asian woman presented to the Emergency Department complaining of acute abdominal pain localized to the left lower quadrant, persisting for several days. The pain was constant, non-radiating, and not associated with fever, nausea, vomiting, or altered bowel habits. On physical examination, the abdomen was soft, with localized tenderness in the left lower quadrant but without signs of peritonism. Laboratory investigations, including complete blood count and inflammatory markers, were within normal ranges or mildly altered, offering limited diagnostic clarity.Given the clinical suspicion of acute diverticulitis, a contrast-enhanced abdominal CT scan was promptly performed. The imaging revealed a well-circumscribed, oval-shaped lesion of fat attenuation, surrounded by pericolonic fat stranding adjacent to the sigmoid colon—findings pathognomonic of epiploic appendagitis. No evidence of diverticular disease or other intra-abdominal pathology was noted.
Results: Based on the imaging findings and absence of systemic signs of infection, a diagnosis of primary epiploic appendagitis was made. The patient was admitted for conservative management, which included bowel rest, intravenous hydration, analgesia, and a short course of empirical antibiotics due to the initial diagnostic uncertainty. Her symptoms gradually improved over the following 72 hours, and she was discharged in stable condition with full resolution of pain. No surgical intervention was required, and follow-up evaluation confirmed complete clinical recovery without recurrence.
Conclusion: Epiploic appendagitis is a rare, benign, and self-limiting inflammatory condition of the epiploic appendages, often underdiagnosed due to its non-specific presentation and overlap with more common conditions such as diverticulitis and appendicitis. Although it typically affects middle-aged men, this case highlights its occurrence in an adult female, emphasizing the need for clinicians to maintain a broad differential diagnosis when evaluating acute abdominal pain. Contrast-enhanced CT imaging remains the gold standard for diagnosis, enabling prompt recognition and appropriate non-surgical management. Greater awareness of this condition may lead to reduced misdiagnosis, avoidance of unnecessary interventions, and improved patient outcomes.

CLINICAL SIGNIFICANCE OF ANTI-SYNTHETASE ANTIBODIES (ASS) IN A COHORT OF PATIENTS WITH RHEUMATOID OR UNDIFFERENTIATED ARTHRITIS

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Introduzione: La sindrome anti-sintetasi (ASSD) è una rara malattia autoimmune, caratterizzata dalla presenza di autoanticorpi specifici contro le amminoacil-tRNA sintetasi. Il quadro clinico è estremamente eterogeneo e può includere miopatia, interstiziopatia polmonare (ILD), artrite, fenomeno di Raynaud, febbre e mani da meccanico. Tuttavia, tali manifestazioni non sono costanti e possono variare considerevolmente in termini di gravità e presentazione. Non è rara inoltre la sovrapposizione con altre condizioni autoimmuni, come l'artrite reumatoide (AR). Numerosi case report hanno descritto casi di ASSD associata a AR, spesso accompagnati da positività sierologica per fattore reumatoide (FR) e anticorpi anti-peptidi citrullinati ciclici (ACPA). In assenza di criteri diagnostici universalmente accettati, sono stati proposti recentemente i criteri classificativi EULAR/ACR CLASS, i cui risultati sono ancora in corso di pubblicazione, sebbene in parte siano stati anticipati.
Obiettivo: Questo progetto mira a individuare, in una popolazione di pazienti con diagnosi di AR o artrite indifferenziata in follow-up reumatologico, i casi di probabile o definita ASSD.
Metodi: Abbiamo analizzato una casistica di pazienti con diagnosi di artrite, in follow-up reumatologico, selezionando una sottopopolazione in base ai seguenti criteri:
Dopo aver selezionato i pazienti con tali caratteristiche, è stata eseguita la raccolta dati tramite:
Risultati: Dopo 4 mesi dall'inizio dello studio, su un database di 304 pazienti, sono stati individuati 174 pazienti che soddisfacevano i criteri di ingresso. Di questi 43 risultavano deceduti o persi al follow-up.
Dei restanti 131, 17 presentavano ILD, mentre 24 avevano in anamnesi il riscontro di una pregressa ANA positività. In nessun paziente era stato posto il sospetto di "mano del meccanico".
Ad aprile 2025, 33 pazienti sono stati sottoposti a prelievo per profilo anticorpale anti-ENA pannello miositi/sintetasi. In 3 casi il prelievo ha dato esito positivo: un paziente è risultato positivo per anti-Jo1 e anti-SSa/Ro52, il secondo per anti-PL12, la terza paziente presentava anticorpi anti-Ribosomial P0.
1° paziente: la diagnosi di AR era stata posta nel 2017, con sinovite erosiva delle piccole articolazioni associata a ILD e positività per FR. Il paziente in passato era stato trattato con methotrexate, golimumab e etanercept con scarsa efficacia terapeutica. A gennaio 2025 è stato indirizzato presso il nostro ambulatorio, dove è stata riscontrata positività ANA 1/160 pattern granulare

citoplasmatico, anti-SSa/Ro52, anti-Jo1. La TC del torace mostrava un quadro ILD tipo NSIP. Clinicamente non riferiva fenomeno di Raynaud, rash cutanei, deficit muscolari. Gli enzimi di necrosi muscolare erano negativi.
2° paziente: diagnosi di AR (ANA positività 1/1280 pattern citoplasmatico, FR a basso titolo e ACPA) in terapia con methotrexate e infliximab. Il profilo anticorpale risultava positivo per anti-PL12 ad alto titolo. In anamnesi si riscontrava esclusivamente un episodio di miopericardite acuta complicata da BAV totale, di natura non identificata.
3° paziente: diagnosi di AR con ILD, FR e ACPA ad alto titolo, in terapia con etanercept. Il riscontro di anticorpi anti-Ribosomial P0 ad alto titolo al momento è poco utile per ulteriore tipizzazione in quanto poco specifici e spesso descritti in associazione a lupus eritematoso sistemico.
Se nel primo paziente la diagnosi di ASSD è definita, nel secondo paziente potrebbe essere sospettata alla luce della pregressa miocardite che seppur un evento raro della ASSD, è comunque tra le manifestazioni cliniche severe che impattano maggiormente la prognosi.
Conclusion: i: al momento attuale su 33 pazienti sottoposti a valutazione sierologica, clinica e radiologica, 2 casi hanno una diagnosi di ASSD definita o probabile. Nel tempo valuteremo ulteriori risultati ampliando la popolazione in studio. Seppur siano risultati preliminari e incompleti, il nostro studio suggerisce l'importanza di una stratificazione più accurata dei pazienti con AR/artrite indifferenziata in cui si associano manifestazioni extra-articolari o refrattarietà alla terapia. L'identificazione di ASSD può aiutare per ottimizzare le scelte terapeutiche e il follow-up, prevenendo complicanze e manifestazioni extra-articolari.

DIAPHRAGMATIC DYSFUNCTION IN A COHORT OF CRITICALLY ILL SUBJECTS ASSESSED IN THE ED: A PILOT STUDY

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Introduction: Diaphragmatic dysfunction is frequently observed in individuals with heart failure and has been linked to increased disease severity among this population. The purpose of this pilot study was to investigate the clinical and laboratory correlations of diaphragmatic dysfunction in a prospective cohort of patients admitted from the emergency department (ED) for acute decompensated heart failure (ADHF).
Patients and Methods: We enrolled all the patients admitted to our ED for ADHF. For each patient, we collected at the ED admission: age, sex, clinical parameters (cardiac frequency, respiratory rate, SpO2, systolic and diastolic pressure), clinical manifestations (NYHA class, orthopnea, acute or progressive onset of symptoms), echocardiographic and lung ultrasound parameters taken with point-of-care ultrasound, BNP and blood gas analysis. Need for CPAP or BiPAP in the acute phase of the disease was also assessed. Diaphragmatic dysfunction (DD) was defined as a reduced excursion of one or both hemidiaphragms (<11 mm) associated with a reduced thickening (<20%) of one or both hemidiaphragms.
Results: we obtained a sample of 26 consecutive patients admitted to the ED for ADHF; mean age was 83.8 (±7.1) years, males represented 76.9% (n=20), diaphragmatic dysfunction was present in 12 (46.2%) patients. We observed that at admission, subjects with DD had a higher prevalence of an acute manifestation (n=8; 66.7%; p<0.0001), a higher prevalence of orthopnea (n=8; 66.7%; p<0.0001), a higher respiratory rate (26.0±4.0 versus 18.57±4.40; p<0.0001), a higher cardiac frequency (94.16±16.3 versus 82.85±11.78; p<0.0001), a higher NYHA category (2.0±0.55 versus 3.5±0.78; p<0.0001), and a higher prevalence of CPAP/BiPAP use (n=8; 66.7%; p<0.0001). Among the echocardiographic variables, we observed a higher pulmonary artery systolic pressure (43.75±11.88 versus 64.00±12.09; p<0.0001). Among the blood gas analysis values, we observed a significantly lower pH at ED admission (7.45±0.03 versus 7.33±0.11; p=0.0013). Right and left diaphragm excursion were significantly correlated with NYHA class (right diaphragm excursion: r2=0.570, p<0.0001; left diaphragm excursion: r2=0.346, p=0.0016; Figure 1, Panels A-B) and respiratory rate (right diaphragm excursion: r2=0.272, p=0.0063; left diaphragm excursion: r2=0.431, p=0.0003; Figure 1, Panels C-D). The percentage of inspiratory increase or right hemidiaphragm was significantly associated with NYHA class (right: r2=0.262, p=0.0075; left: r2=0.022, p=0.468).
Results: we observed that diaphragmatic dysfunction was associated with more severe symptoms, worse NYHA class, worse functional parameters at admission, and higher need for CPAP or BiPAP in ADHF.

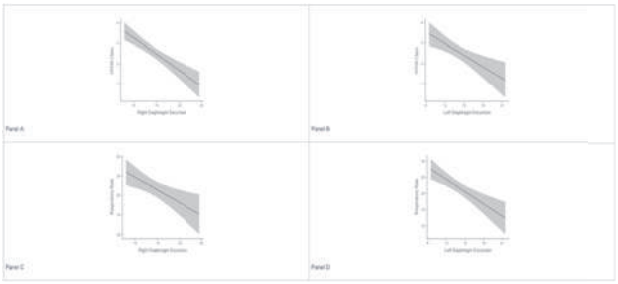

Figure 1: relationship between diaphragm excursion and NYHA class and respiratory rate

PREVALENCE AND ASSOCIATED FACTORS OF STEATOSIS, STEATOHEPATITIS AND FIBROSIS DIAGNOSED WITH NON-INVASIVE METHODS DURING ANNUAL CHECK-UPS IN AN INDUSTRIAL WORKER POPULATION

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Introduction: Steatotic liver disease (SLD) can progress to fibrosis and liver cirrhosis. Its prevalence is rapidly increasing due to the rising incidence of metabolic-associated steatotic liver disease (MASLD), however, different aetiologies should be considered, and the incidental finding of SLD should prompt their evaluation. Screening for SLD in the general population is not recommended, but its association with elevation in liver enzymes (steatohepatitis -SH-) and liver fibrosis is associated with liver-related outcomes. FIB-4 and APRI scores can be used to screen for fibrosis in at-risk populations in primary care settings. In the present study, we used data from annual health check-ups at Bridgestone's factory in Bilbao to assess the prevalence and identify factors associated with these three conditions in this worker population.
Methods: 886 healthy workers were prospectively enrolled during yearly health checkups (from January to December 2024) at the Bridgestone factory (Bilbao, Spain). Ultrasound, anthropometric and biochemical data were collected. Alcohol consumption was assessed using a qualitative questionnaire. 362 patients with all available data were further analysed. Patients were divided into the following groups: no steatosis (Healthy), steatosis and normal LE (SLD), steatosis and elevated LE (SH). Differences between the three groups were evaluated via one-way or Kruskal-Wallis analysis of variance for continuous variables and chi-square for categorical variables after adjustment for multiple comparisons with the Bonferroni test. Multivariable logistic regression was used to search for factors associated with SLD or SH. A multivariable linear regression evaluated factors associated with FIB4 and APRI scores.
Results: The Healthy Group accounted for 68% of the patients, while the remaining patients were divided into the other two groups (SLD 20%; SH 12%). Analysis of variance showed a statistical significant increase in age, BMI, creatinine, haemoglobin, triglycerides and serum glucose between healthy individuals, SLD and SH. A progressive increase in individuals with arterial hypertension, with increased alcohol consumption and male sex, was noted. At post-hoc analysis, the only differences between SLD and SH patients were higher BMI, higher triglycerides and lower HDL.
The prevalence of SLD diagnosed with ultrasound was 31.9%, [95% CI: 27.6%-36.6%]. Also, the prevalence of fibrosis diagnosed with FIB4 or APRI score was: 0.55% [0.15% - 1.9%], defined by a FIB4 score > 2.67; and 0.2% [0.04% - 1.5%], defined by an APRI score > 1.5.
Factors associated with SLD at multivariable logistic regression were: BMI (aOR 1.18 [1.06, 1.33]), hypertension (aOR 2.69 [1.22, 6.03]), alcohol consumption (aOR 2.40 [1.16, 5.12]) and ALT (aOR 1.03 [1.00, 1.06]). Factors associated with SH at multivariable logistic regression were: BMI (aOR 1.33 [1.19, 1.50]) and triglycerides (aOR 1.00 [1.00, 1.01]). Predictors of FIB4 were sex (coefficient: 1.30 [1.15, 1.47]), serum magnesium (coefficient: 0.67 [0.52, 0.84]) and HDL (coefficient: 1.01 [1.01, 1.01]). The only predictor of APRI score was serum magnesium (coefficient: 0.85 [0.76, 0.95]).
DISCUSSION:
Conclusion: The prevalence of SLD and liver fibrosis in this working population was consistent with existing literature. Opportunistic screening with ultrasound and liver enzymes identified a subset of patients at increased risk (SH),

emphasising the value of incorporating liver assessments into routine occupational health evaluations.

INCIDENCE, OUTCOMES AND RISK FACTORS FOR CARBAPENEM-RESISTANT ORGANISMS (CRO) COLONIZATION OR INFECTION IN PATIENTS ADMITTED IN AN INTERNAL MEDICINE WARD

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Background and aim: Carbapenem-resistant Organisms (CRO) generates anincreasing threat in hospitals worldwide in terms of patient management, length/costs of hospital stay, and outcomes.The 2024 "WHO Bacterial Priority Pathogens List" ranks CRO, which includes carbapem-resistant Acinetobacter baumannii and carbapem-resistant Enterobacterales in the highest priority category (critical group). Patients infected by CRO show increased likelihood of morbidity and mortality compared with patients infected by susceptible pathogens. We studied the impact of CRO colonization and infection on a cohort of patients admitted in 2024 from ER to the Internal medicine ward in southern Italy.
Methods: . We identified two groups, i.e., a) the Septic Group (SG) consisting of patients with positivity for detection of most prevalent carbapenemase genes (coding for VIM, IMP, NDM, KPC and OXA-48) by real-time PCR on rectal swab and microbiology evidence of bacteremia;b) the Colonized Group (CG) consisted of patients with positivity for the most prevalent carbapenemase genes and no bacteremia. The burden of comorbidities was assessed by calculating the Charlson comorbidity index (CCI).
Results: Among740admissions,22SG and44CG were identified (8.9% of all hospital admissions).Infections were from K. pneumoniae (n=8,36.4%),A. Baumannii(n=8,36.4%), P. aeruginosa (n=3,13.6%), E. Faecium (n=1,4.5%). A co-infection from different CROs was recorded in5patients (22.7%). Gender distribution was comparable in the two groups(SG:13females [59%]; CG:18females [41%]) but SG patients were youngerthan CG patients(69.2±SEM3.4vs.75.6±2.1years, respectively, p=0.007), and had a lower burden of comorbidities (CCI5.9±0.5and7.1±0.3, in SG and CGrespectively, p=0.04).Despite the median length of stay was above20days in both groups, mean stay wassignificantly longer in SG than in CG (30.1±4.2vs.22.7±2.9days, respectively, p=0.02); in both groups, the median length of stay was longer than non-colonized patients (11.2days, p<0.001). Considering both groups,46patients (69.7%) were institutionalized or have been hospitalized in the past3months.The rate of septic shock was higher in SG patients (n=15,68%), than in those in CG(n=6,13.6%, p<0.0001). Antibiotic therapy (cefiderocol, ceftazidime-avibactam + aztreonam, meropenem-vaborbactam) was administered in all SG patients. In addition,all6patients with septic shock in CG were treated;2of these died. The in-hospital death rate was higher among SG patients (n=12,55%) than CG (n=12,27%, p=0.03).
Conclusions: In internal medicine wards, either colonization or infection from CRO generate long hospitalstay. To address this global epidemic, early identification and active surveillance are needed. With the same comorbidities we show that patients with sepsis were younger and more often institutionalized or recently hospitalized. Patients with CRO infection require expensive antibiotic therapies and have an increased in-hospital mortality. Greater attention and further studies are needed to better characterize population at risk in order to implement efficient prevention strategies.

CANCER INCIDENCE AND MORTALITY IN HOSPITAL PATIENTS BEFORE AND AFTER COVID-19 ERA: A CHANGING LANDSCAPE IN INTERNAL MEDICINE

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Background: The potential oncogenic role of SARS-CoV-2 has recently been suggested, butthe indirect effects of the pandemic on cancer are still largely unexplored. The COVID-19outbreak may have determined,also in not infected subjects,a poorer control of potentially modifiablerisk factors,influencing several aspects of cancer care worldwide.
Methods: We studied the impact of COVID-19 on cancer incidence, mortality, institutionalization and hospital costs among patients acutely admitted in an internal medicine ward comparing administrative data of period before (years 2016-2019, group bCO19) and after (years 2020-2023, group aCO19) COVID-19 occurrence. Cases with acute SARS-CoV-2 infection (1st, 2nd waves) were excluded from analyses.
Results: Data were collected from a total of 5,418 patients older than 15 years (mean age 71.4 yrs, female 44.1%, bCO19=3,557 patients; aCO19=1,861 patients), hospitalized at the Internal Medicine Division involved in COVID-19 pandemic of regional hospital Policlinico of Bari. After propensity score matching, for age, gender and access type,aCO19 group had a higher prevalence of cancer disease than bCO19 group (26.7% vs 22.7%, respectively, p=0.004and higher risk of all-causes mortality (Hazard Ratio (HR): 1.84, 95% confidence interval (CI) 1.47-2.31, p<0.001), institutionalization (HR: 2.39, 95% CI: 1.68-3.38, p<0.001)and longer length of stay (β: 1.25, 95% CI: 0.68-1.83, p<0.001). In addition, aCO19 group showed higher diagnosis-related group (DRG)-based cost of the index hospitalization (β: +729.82 €, 95% CI: 603.81-855.84, p<0.001). A non-significant trend toward higher cancer incidence and cancer-related mortalitywas observed among male and younger subjects (≤ 65 years old). Conversely, after COVID-19 the all cause in-hospital mortality increasedin particular in older adults and female subjects.
Conclusion: During and immediately after the COVID-19 pandemic there was a significant change in the characteristics of patients accessing the medical hospital area, including internal medicine wards. Patients appear more frail, with more severe diseases (higher DRGs and longer hospital stays), and a higher risk of short-term mortality and institutionalization upon discharge.This could be partly explained by a change in the cancer epidemiology with an increase in the incidence and mortality, particularly in male and younger subjects.

CLINICAL COURSE, THERAPEUTIC MANAGEMENT, AND LIPID-LOWERING THERAPY IN A COHORT OF PATIENTS WITH IMMUNE-MEDIATED NECROTIZING MYOPATHY (IMNM)

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Introduzione: La miopatia necrotizzante immuno-mediata (IMNM) è una rara patologia autoimmune appartenente allo spettro delle miopatie infiammatorie idiopatiche (IIM). Clinicamente, si manifesta con debolezza muscolare prossimale simmetrica, a esordio subacuto o rapido, accompagnata da un incremento marcato della creatinchinasi (CPK) sierica, spesso ≥10 volte il limite superiore della norma. Il coinvolgimento extramuscolare è meno comune rispetto ad altre IIM.
La biopsia muscolare mostra necrosi e rigenerazione delle fibre muscolari con infiltrato infiammatorio composto prevalentemente da macrofagi. L'analisi immunoistochimica rivela solitamente la deposizione del complesso di attacco alla membrana (MAC) su fibre non necrotiche e la sovraespressione delle molecole MHC di classe I. La presenza di autoanticorpi specifici, come gli anti-signal recognition particle (anti-SRP) e gli anti-idrossimetilglutaril-coenzima A reduttasi (anti-HMGCR), è tipica della malattia, sebbene circa il 20% dei pazienti risulti sieronegativo pur presentando un quadro clinico e istopatologico compatibile.
Nonostante i criteri classificativi EULAR/ACR del 2017 collochino ancora l'IMNM nel sottogruppo della polimiosite — principalmente a causa della limitata numerosità campionaria — attualmente questa condizione è considerata un'entità clinica distinta con caratteristiche specifiche. A supporto della diagnosi possono essere utilizzati anche i criteri ENMC del 2017.
Casistica: Nella nostra casistica sono stati identificati 16 casi di IMNM, diagnosticati tra gennaio 2014 e oggi, presso la Clinica Medica dell'AOU delle Marche (Ancona). La diagnosi è stata effettuata valutando clinica, profilo immunologico e aumento degli indici di citonecrosi muscolare; tutti soddisfano i criteri ENMC 2017 per la diagnosi di IMNM. La nostra popolazione ha una prevalenza di sesso femminile (10, 62.5%), l'età media alla diagnosi era di 64,5 ± 9,4 anni. Dodici pazienti risultavano positivi agli anticorpi anti-HMGCR e quattro agli anti-SRP. La mediana dei mesi di follow-up è 15 (IQR: 9 – 38).
All'esordio sette pazienti presentavano disfagia, segno clinico di malattia severa; in un caso è stata riscontrata una neoplasia del colon in concomitanza con la diagnosi di miosite. La stessa paziente è uno dei due casi (entrambi anti-SRP positivi) con coinvolgimento polmonare, con quadro di interstiziopatia (ILD) tipo NSIP/OP. La mediana dei valori di CPK alla diagnosi era di 6314 U/L

(IQR: 4865–11072), mentre il punteggio medio all'MMT8 era 133 (IQR: 116–138). Tutti i pazienti, tranne due con positività anti-SRP, avevano una storia di pregressa esposizione a statine.
Il trattamento iniziale ha previsto la somministrazione di prednisone ad alto dosaggio (1 mg/kg/die per 3–4 settimane), con successivo tapering; solo tre pazienti hanno ricevuto boli di metilprednisolone (250-500 mg ev per 3 giorni). La terapia immunosoppressiva steroid sparing di prima linea più utilizzata è stata il metotrexate (7 pazienti), seguito da micofenolato mofetile (3 pazienti), immunoglobuline ad alte dosi (2 g/kg in 5 giorni, in 3 pazienti), ciclosporina (1 paziente). In due casi è stata utilizzata solo terapia steroidea.
Otto pazienti hanno richiesto una terapia di seconda linea, con l'impiego di rituximab, micofenolato mofetile e IVIg. In tre casi è stato necessario ricorrere a una terapia di terza linea con micofenolato e IVIg.
La terapia ipolipemizzante è stata modificata in tutti i pazienti che assumevano statina. Cinque sono stati trattati con inibitori di PCSK9 (evolocumab), due con inclisiran, sei con associazione acido bempedoico/ezetimibe, e quattro con solo ezetimibe. In tutti i casi, il trattamento si è rivelato efficace e ben tollerato, senza effetti avversi segnalati.
Conclusioni: Questi dati confermano la complessità clinica e terapeutica dell'IMNM, che spesso ha un decorso benigno, ma con un alto rischio di resistenza alla prima linea di terapia (nel 50% della nostra casistica). La dislipidemia e il rischio cardiovascolare sono spesso di difficile gestione, anche a causa degli effetti avversi dovuti alla terapia steroidea prolungata. Un attento follow-up del rischio cardiovascolare e l'utilizzo dei nuovi farmaci ipolipemizzanti sono fondamentali nella gestione di questi pazienti.

P	Età diagnosi	Anticorpi	CPK ricovero	CPK follow-up	MMT 8 ricovero	MMT 8 follow-up	Comorbidità	Manifestazioni extra muscolari	Statine ricovero	Steroid sparing			Terapia ipolipemizzante attuale
										I linea	II linea	III linea	
#1/F	56,33	HMGCR	13103	32	92	135	DM tipo II, IAS, dislipidemia mista	Disfagia	Atorvastatina	IVIg	RTX	MMF	PCSK9+, ezetimibe
#2/F	60,36	HMGCR	6468	90	142	150	IAS, dislipidemia mista		Lovastatina	MTX			Inclisiran
#3/F	71,96	HMGCR	3332	24	134	150	IAS, dislipidemia mista		Atorvastatina, Rosuvastatina	MTX			Acido bempedoico, ezetimibe
#4/M	59,50	HMGCR	5727	652	118	148	Sindrome metabolica, depressione maggiore		Atorvastatina	MTX	MMF	IVIg	PCSK9+
#5/F	69,87	HMGCR	6569	392	140	144	Dislipidemia mista	Disfagia	Rosuvastatina	MTX	IVIg		PCSK9+, ezetimibe
#6/F	64,78	HMGCR	11293	51	132	148	IAS, dislipidemia mista		Atorvastatina	MMF	6MPDN		Ezetimibe
#7/F	60,06	HMGCR	8722	47	139	150	DM tipo I, tiroidite, sdr metabolica, talassemia minor	Disfagia	Atorvastatina/ezetimibe	MMF			Acido bempedoico, ezetimibe
#8/M	81,31	HMGCR	11000	975	138	145	IAS, dislipidemia mista		Atorvastatina				Acido bempedoico, ezetimibe
#9/M	68,20	HMGCR	4254	34	129	148	Sdr metabolica, cardiopatia ischemica, stenosi aortica	Disfagia	Atorvastatina	MTX			Acido bempedoico, ezetimibe, PCSK9+
#10/F	71,00	HMGCR	6160	56	135	146	Ipotiroidismo, dislipidemia mista, aterosmosi carotidea, IAS, maciulopatia		Atorvastatina	MTX	IVIg		Acido bempedoico, ezetimibe, inclisiran
#11/M	75,03	HMGCR	4854	300	135	150	Obesità I, IAS, dislipidemia mista, aterosmosi carotidea, HBV cronica latente, embolia polmonare		Atorvastatina	MTX			Ezetimibe
#12/M	68,22	HMGCR	13324	150	110	145	Osteoporosi, dislipidemia mista, osteonecrosi testa del femore	Disfagia	Atorvastatina	IVIg	AZA	6MPDN	
#13/F	62,81	SRP, ANA, Sa/Ro	11940	239	125	131	Osteoporosi, IAS	Disfagia	Rosuvastatina	MMF			PCSK9+
#14/F	43,04	SRP, ANA, Sa/Ro	4936	123	76	150	HBV cronica latente, gastrite cronica atrofica, tiroidite, IAS, scompenso cardiaco cronico	Disfagia	No	IVIG	MMF		
#15/M	54,49	SRP	5736	448	110	148	HBV cronica latente, Fa, tiroidite, IAS, rottura tendini rotulei, osteoporosi	ILD, Cuore	No	CsA	IVIg	MMF	Acido bempedoico, ezetimibe
#16/F	69,26	SRP	1000	622	146	148	Tiroidite Hashimoto, lichen sclerosu, dislipidemia mista, neoplasia del colon	ILD	Atorvastatina				

Tabella 1. Caratteristiche cliniche e terapia della nostra casistica. AZA: azatioprina; CsA: ciclosporina A; DM: diabete mellito; IAS: ipertensione arteriosa sistemica; ILD: interstitial lung disease; IVIg: immunoglobuline endovena; MMF: micofenolato mofetile; MTX: metotrexato; RTX: rituximab; 6MPDN: 6-metilprednisolone.

OXIDATIVE STRESS MAY CONTRIBUTE TO ENHANCED THROMBOPOIESIS THROUGH MIR-150: IMPLICATIONS FOR ASPIRIN RESPONSE

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Background: Variability in platelet cyclooxygenase-1 (COX-1) turnover significantly affects individual responses to aspirin (ASA). Given ASA's short half-life, increased platelet (PLT) production can lead to a suboptimal antiplatelet effect over a 24-hour period. We previously demonstrated that poor ASA responders display enhanced megakaryopoiesis (MK) and increased proplatelet formation, leading to a more rapid restoration of COX-1 activity. Type 2 diabetes mellitus (T2DM) is characterized by enhanced oxidative stress, which may disrupt the platelet microRNA (miRNA) profile, thereby enhancing platelet reactivity and contributing to resistance to antiplatelet therapy. In this study, we evaluated the role of CCL5 (C-C motif chemokine ligand 5, also known as RANTES), due to its known role in promoting MKs, and miR-150, a miRNA involved in guiding MK-erythroid progenitor fate by favoring megakaryocytic over erythroid differentiation in patients with shorter duration of aspirin effect over the 10-24 hours dosing interval, due to accelerated PLT COX-1 recovery.
Objectives: This study aimed at assessing the extent of lipid peroxidation (measured by 8-iso-PGF2α), circulating CCL5 and their association with miR-150 levels in individuals exhibiting showing faster recovery of PLT cyclooxygenase activity over 24 hours.
Methods: A total of 100 high cardiovascular (CV) risk T2DM patients undergoing chronic treatment with low-dose ASA (100 mg/day) for CV prevention were enrolled. Blood samples were collected at 10 hours (T10) and 24 hours (T24) following a witnessed ASA administration. Patients were stratified into tertiles based on the slope of serum thromboxane B_2 (TXB_2) levels, and comparisons were made between the first and third tertiles.
Urine and fasting blood sampling were performed. The analysis included evaluation of PLT-associated miR-150 (as index of megakaryopoiesis), circulating CCL5 levels (as a marker of PLT activation), and urinary 8-iso-prostaglandin F2α (8-iso-PGF2α, as biomarker of lipid peroxidation and oxidative stress).
Results: T2DM patients with accelerated COX-1 recovery showed higher levels of urinary 8-iso-PGF2α (p=0.019) and circulating CCL5 (p=0.017), which were directly correlated (rho=0.273, p=0.032), **Figure 1**. CCL5 levels were also positively correlated with thrombopoietin (ρ = 0.399, p = 0.022) and platelet count (ρ = 0.286, p = 0.002). Both thrombopoietin levels and platelet counts were significantly higher in patients in the third tertile (p = 0.023 and p = 0.047, respectively), **data not shown**. Circulating miR150-5p was also upregulated in 3rd tertile (p=0.058) and directly correlated (rho=0.274, p=0.063) with 8-iso-PGF2a, **Figure 2**. No significant difference was observed for miR-150-5p levels in PLTs. However, PLT miR-150-5p levels were directly correlated with CCL5 (rho=0.262, p=0.042), **data not shown.** TargetScan analysis identified **prostaglandin F receptor** (**FP**) as the target gene for miR150-5p.
Conclusions: In patients with type 2 diabetes at high cardiovascular risk, a reduced response to low-dose aspirin is associated with a faster recovery of platelet COX-1 activity. Our findings indicate that elevated oxidative stress, reflected by increased urinary 8-iso-PGF2α, is accompanied by higher levels of CCL5 and circulating miR-150-5p—factors potentially involved in enhanced thrombopoiesis. The direct correlations among oxidative stress, CCL5, and miR-150-5p suggest a mechanistic link whereby oxidative stress may drive megakaryocyte activation and accelerated platelet production. These markers could help identify patients with a reduced response to aspirin and support new strategies to improve antiplatelet treatment in high-risk individuals.
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Figure 1

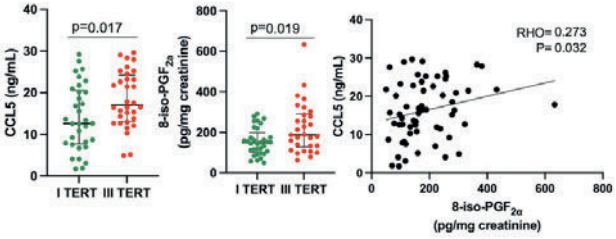
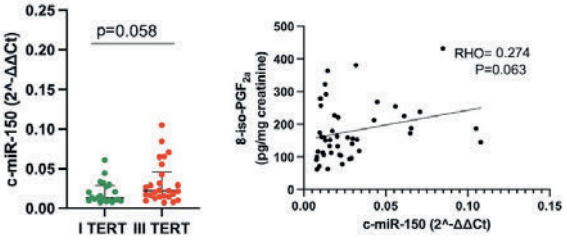


Figure 2



CASE REPORT: JAK INHIBITORS TREATMENT IN JUVENILE DERMATOMYOSITIS WITH CALCINOSIS

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Introduzione: Le forme giovanili di miopatie infiammatorie idiopatiche (IIM) sono patologie rare che si manifestano con un ampio spettro clinico. La forma più comune e più conosciuta è la dermatomiosite giovanile (JDM) caratterizzata da lesioni cutanee tipiche (papule e segno di Gottron, rash eliotropo, calcinosi) e debolezza muscolare prossimale. Agli esami di laboratorio si riscontra un

aumento degli enzimi di citonecrosi muscolare, mentre la RMN e la biopsia muscolare sono utili per confermare la natura infiammatoria del danno con reperti quali edema muscolare e infiltrato perivascolare e del perimisio con alcune fibre necrotiche. La sierologia immunitaria presenta anticorpi miosite specifici in quasi il 70% dei pazienti e i più frequenti sono TIF1-gamma, anti-NXP-2, anti-MDA5 e gli anticorpi anti-sintetasi. La terapia è basata sull'uso di corticosteroidi ad alte dosi (1mg/Kg/die o boli), associato a immunosoppressori/immunomodulanti quali methotrexate, azatioprina, ciclofosfamide, immunoglobuline ad alto dosaggio (IVIg), inibitori della calcineurina.
La calcinosi dei tessuti molli è una complicanza frequente soprattutto nei pazienti con anticorpi anti NXP-2, si può presentare con masse calcifiche profonde o superficiali che coinvolgono masse muscolari, tendini o cute. L'approccio terapeutico è spesso difficile, è riportato l'utilizzo di diltiazem, IVIg, costicosteroidi intralesionali, bifosfonati, infliximab e abatacept, con risultati alterni. Nei casi severi è spesso necessario il trattamento chirurgico.
Case report: Descriviamo il caso di una paziente affetta da JDM NXP-2 positiva, che ha sviluppato panniculite e calcinosi sottocutanee dopo 5 anni di remissione, attualmente in terapia con JAK-inibitori.
La storia clinica iniziava nel 2011 quando la paziente all'età di 11 anni sviluppava rash eliotropo, edema palpebrale, febbre e mialgie. Il riscontro di CPK elevate (2888 U/l), ANA positività 1/640, elettromiografia indicativa di sofferenza muscolare primitiva, poneva il sospetto di JDM, confermato dalla biopsia muscolare. La paziente veniva trattata con steroide ad alto dosaggio (1 mg/kg/die) con lento tapering, associato a IVIg (2g/kg/mese) e micofenolato mofetile. Dopo remissione completa della malattia la terapia steroidea veniva sospesa nel 2013, successivamente si sospendevano anche il micofenolato mofetile (nel 2014) e le immunoglobuline (2015). Negli anni successivi la sierologia immunitaria riscontrava positività per anti-NXP2. Contestualmente la paziente nel 2015 riceveva una diagnosi di rettocolite ulcerosa su reperto istologico, trattata con budesonide e mesalazina con beneficio e in assenza di recidive.
Nel 2019 dopo comparsa di nodularità sottocutanee su coscia e gomito, eseguiva una RM bacino che evidenziava la presenza di fenomeni di cellulite-adiposite con aspetti di tipo liponecrotico-fibrotico. La biopsia della coscia descriveva un quadro compatibile con panniculite. La paziente non lamentava debolezza muscolare né rash cutanei e gli esami ematici non riscontravano elevazione degli indici di necrosi muscolare. Data la localizzazione delle lesioni, l'evoluzione in nodularità calcifiche e la lipodistrofia, il quadro è stato interpretato come recidiva cutanea di JDM con calcinosi ed è stata intrapresa terapia con methotrexate (15 mg/sett) con parziale beneficio. Successivamente è stata associata terapia con idrossiclorochina (200 mg/die) e alendronato (70 mg/settimana).
Per la progressione e il peggioramento delle calcificazioni, presenti soprattutto in regione trocanterica e lungo il decorso del bicipite femorale, da gennaio 2024 a novembre 2024 la paziente è stata sottoposta a terapia con IVIg (90g/mese) con poca efficacia. Durante la terapia con IVIg ha sviluppato nuove lesioni sottocutanee, presenti anche in zona brachiale, in sede di infusione endovenosa del farmaco.
Alla luce della costante seppur lenta progressione della sintomatologia cutanea e al fine di evitare l'uso di ulteriori terapie endovenose, è stata intrapresa terapia con JAK-inibitori. Da gennaio 2025 la paziente è in terapia con baricitinib 4 mg/die, con attuale stabilità della sintomatologia cutanea. Il successo terapeutico nella nostra paziente sarà rivalutato nel tempo con esame clinico e rivalutazione radiologica.
Conclusion: i: Nella DM le analisi trascrittomiche dimostrano una sovraespressione dei geni regolati dall'interferone (IFN), confermandone il ruolo nello sviluppo della patologia. L'azione dei JAK-inibitori sulla trasduzione del segnale dell'IFN rappresenta il razionale del loro utilizzo nella DM e le sempre maggiori evidenze sull'efficacia terapeutica (in alcuni report anche sulle calcificazioni dei tessuti molli correlate), li rendono un'alternativa molto utile nella gestione dei pazienti con JDM.

INTRAVASCULAR LEIOMYOMATOSIS EXTENDING TO THE RIGHT ATRIUM: A CASE REPORT WITH A MULTIDISCIPLINARY MANAGEMENT

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Introduction: Intravascular leiomyomatosis (IVL) is a rare condition, with approximately 400 cases reported in the literature since its first description in 1896 [1]. It is characterized by the intravascular proliferation of smooth muscle cells, often with a branching pattern that can extend from pelvic veins to thoracoabdominal vessels. Although benign in histological terms, IVL can clinically mimic a malignancy and lead to potentially fatal complications. The majority of cases of IVL have been reported in women, especially in the fourth decade of life, frequently associated with uterine leiomyomas [2], [3]. The treatment of choice is surgical resection, aiming to reduce morbidity and mortality associated with vascular involvement and minimize the risk of recurrence [4].
Case presentation: We report the case of a 48-year-old woman who presented in December 2022 with dyspnea and palpitations. A transthoracic echocardiogram revealed a right atrial mass, prompting further evaluation. A total-body CT scan identified a large pelvic mass, likely of uterine origin, with intravascular extension involving the ovarian veins, the right internal and common iliac veins, and the inferior vena cava (IVC), reaching the right atrium. Pelvic mass biopsy confirmed a benign leiomyoma and intravascular leiomyomatosis. Following multidisciplinary discussion, the patient underwent an initial surgery to remove the tumor from the vascular structures. In June 2023, resection was performed from the atriocaval junction up to the confluence of the suprahepatic veins. Histological examination confirmed IVL. A radiological follow-up in May 2023 revealed an increase in pelvic mass size and recurrent intravascular extension to the right atrium (Figure 1). After re-evaluation, a three-stage surgical procedure was performed, including complete hysteroannessiectomy and tumor removal from the right iliac vein, IVC, and right atrium. The surgery was completed without complications. Postoperative histology confirmed IVL in all specimens. A follow-up CT in July 2023 showed no residual disease, although a focal filling defect in the IVC—just above the iliac vein confluence and at the renal vein junction—suggested chemical thrombosis. The patient was started on anticoagulant therapy, which was well tolerated, without thromboembolic recurrence or major bleeding. Complete recanalization of the thrombosis was achieved.
Conclusion: This case illustrates the complex and rare nature of IVL, highlighting the critical role of a multidisciplinary management for diagnosis, treatment and follow-up. Postoperative clinical and radiological follow-up is essential to detect complications such as thrombosis and especially recurrence, which occurs in 16–30% of cases, particularly when complete surgical excision is not achieved [5]. Additional studies are needed to define standardized surgical and therapeutic protocols for the management of IVL.

A RARE CASE OF SCABIES COMPLICATED WITH TRANSIENT ABSOLUTE B LYMPHOCYTOPENIA AND SEVERE LYMPHEDEMA OF LOWER LIMBS

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Introduction: Scabies, a contagious skin condition, is a universal disease caused by a mite, Sarcoptes scabiei var. hominis, clinically characterized by itching essentially in areas with thin skin with possible complications due to scratching lesions and secondary bacterial infections. It is transmitted by prolonged direct skin-to-skin contact and by indirect contact with infested objects. Scabies has become a growing concern, with its prevalence increasing in recent years. Factors such as natural disasters, wartime conditions, and irregular migration contribute to its spread, particularly in settings with poor hygiene. Although traditionally associated with regions of lower socioeconomic status, scabies is observed globally, including in developed countries. The condition disrupts skin integrity, predisposing individuals to bacterial infections (impetigo). and Streptococcus pyogenes are commonly implicated bacteria in these infections, the latter of which may result in kidney disease and rheumatic heart disease. Scabies also impacts quality of life: itch and visible rash often lead to poor sleep, stigmatization and social exclusion, interrupting school and work attendance. The direct spread of these bacteria contributes to the prevalence of bacterial infections in scabies cases. Furthermore, complement inhibition induced by the scabies may facilitate the occurrence of these bacterial infections.
Clinical case: A 68 years old allergic man, presented to our Department for intense itching on his lower legs especially intense at night. The symptoms had been persistent for the last two weeks despite therapy on antihistaminic and steroid drugs. The patient also received antihelmintes (Albendazole) treatment for possible intestinal worn infection, without relief. He reported a history of hypertension on sartans and previous cholecistectomy and prostate hypertrophy and allergic rhinitis. Since his blood examen revealed a mysterious absolute B-lymphocyte deficiency with eosinophilia, while elevated was the CRP level, but normal all the rest of laboratory evaluation, we suspected a lymphoma and the patient underwent to total body CT-scan and PET evaluation, which resulted negative, and dermatological visit that showed a widespread erythematous-scaly- eruption, all over the body, in particular the back, abdomen, upper and especially lower limbs involved in the right side in a evident lymphedema, confirmed by Doppler-ultrasound evaluation. The dermatologist places clinical suspicion between Sneddon-Wilkinson dermatitis, pustular psoriasis and paraneoplastic syndrome and requests histological examination from skin biopsies. Skin biopsies was taken from his right upper forearm for histopathology examination and later skin scrapings from same late expressing interdigital papules. These both revealed the presence of a female Sarcoptes scabiei! We made diagnosis of scabies and the patient started therapy with oral ivermectin

(two cycles) and topical application of benzyl benzoate, moreover it needed treatment on antibiotics (vancomycin) against the lymphedema due to Staphylococcus aureus. Finally, three months after the onset of symptoms, at follow-up he appeared greatly improved and his mysterious B lymphocytopoenia resulted completely disappeared!
Conclusions: Human, caused by the mite, is a contagious skin condition prevalent in regions with low socioeconomic status, crowded living conditions, and following wars or natural disasters. Clinical scabies is often intensely itchy and distressing, with signs on examination including nodules, papules and s-shaped mite burrows. The latter can be seen with the naked eye, but dermatoscopy may aid diagnostic confirmation as can light microscopy identification of mites, eggs, or faeces in skin samples scraped from affected areas. Rashes may occur anywhere on the body, with burrows commonly observed on the hands (particularly finger-webs), breasts and genitals. It manifests as itchy lesions, disrupting skin integrity and predisposing individuals to skin infections. Commonly available tests are not very sensitive in scabies diagnosis. Diagnosis is therefore mainly based on simple examination and history and may be difficult, especially in older adults. Skin scraping followed by microscopy can be used to confirm diagnosis. However negative findings should not be taken to indicate absence of infestation due to its low sensitivity. Individuals who have been diagnosed with scabies should be treated promptly to alleviate symptoms and reduce risk of complications. This should never be delayed by waiting for contacts to be treated. Ivermectin 3 mg tablets are licensed for the treatment for scabies once diagnosis has been confirmed clinically or by parasitological examination. Itching alone, without a formal diagnosis of scabies, does not justify treatment with ivermectin. The association between and , caused by and, is well-established.

THE SILENT GIANT: AN UNKNOWN ABDOMINAL MASS

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Case report: A 65-year-old man was hospitalized for fever resistant to ciprofloxacin during the last 10 days. Blood tests revealed an acute renale failure (creatinine 6.9 mg/dL, eGFR 8 mL/min), with acute inflammation (CRP 161.3 mg/L, neutrophilic count 21.04x103/uL). Physical examination revealed a painless, large, hard-elastic mass in the left abdominal quadrants, with ultrasonographic (US) grade II hydronephrosis due to a compressing hyperechogenic mass of 25 cm. Urine culture was positive (E. Coli) and meropenem therapy was started. The abdominal CT scan confirmed the presence of complex cyst, Bosniak classification IIF (Figure 1). A nephrostomy was thereafter positioned, with drainage of 6000 cc of serous fluid with negative culture and normal chemical-physical examination. Both US and TC scan documented the complete resolution of hydronephrosis and disappearance of the cystic lesion, along with normalization of blood test (Figure 2). After 2 days the drainage was closed and the bladder catheter removed. An episode of urinary retention occurred, with relapse of liquid drainage and increased creatinine concentration on drainage (55 mL/min), confirming the connection of the cyst with the urinary tract. US confirmed an acute urinary retention, and a bladder catheter was re-positioned, with start of therapy with silodosin. After a multiple-session ethanol sclerotherapy the patients was discharged, and scheduled for urological follow up.
Conclusion: Renal cysts (RC) are frequently diagnosed in about 10% of the general population, often as incidentaloma, and usually do not require treatment. Further assessment is needed in the presence of associated symptoms/signs due to complications in about 8% of cases. The management relies on accurate, comprehensive and multidisciplinary evaluation, as soon as even early and mild symptoms/signs develop, suggesting potentially lethal complications. More and more often acute, complex and critical patients are populating the internal medicine wards, and internists are called to respond to this multi-level challenge.

SIDE EFFECTS OF LONG-TERM LITHIUM THERAPY: A CASE REPORT OF IATROGENIC HYPERPARATHYROIDISM AND NEPHROGENIC DIABETES INSIPIDUS

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Background: Lithium is a mood stabilizer and the first-line therapy for bipolar disorder. However, long-term lithium therapy can lead to severe endocrine and renal complications. Lithium enters the cells of the collecting duct through sodium-channels (ENaC) and inhibits the action of antidiuretic hormone (ADH) inducing nephrogenic insipidus diabetes. Furthermore, lithium inhibits calcium-sensing receptors and, when administered chronically, can lead to parathyroid hyperplasia or adenomas with manifestations identical to those of primary hyperparathyroidism.
Discussion: We present the case of a 78-years old female affected by bipolar disorder treated with lithium since 2017. The patient was admitted to the Intensive Care Unit (ICU) in a comatose state secondary to hypernatremia. She underwent endotracheal intubation and received intravenous hydration alongside the discontinuation psychiatric medications.
The following investigations were performed: coltural examinations on cerebral spinal fluid, blood and urine, all negative for infections, and cerebral MRI which showed previous subcortical ischemic lesion and pontine hyperintensity indicative of pontine myelinolysis.
After regaining consciousness, the patient was extubated and transferred to our ward. She appeared agitated, confused and partially cooperative with a depressed mood and psychomotor restlessness lithium therapy was therefore re-introduced.
After restoration of lithium therapy, we assisted to a severe worsening of laboratory tests: serum creatinine increase (1,89 mg/dL), hypernatremia (154 mmol/L) and hypercalcemia (13,6 mg/dL), even if lithium serum-concentration was lower than normal value (0.31 mmol/L v.n. 0.50 – 1.20). Lithium therapy was discontinued in suspicion of an iatrogenic effect and aggressive intravenous hydration was started.
To further investigate hypernatremia, we tested urinary sodium (277 meq/24h), plasma osmolality (305 mOsm/kg) and urinary osmolality (167 mOsm/kg): considering hypotonic urine, diabetes insipidus was suspected. Due to advanced patient's age and poor compliance, water deprivation test was not practicable. So, we measured copeptin serum-concentration, showing an elevated value (60,2 pmol/L, normal value less than 12.5 pmol/L), indicative of nephrogenic diabetes insipidus.
Amiloride was administered at a dose of 5 mg/day. Thiazide diuretics were excluded as, although they can lower serum sodium, they may also increase plasma calcium levels. Gradually, sodium serum concentration decreased.
Concerning the founding of hypercalcemia, a paraneoplastic etiology was firstly ruled out by performing an FDG-PET scan which showed no evidence of neoplastic uptake. Laboratory tests revealed high parathormone (PTH) levels and low vitamin D, indicative of primary hyperparathyroidism. Parathyroid ultrasound, scintigraphy and choline-PET scan were performed, and they confirmed parathyroid hyperactivity (adenoma vs parathyroid hyperplasia). High dose of cinacalcet was administrated. Due to lack of response on lowering hypercalcemia, we added low dose zoledronic acid, considering the patient's impaired renal function, resulting in normalization of serum calcium levels.
With the normalization of plasma sodium and calcium levels, renal function also returned to normal. Additionally, the patient appeared more lucid and responsive. However, memory deficits and perseverative thinking persisted. Lithium was permanently discontinued, and alternative treatment was initiated with sertraline, pregabalin, duloxetine, and quetiapine resulting in a moderate improvement in mood stability.
Conclusion: This case illustrates potential side effects of long-term lithium therapy, including renal failure, hypernatremia due to nephrogenic diabetes insipidus, and hypercalcemia secondary to primary hyperparathyroidism. Notably, these complications occurred despite the patient's serum lithium levels were not above the therapeutic range.
Our patient was treated with aggressive hydration, cinacalcet, zoledronic acid and amiloride, leading to normalization of serum creatinine, sodium, and calcium levels.
In conclusion, while lithium remains a first-line treatment for bipolar disorder, its long-term use may lead to serious adverse effects. Therefore, it is essential to regularly monitor blood tests, in particular renal function and serum electrolyte levels, in patient who takes chronic lithium therapy.

OBESITY IS ASSOCIATED WITH A HIGHER GLUCOSE-INDUCED SECRETION OF THE INTESTINAL HORMONE NEUROTENSIN

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Preclinical studies have demonstrated that neurotensin (NT), a peptide hormone released by intestinal N cells that promotes intestinal fatty acid absorption, inflammation, and insulin resistance, is involved in the development of obesity and its complications. Accordingly, higher fasting levels of pro-neurotensin

(pro-NT), a stable NT precursor fragment produced in equimolar amounts relative to NT, have been found in individuals with cardiometabolic disorders, including obesity, type 2 diabetes, and hepatic steatosis. Preclinical evidence also suggests that luminal glucose may stimulate NT release via a sodium-glucose transporter 1 (SGLT-1)-dependent mechanism. Since we have previously found that individuals with obesity exhibit a higher abundance of SGLT-1 in the duodenum compared to normal-weight individuals, it is plausible to hypothesize that subjects with obesity show an augmented NT secretion in response to oral glucose intake. To test this hypothesis, we studied 13 non-diabetic participants who underwent comprehensive anthropometric and biochemical assessments, including a 75 g oral glucose tolerance test (OGTT) with blood sampling at 0, 30, 60, 90, and 120 minutes for glucose, insulin, and pro-NT measurements. Participants were classified based on the presence or absence of obesity (defined as a BMI ≥30 kg/m^2) into two groups: obese (OB, n=7; M/F=3/4; age=51±10 years; BMI=33±3 kg/m^2) and non-obese (noOB, n=6; M/F=2/4; age=47±12 years; BMI=25±2 kg/m^2). OB subjects exhibited a worse metabolic profile, including higher levels of total cholesterol, triglycerides, 2-hour post-load glucose and insulin, and lower HDL levels compared to the noOB group. Notably, circulating levels of pro-NT were significantly and progressively increased at 60, 90, and 120 minutes after the glucose load compared to baseline in OB subjects. In contrast, no significant changes in pro-NT levels during OGTT were observed in the noOB group. Furthermore, the area under the curve (AUC) for pro-NT during OGTT was significantly higher in OB subjects compared to the noOB group (376.4±60 vs 289.9±57; P=0.04). Next, we investigated whether exposure to high glucose (HG) directly induces intestinal NT secretion in OB subjects. Duodenal mucosa specimens, obtained during upper gastrointestinal endoscopy from 3 OB subjects (M/F=1/2; age=43±21 years; BMI=37±7 kg/m^2) and 4 noOB subjects (M/F=3/1; age=46±22 years; BMI=25±4 kg/m^2), were cultured in the presence of HG (50 mM) or mannitol (50 mM), used as a hyperosmolarity control, for 8 hours. Exposure to HG resulted in a significant 1.5-fold increase in pro-NT release in the culture medium of duodenal specimens from OB subjects compared to mannitol-treated controls (P=0.04). By contrast, no significant changes in pro-NT release were observed in the noOB group. In conclusion, these findings demonstrate that obesity is associated with enhanced glucose-induced secretion of the gut hormone NT, offering new insights into the pathogenesis of obesity-related disorders.

INSUFFICIENT WEIGHT LOSS AFTER BARIATRIC SURGERY: ROLE OF LIVER HISTOLOGY AND GENETIC SUSCEPTIBILITY

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Background: Obesity affects over 890 million people globally (WHO 2022), with a prevalence of 11.5% in Italy. Bariatric metabolic surgery (BMS) is the most effective long-term weight loss strategy, yet a substantial proportion of patients experience insufficient weight loss (IWL), sometimes requiring revisional procedures. IWL is driven by multiple factors, including male sex, high preoperative BMI, metabolic comorbidities, psychological factors, and poor follow-up. Emerging evidence suggests that genetic variants, particularly those in the Insulin Receptor Substrate 1 (IRS1) gene—a key mediator of insulin signaling—may influence weight loss outcomes. Specifically, the IRS1 rs2943641 variant has been associated with insulin resistance, abdominal obesity, and differential responses to dietary fat intake, with the C allele linked to higher body fat and the T allele appearing protective. The impact of liver-related comorbidities—particularly metabolic dysfunction-associated steatotic liver disease (MASLD) and fibrosis—on insufficient weight loss (IWL) after BMS remains unclear, as does the specific contribution of IRS1 variants. This study aims to investigate the prevalence and predictors of IWL in a cohort of bariatric patients with intraoperative liver biopsy and IRS1 genotyping.
Material and methods: This retrospective study included consecutive patients who underwent BMS at Policlinico Hospital of Milan between January 2008 and December 2023, with available intraoperative liver biopsy and weight data at 12–18 months. Baseline anthropometric, clinical, and biochemical data were collected. Insufficient weight loss (IWL) was defined according to Reinhold criteria as either <50% excess weight loss—calculated as the percentage of weight lost relative to excess weight, defined as the amount above the weight corresponding to a BMI <25 kg/m^2—or a postoperative BMI >35 kg/m^2. IWL was assessed at 12–18 months, the expected peak period of weight loss. MASLD (>5% steatosis), borderline MASH (NAFLD Activity Score 3-4), MASH (NAFLD Activity Score ≥5), and significant or advanced fibrosis (fibrosis stage ≥2 or ≥3, respectively) were defined histologically. Genotyping of the IRS1 rs2943641 variant was performed using the TaqMan allelic discrimination assay.
Results: A total of 308 patients were included (77.9% female; median age 44 years [IQR 37–50]; median BMI 42.1 kg/m^2 [IQR 38.8–46.9]); 143 (46.4%) underwent gastric banding, 130 (42.2%) gastric bypass, and 35 (11.4%) sleeve gastrectomy. Liver histology revealed MASLD in 260 patients (84.7%), borderline MASH in 107 (34.8%), definite MASH in 50 (16.3%), significant fibrosis in 23 (7.5%), and advanced fibrosis in 5 (1.6%). The prevalence of insufficient weight loss (IWL) at 12–18 months was 29.5%. IWL was significantly more frequent among patients who underwent gastric banding (75.8%) compared to those who received gastric bypass (23.1%) or sleeve gastrectomy (1.1%) ($p < 0.001$).Compared to patients without IWL, those with IWL had a higher preoperative BMI (median 46.3 vs 40.9 kg/m^2, $p < 0.001$), a greater prevalence of hypertension (54.1% vs 29.5%, $p = 0.008$), and higher rates of significant (12.1% vs 5.6%, $p = 0.048$) and advanced fibrosis (4.4% vs 0.5%, $p = 0.013$). No significant differences were observed in the prevalence of MASLD, MASH, or other metabolic comorbidities. IRS1 genotyping was available for 109 of the 308 patients. Compared to those without IWL, patients with IWL were significantly less likely to carry the IRS1 rs2972146 T allele (78% vs 95%, $p = 0.009$). In multivariable analysis (adjusted for sex, age, hypertension, and significant fibrosis), both higher preoperative BMI (OR = 1.22 per kg/m^2, 95% CI: 1.11–1.34, $p < 0.001$) and undergoing gastric banding (compared to sleeve or bypass; OR = 16.61, 95% CI: 3.79–72.87, $p < 0.001$) were independently associated with IWL, while carrying the IRS1 rs2972146 T allele remained significantly protective (OR = 0.18, 95% CI: 0.04–0.81, $p = 0.025$).
Conclusions: In this well-characterized bariatric cohort with integrated liver histology and genetic profiling, IWL was highly prevalent, affecting nearly one-third of patients at 12–18 months. Gastric banding and higher preoperative BMI were independently associated with IWL, while liver-related and metabolic comorbidities were not. Notably, the IRS1 rs2972146 T allele—linked to insulin signaling and adiposity regulation—was independently protective against IWL, suggesting that carriers of the C allele may require closer monitoring due to reduced weight loss response. These findings highlight the importance of genetic background, particularly insulin signaling, in shaping weight loss outcomes and support a precision medicine approach to bariatric patient selection and follow-up.

PREVALENCE AND RISK FACTORS OF UNDIAGNOSED LIVER FIBROSIS IN THE GENERAL POPULATION OF THE VENETO REGION: RESULTS FROM THE LIVERSCREEN VENETO PROGRAM

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Background: and Aims: Chronic liver disease (CLD) causes a substantial healthcare burden. CLD is usually asymptomatic in early stages and therefore is usually diagnosed in advanced stages, when cirrhosis and its complications are already established and available treatments are less effective. Therefore, a strategy for the screening of CLD is a relevant unmet need. The aim of our study was to assess the prevalence and risk factors of CLD with liver fibrosis in a cohort of individuals from the Veneto region.
Method: From October 2020 to January 2025, 3,003 subjects resident in Veneto older than 40 years, without history of CLD, active malignancies or severe extrahepatic diseases were included in the study. During the first evaluation, demographic and clinical data were collected, including alcohol consumption and metabolic risk factors. Standard lab parameters (blood count, transaminases, albumin, cholesterol, triglycerides) were also collected. Liver fibrosis was assessed by liver stiffness measurement (LSM) using vibration controlled transient elastography (Fibroscan®, Echosens, France). Subjects with LSM ≥8kPa, and/or ALT≥1.5 the upper normal limit were referred for a second evaluation of liver disease.
Results: Mean age was 58.7±8.8 years, 59% were women. Most subjects had at least one metabolic risk factor (38.1%), including obesity (12.5%), metabolic syndrome (13.0%), type 2 diabetes [T2D] (2.2%), alcohol consumption exceeding the limit of 14 UA for women and 21 UA for men (3.3%). The prevalence of LSM≥8kPa was 4.3%, LSM≥10kPa was 2.1% and LSM≥15kPa was 0.7%.

Prevalence of patients with ALT≥1.5 the upper normal limit was 2.1%). At multivariate analysis, age (OR 1.03, 95% CI 1.01-1.06, p=0.003), female sex (OR 0.63, 95% CI 0.43-0.91, p=0.015) and BMI (OR 1.19, 95% CI 1.15-1.24, p<0.001) were found to be independent predictors of LSM≥8 kPa, while age (OR 1.05, 95% CI 1.02-1.09, p<0.001), BMI (OR 1.21, 95% CI 1.16-1.27, p<0.001) and high-risk alcohol consumption (OR 2.42, 95% CI 1.00-5.84, p=0.050) were found to be independent predictors of LSM≥10 kPa. Two-hundred and seventeen patients (7.2%) had criteria for a second evaluation, but only 196 (90.3%) were performed (mainly due to patients' refusal). At the end of the second evaluation, a steatotic liver disease was confirmed in 101 patients (51.5%) and ALD in 25 patients (12.8%).
Conclusion: In the population of the Veneto Region there is a high prevalence of undiagnosed liver fibrosis mainly related to steatotic liver disease due to metabolic risk factors and/or high-risk alcohol consumption. A strategy for early detection of liver fibrosis in high-risk population could help reducing the burden of CLD.
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HIGHER CIRCULATING LEVELS OF THE GUT-DERIVED HORMONE FGF19 CONFER CARDIOVASCULAR PROTECTION

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Growing evidences have suggested the important role of several intestinal hormones in regulating cardiovascular health. Fibroblast growth factor 19 (FGF19) is an endocrine hormone secreted by ileal enterocytes in response to lumen bile acids, exerting several beneficial effects on energetic homeostasis, and cardiovascular system. Lower circulating levels of FGF19 have been found in subjects with type 2 diabetes, and cardiovascular organ damage. However, it remains to be ascertain whether the association between reduced levels of FGF19 and cardiovascular diseases (CVDs) is independent of cardio-metabolic risk factors. To address this issue, we examined 77 non-diabetic subjects, who underwent to a detailed medical history, anthropometric and biochemical characterization including a 75 g oral glucose tolerance test. Fasting FGF19 concentrations were assessed on serum samples by using specific ELISA assay. Study participants were classified as having or not CVDs, defined as presence of coronary artery disease and/or cerebrovascular disease and/or peripheral arterial disease (35 subjects with CVDs and 42 subjects without CVDs). Subjects having CVDs were significantly older, and exhibited a worse cardio-metabolic risk profile with increased values of BMI, waist circumference, triglycerides and lower HDL cholesterol levels, in comparison to those without CVDs. Conversely, no difference in glucose tolerance status was observed amongst the study groups. Importantly, we found that individuals with CVDs have significantly lower circulating FGF19 levels, even after adjusting for age, sex and BMI (291±49 vs 120 ± 28 pg/ml, P=0.02). In a logistic regression analysis model including age, sex, BMI, lipid profile, blood pressure, and glucose tolerance status, higher fasting serum FGF19 concentrations were associated with a reduced risk of having CVDs (OR:0.66; 95%CI 0.45-0.95; P=0.03). In conclusion, our findings suggest that augmented circulating levels of the gut-derived hormone FGF19 confer a protection against CVDs regardless of other cardio-metabolic risk factors, and lay the basis for future studies aimed to explore FGF19 signaling as a potential therapeutic strategy for CVD treatment.

AORTIC GRAFT AND ENDOGRAFT INFECTIONS: A 20-YEAR RETROSPECTIVE OBSERVATIONAL STUDY

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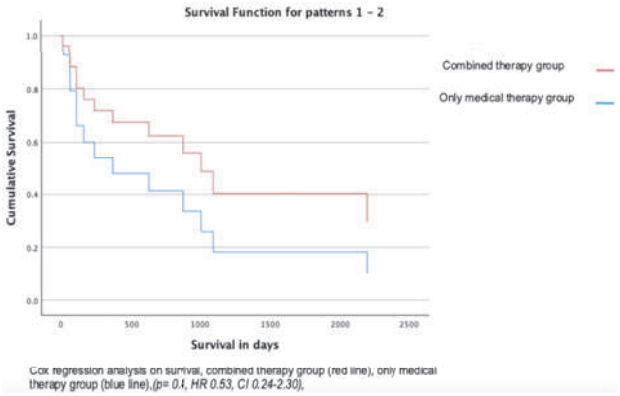
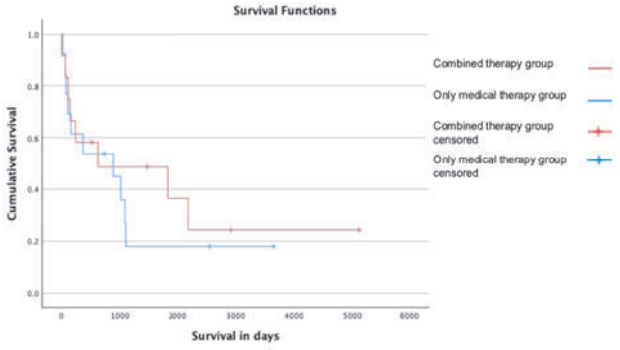
Background: Vascular graft and endograft infections (VGEI) are rare but severe conditions occurring in 1-5% of patients with a previous vascular graft or endograft implant, showing high mortality and morbidity rates. Diagnosis is challenging, as clinical presentation in often subtle and misleading. Whether Gram-positive bacteria have always been considered the leading pathogens, recently, an increase of Gram-negatives has been reported. Surgical removal of the infected graft and appropriate antibiotic therapy represent the cornerstone of treatment. However, when a complete removal is not feasible, long-term antibiotic therapy with or without conservative surgery remains the only treatment option. With regards to clinical and microbiological characteristics and long-term survival, few data are present in literature with conflicting results. To address this lack of evidence with the aim of providing insights on the topic we conducted a large study based on a 20 years' single center clinical experience on VGEI.
Methods: This is a single-center observational retrospective study, including all patients admitted for or with a diagnosis during hospital stay of VGEI between 2005 and 2024, at the Unit of Internal and Transplant Medicine, Monaldi Hospital, University of Campania "Luigi Vanvitelli". All patients fulfilling MAGIC criteria for suspected or definite intracavitary VGEI were included; exclusion criteria consisted in evidence of native infective aortitis or a concomitant aortic valve implantation. Collected data included: general data, blood chemistry and microbiological parameters, radiological data, surgical procedures, and mortality. Combined therapy was defined as any kind of surgical treatment together with antimicrobial therapy. Continuous variables were presented as median and interquartile range (IQR) and categorical variables as numbers and percentages. Continuous variables and categorical variables were analyzed with Mann-Whitney and chi-square test or Fisher test, respectively. A p-value ≤0.05 was established for statistical significance. Survival was estimated using Kaplan Meier curves and groups were compared with log rank tests. Finally, Cox regression analysis for survival was performed after propensity score adjustments.
Results: During the study period (2005-2024) 57 patients received a diagnosis of VGEI of these 37 patients met the inclusion criteria and were enrolled. Study subjects were predominantly male (91.1%) with a median age of 71 years. All baseline characteristics and outcomes are reported in Table 1. Regarding radiological diagnosis, 34 patient (91%) underwent at least one radiological investigation (PET-CT scan or contrast enhanced CT scan) with radiological criteria for graft infection met in 27 (79.4%) of them. From a microbiological standpoint, microbiological diagnosis was possible in 31 patients (86%) mostly (63%) from blood cultures, while negative-cultures VGEI accounted for 13.5% of the study population. VGEIs were caused by a single germ in 19 patients (51%), whilst polymicrobic infections were reported in 32% of the cases. Among monomicrobic infections, Gram-positives were the most common pathogens (73.7%) on the other hand, Gram-negatives were found in 26.3% of cultures. Comparing polymicrobic and monomicrobic infections, abdominal aortic graft (p=0.012), Gram-negative bacteria (p=0.001) and the presence of a fistula (p=0.019) were more common in polymicrobic infections whereas monomicrobic infections were more often associated with thoracic graft (p=0.012). Conversely, abdominal VGEIs were associated with Gram-negative infections (p=0.003). Regarding management, medical therapy alone was the treatment of choice for 51% of the study population whereas 49% of patients were treated with a combined therapy. A successful graft removal was obtained in 22% of patients in the combined therapy group, on the other hand, a palliative surgery approach was chosen in 39% of cases. Unfortunately, data regarding type of surgery weren't available in the remaining 39% of patients. Median duration of antibiotic therapy was 27 weeks (IQR 11.5-81) and median length of follow-up from diagnosis was 675.5 days (IQR 108-1723.7), with 18 (48.6%) patients followed up until death. Median survival time was 160 days [67.5-945] and mortality at 30 days, 1 year and 3 years was 7.7%, 42.6% and 72%, respectively. There were no statistically significant differences in survival time according to therapy approach (p=0.58), as well as VGEIs localization (p=0.75). Conversely, a shorter survival emerged in Gram-negative sustained infections compared with non-Gram-negative ones (p=0.04, HR 8.97, CI: 1.05-76.84).
Conclusions: In our study VGEIs remain a potentially fatal condition specially, when caused by Gram-negative pathogens. Influencing microbiological patterns, infected graft localisation should be considered when empirical antibiotic therapy is chosen, and an optimal management should prioritize microbiological diagnosis that may allow a targeted antibiotic therapy. In our experience a conservative approach did not lead to a lower survival, but further studies are needed to address this question.

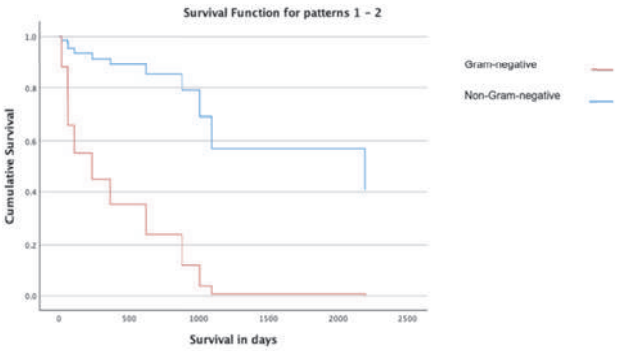
Characteristics	Combined therapy, n 18	Only medical therapy, n 19	P-value
Age, years, median [IQR]	71 [60-75,7]	70 [65-70,5]	0.79
Male gender, n (%)	15 (83%)	19 (100%)	0.10
Charlson comorbidity index, median [IQR]	**4 [1.5-4.5]**	**6 [3-8.25]**	**0.006**
Vascular Graft, n (%)	12(70%)	9 (56.2%)	0.45
Endograft, n (%)	5 (29,4%)	7 (43.7%)	0.45
Thoracic, n (%)	5 (27%)	6 (31,5%)	0.71
Abdominal, n (%)	13 (72%)	10 (52,6%)	0.71
Thoraco-abdominal, n (%)	-	3 (15,7%)	0.230
Time to infection, years, median [IQR]	3 [1-9]	2.3 [0,2-6]	0.45
Length of follow up, days, median [IQR]	568 [117-2095,7]	730 [90-1067.5]	0.76
Survival time, days, median [IQR]	189.4 [72.7-1514]	159.9 [67.5-945]	0.88
30-day mortality, n (%)	1 (8%)	1 (7%)	1
1-year mortality, n (%)	5 (41%)	6 (42%)	1
3-year mortality, n (%)	6 (54%)	12 (85%)	0.18



Cox regression analysis on survival, combined therapy group (red line), only medical therapy group (blue line), *(p= 0.1, HR 0.53, CI 0.24-2.30)*.



Log Rank test on Kaplan-Meyer, combined therapy group (red line), only medical therapy group (blue line) *(p=0.58)*



Cox regression analysis on survival, Gram-negative (red line), non-Gram-negative (blue line) *(p=0.04, HR 8.97, CI 1.05-76.84)*

OCCURRENCE AND MANAGEMENT OF OPIOID-INDUCED CONSTIPATION (OIC) IN PATIENTS WITH CANCER ADMITTED TO THE INTERNAL MEDICINE WARD. NEED TO BE AWARE

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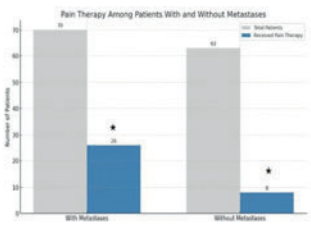
Background: Chronic opioid-based analgesic therapies are often necessary in neoplastic patients developing severe pain. OIC is a bothersome complication, can develop in 40-80% of cases and is the consequence of the agonist action of opioids on enteric μ-receptors. This step leads to increased colonic non-propulsive contractions, inhibition of water and electrolyte excretion, increased fluid absorption and anal sphincter tone with impaired defecation reflex, delayed gastrointestinal (GI) transit, and hardening of stools. OIC can become a major side effect with impact on quality of life (QoL) and risk of opioid therapy discontinuation. We assessed the impact of constipation in neoplastic patients receiving opioid-based pain therapy in internal medicine environment.
Method: We screened for neoplastic patients admitted in 2024. Constipation was defined according to Rome IV criteria, number of bowel movements per week, and Bristol stool scale for consistency (score 1-7).
Results: Among133patients (mean age74.1±SD10years),78were females (58.6%) and55were males (41.4%). The most prevalent cancers were from lung (N=23), urogenital tract (N=22), hematologic (N=21), GI (N=21), breast (N=17), and miscellanea (N=29). Metastases were present in70patients and absent in63patients. Pain therapy with opioids was necessary in34(25.6%) patients, and in67.6% by transdermal route. The most frequently used opioids were Fentanyl and oxycodone±naloxone/naltrexone. The prevalence of pain therapy was higher in patients with metastases than without metastases (37.1% vs.12.7% respectively, p=0.00025), irrespective of tumor type. Constipation per se was present in34patients (25.6%), while19patients (55.9%) had OIC. The prevalence of constipation was significantly greater in patients using opioid therapy (55.9% vs.15.2%, p<0.0001), with a trend especially with fentanyl (72.2% in fentanyl-based therapy vs37.5% in non-fentanyl group, p=0.091). By using a logistic regression model, regardless of age and sex, fentanyl use became a significant predictor of constipation (p<0.0001, OR=13.755). In the OIC group,11(60%) patients required both first-line laxatives (PEG) as well as the Peripherally Acting Mu-Opioid Receptor Antagonist (PAMORA) Naldemedine (Shionogi, Italy) which further improved OIC in63% of patients by one week. This finding was subsequently confirmed at post-discharge follow-up.
Conclusions: Patients with a wide range of tumors are continuously admitted to internal medicine wards, and several patients will require opioid-based analgesic therapies. Patients with metastases more often require pain therapy and develop OIC. Beside first-line therapy, which includes increased water and fibers intake, physical activity, as well lubricants, osmotic and stimulant laxatives, selective PAMORAs (e.g. naldemedine with the highest quality of evidence) must be part of therapy, and ameliorates OIC (1). This study is part of a larger ongoing survey on OIC involving internal medicine units and specialistic referral centers.



* p=0.00025 * p<0.0001

(1) Varrassi G, Casale G, De Marinis MG, Dentali F, Evangelista P, Gobber G, Lanzetta G, Lora Aprile P, Pace MC, Portincasa P, Radaelli F, Ungar A. Improving Diagnosis and Management of Opioid-Induced Constipation (OIC) in Clinical Practice: An Italian Expert Opinion. J Clin Med. 2024 Nov

DAL TRATTO GASTROINTESTINALE AL CERVELLO: UN RARO CASO DI ASCESSO CEREBRALE

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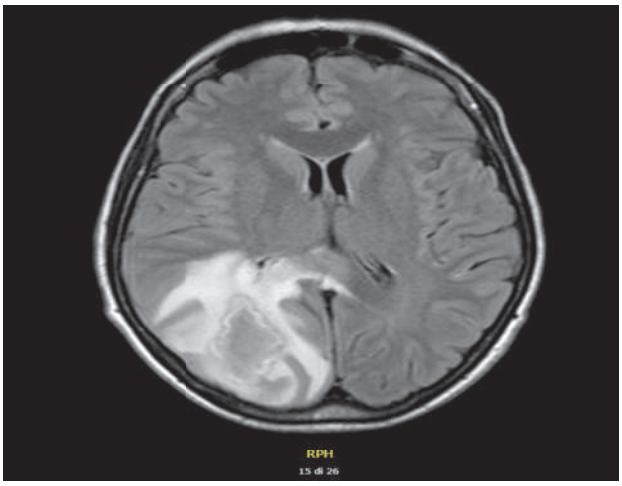
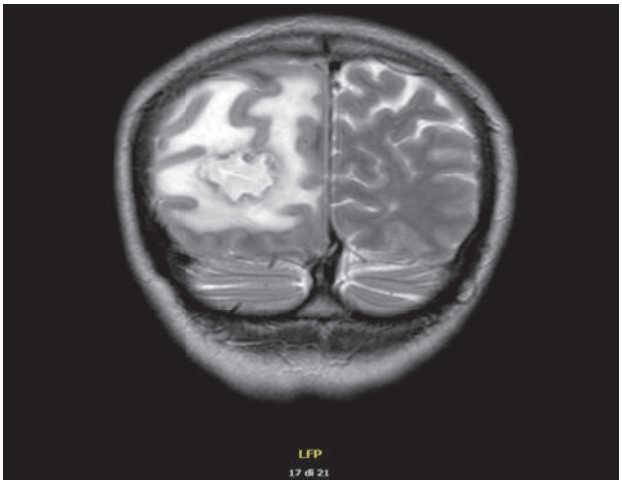
L'ascesso cerebrale è una raccolta circoscritta di materiale purulento all'interno del parenchima encefalico, risultante da un processo infettivo localizzato. La

sua eziologia prevede generalmente una diffusione batteriemica per contiguità (otiti, sinusiti ecc) o a distanza (endocarditi, sepsi ecc). In misura minore la genesi può derivare da pratiche chirurgiche e/o invasive.Il presente caso clinico descrive una paziente di 63 anni ricoverata presso la nostra U.O.C. per riscontro di polmonite acquisita in comunità nel contesto di nota cirrosi epatica scompensata secondaria a colangite biliare primitiva.Qualche giorno prima dell'evento respiratorio veniva riportato accesso presso altro nosocomio per l'insorgenza di crisi epilettiche con riscontro imaging di lesione cerebrale di non chiara natura e conseguente inizio di terapia anticomiziale.Tale lesione, localizzata in zona parieto-occipitale destra, inizialmente di sospetta natura eteroplastica, si è rivelata essere un ascesso cerebrale dopo esecuzione di RMN encefalo.Veniva pertanto iniziata antibioticoterapia ad ampio spettro (metronidazolo e ceftriaxone poi sostituito da meropenem), esami colturali (emocolture, conta cellule su liquido ascitico, lavaggio alveolo bronchiale, quantiferon, HIV, CMV DNA, urinocoltura) per identificare l'agente eziologico e strumentali (ecografia addome e TC total body) per l'eventuale focolaio flogistico. L'assenza di una causa infettiva manifesta, la negatività degli isolamenti colturali e l'assenza di un quadro imaging suggestivo, tuttavia, ci portava a rivalutare la storia clinica della paziente dalla quale è emersa recente legatura di varici esofagee per emorragia digestiva superiore (EDS) e successiva sclerotizzazione, portandoci a identificare tale procedura come causa eziologica dell'ascesso cerebrale. Durante la degenza, per recidiva di EDS da varici esofagee è stata sottoposta a TIPS (Transjugular Intrahepatic Portosystemic Shunt) con successiva revisione a causa di episodi di encefalopatia epatica post-TIPS. A seguito di rivalutazione multidisciplinare, per la complessità del quadro clinico e la fragilità della paziente, non veniva posta indicazione a trattamento neurochirurgico ma si confermava il prosieguo della sola terapia antibiotica e rivalutazione imaging seriata, con iniziale buona risposta clinica.La fragilità e la progressiva immunodepressione della paziente, secondaria alla cirrosi epatica scompensata e al trattamento farmacologico, nonostante la somministrazione di fattori di crescita, ha causato successive e secondarie frequenti infezioni urinarie e polmonari: Klebsiella pneumoniae (isolata in urinocoltura) e Aspergillus spp. (24.746 copie/ml di DNA Aspergillus in BAL). La coltura del BAL ha evidenziato, inoltre, la presenza di Candida glabrata, Pseudomonas aeruginosa, Staphylococcus aureus, Enterococcus faecium e Enterococcus faecalis. Per cui è stata praticata antibioticoterapia mirata con ceftazidima/avibactam, vancomicina, voriconazolo.Tale quadro clinico è stato ulteriormente complicato da un'insufficienza renale acuta di origine parenchimale, associata a farmaci, e con una componente pre-renale secondaria alla disidratazione e alla sepsi, e conseguente stato anasarcatico. È stato quindi intrapreso un trattamento di supporto con diuretici, albumina, paracentesi detentiva (08/11/2023) e ossigenoterapia, con scarso beneficio clinico e laboratoristico. Nonostante un approccio terapeutico multidisciplinare, la paziente ha mantenuto delle condizioni cliniche generali scadenti. La situazione è stata ulteriormente complicata da uno stato psichico alterato, con fasi di lucidità interrotte da periodi di sopore profondo, episodi di encefalopatia e dalla persistenza della lesione cerebrale.Considerata la malattia epatica avanzata (classe Child Pugh C 10), l'immunosoppressione, il progressivo decadimento delle condizioni cliniche generali e l'insorgenza di insufficienza multiorgano, la paziente è stata avviata a cure palliative presso Hospice per avvio di cure di fine vita. Questo caso clinico sottolinea l'importanza di considerare complicanze infettive rare ma gravi, come l'ascesso cerebrale, in pazienti sottoposti a sclerotizzazione di varici esofagee. La letteratura riporta, infatti, rari casi di ascesso cerebrale post trattamento endoscopico di varici esofagee, nonostante sia nota una percentuale di batteriemie post legatura o sclerotizzazione compresa tra l'1% e il 25% con una media dell'8.8%, che suggerisce pertanto la necessità di una profilassi antibiotica periprocedurali. E' necessario, pertanto, una marcata attenzione per una diagnosi precoce ed un intervento terapeutico tempestivo al fine di ridurre la morbidità e la mortalità associate.





NON-INVASIVE TESTS FOR LIVER FIBROSIS ARE INHACCURATE TO SCREEN FOR ADVANCED FIBROSIS IN GENERAL ADULT POPULATION

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Background: and aims: Chronic liver disease (CLD) is asymptomatic for many years before its clinical manifestation, which often occurs in the terminal stages of the disease and is therefore associated with high mortality. Therefore, screening and diagnosis is key to reduce the burden of CLD. Over the years, non-invasive tests based on blood tests have been developed to identify CLD with fibrosis. The use of these non-invasive tests, although recommended by the most recent guidelines, still has some limitations. The aim of this study was the comparison of the performance of AST to Platelet Ratio Index (APRI test), fibrosis-4 index (FIB-4) and NAFLD fibrosis score (NFS) to identify advanced fibrosis in a large cohort of healthy subjects from the Veneto Region.
Method: From October 2020 to January 2025, 3,003 subjects resident in Veneto older than 40 years, without history of chronic liver disease, active malignancies or severe extrahepatic diseases affecting short-term prognosis were included in the study. During the first evaluation, demographic and clinical data were collected, including alcohol consumption and metabolic risk factors. Standard lab parameters (blood count, transaminases, albumin, cholesterol, tryglicerides) were also collected and non-invasive tests were subsequently calculated. Liver fibrosis was assessed by liver stiffness measurement (LSM) using vibration controlled transient elastography (Fibroscan®, Echosens, France). LSM≥8.0 kPa was considered as the cutoff for significant fibrosis and compared to validated cutoffs for non-invasive tests (i.e. ≥0.7 for APRI, ≥1.3 for Fib-4 and ≥ -1.455 for NFS).
Results: Mean age was 58.7±8.8 years, 59% were women. Most subjects had at least one metabolic risk factor (38.1%), including obesity (12.5%), metabolic syndrome (13.0%), type 2 diabetes [T2D] (2.2%), hazardous alcohol consumption (>14/21 UA for women/men (3.3%). The prevalence of LSM≥8kPa was 4.3%,

LSM≥10kPa was 2.1% and LSM≥15kPa was 0.7%. Prevalence of patients with ALT≥1.5 the upper normal limit was 2.1%. Median value for APRI was 0.25 (IQR 0.20-0.32), for FIB-4 1.27 (IQR 0.99-1.63) and for NFS -1.97 (IQR -2.66,-1.30). All three non-invasive tests appeared not highly efficient in terms of discrimination of LSM≥8kPa (AUROC for APRI 0.58, 95% CI 0.53-0.64, p=0.001, AUROC for FIB-4 0.58, 95% CI 0.53-0.63, p=0.003, AUROC for NFS 0.65, 95% CI 0.61-0.70, p<0.001, see Table 1).
Conclusion: The non-invasive tests currently available to screen for CLD have poor accuracy in the general population. There is therefore the need to develop new biomarkers and/or their combination to screen for CLD in the general population.

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	APRI	FIB-4	NFS
Sensibility	3.9%	55.1%	3.9%
Specificity	99.2%	52.6%	98.6%
PPV	18.5%	4.9%	10.9%
PNV	95.9%	96.4%	95.9%
AUROC (95% CI)	0.58 (0.53-0.64)	0.58 (0.53-0.63)	0.65 (0.61-0.70)

Table 1. Accuracy of non-invasive tests for LSM≥8kPa (n=3,003)

	APRI	FIB-4	NFS
Sensibility	6.5%	50.0%	7.6%
Specificity	99.1%	83.8%	97.2%
PPV	50.0%	7.7%	16.1%
PNV	93.6%	93.6%	93.6%
AUROC (95% CI)	0.61 (0.53-0.68)	0.56 (0.48-0.64)	0.67 (0.61-0.73)

Table 2. Accuracy of non-invasive tests for LSM≥8kPa in patients with at least one risk factor (obesity, high risk alcohol consumption, diabetes, n=980)

THE PROGNOSTIC ROLE OF LIVERRISK SCORE IN PATIENTS WITH COMPENSATED CIRRHOSIS

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Introduction: The LiverRisk score is a non-invasive test that has been recently proposed for assessing the risk of compensated advanced chronic liver disease and liver-related events in patients without known chronic liver disease. Recently, its diagnostic and prognostic ability in tertiary settings was questioned.
Aim: The aim of this study was the evaluation of the ability of LiverRisk score in predicting first decompensating event and mortality in outpatients with compensated cirrhosis.
Material and methods: 271 outpatients with compensated cirrhosis and different etiologies evaluated at the Care Management Program of the University Hospital of Padova from 2004 to 2023 were enrolled in the study. LiverRisk score was calculated for each patient using biochemical parameters at inclusion. Patients were followed until death, liver transplantation or the end of follow up (October 2023).
Results: 271 outpatients (64% males, mean age 56.7±13.0 years, mainly HCV cirrhosis [48.7%], median MELD and CTP 8 and 6, respectively) were included in the study. During follow up, 60 patients developed ascites (22.1%, and 6 developed refractory ascites), 30 hepatic encephalopathy (11.1%), 17 variceal bleeding (6.3%). Fifty-six patients died (20.7%, 33 for hepatic cause) and 31 were transplanted (11.4%). At multivariable analysis (adjusted for age, MELD, varices at inclusion and effective etiological treatment), LiverRisk score was associated with development of decompensation (HR 1.08, 95% CI 1.02-1.14, p=0.015) and in particular with development of ascites (HR 1.07, 95% CI 1.02-1.13, p=0.012), but not with mortality (HR 1.06, 95% CI 0.96-1.18, p=0.245).
Conclusions: LiverRisk score is associated with a high risk of decompensation in patients with compensated cirrhosis, however it is not significantly associated with mortality.

ACTN1-RELATED THROMBOCYTOPENIA AND SEVERE HYPERHOMOCYSTEINEMIA: A CASE REPORT

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ACTN1-related thrombocytopenia (ACTN1-RT) is one of the most recently identified forms of inherited thrombocytopenia (IT) and is esteemed to be the fourth most frequent form of IT worldwide. ACTN1-RT is characterized by platelet macrocytosis and mild thrombocytopenia. Its risk of bleeding, either spontaneous or upon hemostatic challenge, is considered negligible. Therefore, ACTN1-RT is classified as a benign form of IT.
Hyperhomocysteinemia (HHcy) due to cystathionine β-synthase (CβS) deficiency is transmitted in an autosomal recessive fashion and is characterized by skeletal, ocular, neurological and thrombotic manifestations. Recurrent severe arterial and venous thromboembolism is the principal complication of HHcy and could manifest early in life with even a moderate elevation in blood homocysteinemia (Hcy).
In this report we describe the case of a 35 year-old man with a personal and familiar history of ACTN1-RT (confirmed by identification of heterozygous, exon 10, 1019 C>T ACTN1 mutation) without bleeding events who was sent to our attention in January 2024 for occurrence of severe HHcy. The patient exhibited mild thrombocytopenia (platelets count: 75-80.000 U/L), markedly elevated levels of serum Hcy (209 mmol/L) and underwent bilateral eye surgery for ectopia lentis. He never developed arterial or venous thromboembolic events. Angio-TC and ultrasound imaging were performed to exclude signs of significant vascular and connective tissue involvement and next-generation sequencing (NGS) resulted in two heterozygous CβS mutations (exon 10, 833T>C and exon 14 1224 G>A). The former was also identified in the proband's father while the latter in his mother and sister. However, none of his first-degree relatives exhibited vascular or connective tissue related clinical events nor severe HHcy. After supplementation of pyridoxine, normalization of homocysteine levels was achieved. By February 2025, the patient is asymptomatic and didn't develop any significant thrombotic or bleeding event. The CβS mutations detected in our patient were classified, respectively, as pyridoxine sensible pathogenetic (if present in homozygosity or compound heterozygosity) and probably pathogenetic. Therefore, they could likely explain the clinical phenotype. Interestingly, he never developed thrombotic events despite severe HHcy. Even though CβS-related HHcy may exhibit clinical heterogeneity we speculate that the concurrent presence of ACTN1-RT could have prevented the development of severe cardiovascular complications determining a milder than expected phenotype.
ACTN1 1019 C>T mutation is classified as likely pathogenetic and is associated with thrombocytopenia in the existing literature. The effects of ACTN1-RT related mutations on platelet aggregation are vastly unknown: ACTN1 encodes for one of the two nonmuscle isoforms of α-actinin but its role in platelet biogenesis is not well defined and does not appear to be responsible for clinically relevant bleeding in humans. However, megakaryocyte–specific α-actinin-1 knockout mice models exhibit impaired platelet function, decreased thrombus formation, and inhibited mitochondrial function. Moreover, the role of HHcy in atherosclerosis has been extensively studied and many mechanisms are involved (e.g.: endothelial cell damage, induction of a coagulant favorable state, vascular cell dysplasia) including platelet generation of thromboxane A2. In conclusion, we speculate the existence of a possible role of platelet disfunction in the prevention of major vascular events in the case presented. Therefore, this report could be used to advocate the need to better understand the biologic role of ACTN1 in platelet function to potentially expand the indications of existing antiplatelet drugs or to lead the development of novel therapies in the management of HHcy and other disorders.

THE PROGNOSTIC ROLE OF C-REACTIVE PROTEIN / ALBUMIN RATIO ON INCIDENCE OF MACE IN PATIENTS WITH CHRONIC HEART FAILURE

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Background: The prognostic role of serum albumin (SA) in patients with heart failure (HF) has been extensively studied. However, C-reactive protein (CRP) to SA ratio (CRP/SA) is emerging as a potential combined inflammatory marker to predict major adverse cardiovascular events (MACE). The aim of this study was to evaluate the long-term prognostic value of the CRP/SA ratio

in predicting MACE in a population of outpatients with chronic HF.
Methods: This retrospective analysis included 500 patients with a diagnosis of chronic HF. The CRP/SA ratio was calculated by dividing the CRP value by the serum albumin value, and the study population was diveded according to median value of CRP/SA ratio (1.19) into two groups: CRP/SA < 1.19 (n = 249) and CRP/SA ≥ 1.19 (n = 251). During a median follow-up of 5.2 years, MACE (non-fatal ischemic stroke, non-fatal myocardial infarction, coronary revascularization or coronary artery bypass grafting, and cardiovascular death), and all-cause mortality were assessed.
Results: The study population had a MACE incidence of 3.6 events/100 patients/year; Patients with CRP/SA ≥ 1.19 had a MACE incidence of 5.9 events per 100 patient-years, compared to 1.2 events per 100 patient-years in those with CRP/SA < 1.19 (p < 0.001). Multivariate analysis confirmed that CRP/SA ≥ 1.19 was associated with an approximately 6.5 times increased risk of MACE (HR 6.513, CI 95% 3.928 – 10.797; p<0.001). In addition, use of SGLT2i, statins and a reduction of 1 mg/dl of uricemia were associated with a reduction of risk of MACE of: 62%, 57% and 17%, respectively. While, a history of chronic kidney disease (CKD) and a ten years' increase of age were independently associated with a higher risk of MACE, respectively by 2.35 and 24%.
Conclusions: The CRP/SA ratio is confirmed to be a powerful prognostic marker in patients with chronic heart failure, associated with a significantly increased risk of MACE. Its use could improve risk stratification and enable more personalized treatment in outpatient settings.

CAPNOCYTOPHAGA CANIMORSUS SEPSIS IN AN IMMUNOCOMPETENT PATIENT: A CLINICAL CHALLENGE

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Capnocytophaga canimorsus is a fastidious gram-negative bacillus that is part of the normal oral microbiota of up to 74% of dogs and 57% of cats. Despite its commensal nature in animals, it can cause severe human infections, especially in immunocompromised patients, following bites, scratches, or even close contact with animals.
Human infections are rare, with an estimated incidence of 0.5 to 0.67 cases per million people yearly. Clinical manifestations can range from mild flu-like symptoms to septic shock, meningitis, endocarditis, or DIC.
A 58-year-old woman presented to our Emergency Department after three days of progressive confusion, generalized weakness, and dizziness. Past medical history included right nephrectomy for renal carcinoma (2015), bronchial asthma treated with inhaled corticosteroids and bronchodilators, appendectomy and active tobacco use (15 cigarettes/day). She denied allergies and G6PD deficiency. No clinical or laboratory evidence of immunodeficiency was found.
On admission, the patient was febrile (38°C), hypotensive (BP 90/65 mmHg) and appeared confused. Initial laboratory results showed mild neutrophilic leukocytosis, marked thrombocytopenia (platelet count 43,000/mm^3 on citrate), elevated inflammatory markers (CRP 298.6 mg/L, PCT 24.3 ng/mL), and renal impairment (creatinine 1.31 mg/dL, eGFR <45 mL/min/1.73 m^2). Broad-spectrum empirical antibiotic therapy with intravenous piperacillin-tazobactam was promptly initiated after blood cultures were drawn.
Imaging studies, including chest X-ray, abdominal ultrasound, and transthoracic echocardiography, showed no signs of localized infection. After four days of incubation, three sets of blood cultures subsequently grew Capnocytophaga canimorsus. Upon re-questioning, the patient recalled a minor bite from her household dog on her left hand approximately 7 days prior to symptom onset. The wound was healing well at the time of examination, with no signs of local inflammation.
The patient's clinical condition improved with continued antibiotic therapy and hemodynamic stability was achieved within 24 hours and laboratory values gradually normalized. Platelet count began to recover by day six. She completed an 8-day course of antibiotics and was discharged in fair general condition with outpatient follow-up.
This case illustrates that although Capnocytophaga canimorsus is classically associated with severe infections in asplenic or immunocompromised individuals, it can also lead to severe sepsis in immunocompetent patients. Its pathogenicity is partly due to its ability to evade host immune defenses by degrading immunoglobulins and resisting phagocytosis.
Diagnosis is frequently delayed because the organism requires enriched media and CO_2 incubation and may take up to 14 days to grow in standard blood culture systems. This diagnostic challenge highlights the need for high clinical suspicion, particularly in the context of recent animal exposure.
The absence of overt local wound signs and the patient's intact immune status can be misleading. Early empirical antimicrobial therapy with a beta-lactam/beta-lactamase inhibitor combination likely contributed to the favorable clinical outcome. Therefore, timely initiation of broad-spectrum antibiotics remains a cornerstone of management in patients with systemic signs of infection and a history suggestive of zoonotic exposure. A thorough anamnesis, including pet contact, is essential in diagnosing sepsis of unknown origin.

ACQUIRED ANGIOEDEMA ASSOCIATED WITH B-NON HODGKING LYMPHOMA: A CASE REPORT

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Introduction: Acquired angioedema (AAE) is a rare disease, partially also due to underdiagnosis. Clinical manifestations consist in angioedema affecting the skin, the gastrointestinal tract and the upper airways. The first episode happens at a median age of 60 years and no family history is reported. In this disorder C1 inhibitor (C1-INH) activity is thought to be reduced due to its consumption or its neutralization by autoantibodies. An associated disorder is detected at the presentation, or it develops thereafter, in almost 80% of cases. The most common etiologies are hematological neoplasms. Its treatment relies upon on-demand drugs targeting kallikrein-kinin pathway and long-term prophylaxis along with treatment of the associated etiology. However, most of the indicated therapies are off label and the optimal management strategy is not established in most cases.
Case report: In October of 2022 a 60 year old woman was sent to our attention for lymphocytosis and a history of recurrent angioedema.
From November of 2021 a history of recurrent, severe angioedema episodes involving the upper airways and requiring observation in intensive care unit was reported. No significant comorbidities nor allergies were present. Family history of angioedema was absent. However, preexisting transient lymphocytosis (5.000 u/L) and monocytosis (1,400 u/L) were reported.
The initial diagnostic work-up showed only relative lymphocytosis, hypogammaglobulinemia (IgG: 533), elevated beta-2-microglobulin (3.98 mg/dL) and type I cryoglobulinemia. C1-INH levels (0.08 mg/dL) and activity (22%) were reduced and C4 was depleted (< 15.4 mg/dL). Lymphocyte flow-cytometry on peripheral blood was performed and showed clonal expansion of CD10-, CD5-B lymphocytes. Abdomen echotomography was negative for organomegalies and lymphadenopathies. Serology for HIV, HBV and HCV were negative too. TC scan resulted negative for relevant lymphadenopathies and pathological masses while bone marrow was compatible with marginal lymphoma.
After multidisciplinary discussion, from April to July of 2023 a total of 8 doses split into 2 cycles of IV Rituximab were administered. Treatment was well tolerated, and clinical and flow-cytometric response was obtained. Moreover, an increase in C1-INH and C4 levels occurred. Contextually, prophylaxis with tranexamic acid was started.
During follow-up, no further episodes of severe entity occurred, C1-INH levels remained stable and peripheral blood lymphocyte flow-cytometry was confirmed negative for clonal restriction of B lymphocytes.
However, two mild recurrences occurred when prophylactic treatment was interrupted. On both episodes, C4 levels returning to the reference levels in about 1 month after resolution were observed. Interestingly, the last recurrence was anticipated by C4 levels decreasing roughly two weeks before. Unfortunately, C1-INH measurement during acute attacks was not available.
From August 2023, the patient underwent radical mastectomy, axillary lymphadenectomy and subsequent hormonal therapy for invasive ductal carcinoma. The patient is still in follow-up, in hematological and oncological response and didn't show new recurrences.
Discussion and conclusions: In the case presented the existence of an associated condition was mainly suggested by epidemiological awareness of the high prevalence of Non-Hodgkin Lymphomas among AAE patients. This emphasizes the importance of keeping a high level of suspicion to detect and treat AAE associated conditions which in turn allows to reduce recurrences.
Reduced C1-INH and C4 levels were useful in establishing the diagnosis. Moreover, C1-INH activity increase was observed after treatment with IV Rituximab. Matched clinical and biochemical response is described only in a part of patients treated with IV Rituximab and could possibly reflect heterogeneity in terms of etiology and pathological mechanism. An increase in C4 levels was observed one month after the completion of the therapy. This trend was also observed in correspondence of angioedema recurrence during which C4 depletion was followed by a raise to the reference interval in roughly one month. Interestingly, the last recurrence of angioedema was anticipated by C4 consumption two weeks before. This finding could possibly suggest the potential

role of C4 levels as a predictor of recurrence.
We observed a good response to Rituximab. However, clinical trials are needed to establish an optimal therapeutic strategy. In our case Rituximab was proved to be effective but a role in the loss of immunosurveillance that eventually led to the development of breast cancer cannot be excluded. Moreover, two mild episodes of angioedema occurred during follow-up, raising possible doubts about the real long-term efficacy of treatment.

HROMBOCYTHEMIA ASSOCIATED WITH A NON-CANONICAL JAK2 MUTATION: A CASE REPORT

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Myeloproliferative neoplasms (MPNs) are hematologic malignancies involving the clonal expansion of myeloid lines in the bone marrow. Key genetic variations linked to MPNs include JAK2-V617F, JAK2 exon 12 mutations, MPL and calreticulin mutations. However, some patients with myelofibrosis (MF) and essential thrombocythemia (ET) are "triple negative" due to potential non-canonical mutations, as illustrated by the patient in this case-report.
In January 2024, a 23-year-old female presented at our Internal Medicine Division with elevated platelet levels discovered during routine blood tests. Her medical history showed good health, with only a paracetamol allergy and a past asymptomatic SARS-CoV-2 infection. Previous tests from 2018 to 2021 indicated normal platelet counts, but by January 2024, levels had risen to 540,000/μL. While her white blood cell count was slightly elevated, her hemoglobin was within normal limits, and she reported no bleeding symptoms or recurrent infections. C-reactive protein was negative, and iron balance was normal. Examinations, including abdominal and chest ultrasounds, showed no significant findings. Given the suspected MPN, tests for BCR/ABL, JAK2, MPL and calreticulin mutations were negative, though platelet levels had jumped to 600,000/μL, prompting a bone marrow biopsy. Histology indicated megakaryocyte hyperplasia and mild fibrosis, consistent with essential thrombocythemia. Next-generation sequencing revealed CBL 1227+4C>T and JAK2 3188G>A mutations. A diagnosis of essential thrombocythemia was confirmed, and low-dose antiplatelet therapy was initiated. By February 2025, the patient remained asymptomatic, with platelet levels at 540,000/μL.
In addition to driver mutations, the presence of other somatic mutations in other genes may be observed in MPN patients. Variations may affect genes involved in signal transduction (CBL, LNK/SH2B3), chromatin remodeling (TET2, EZH, IDH1/2, ASXL1, DNMT3A), RNA splicing (SF3B1, ZRSR2), and tumor suppression (TP53). The identification of these collateral mutations is important for prognosis; for example, in myelofibrosis, CBL mutations are associated with reduced overall survival after transplantation.
The CBL 1227+4C>T genomic variant (rs 201747825) is an intronic mutation that has been reported eight times in the ClinVar database as "benign". At the time of writing, this variant had only been reported as an "additional mutation" in one patient in a 2018 paper investigating therapeutic alternatives in juvenile myelomonocytic leukemia. However, it was not associated with any particular clinical events.
The JAK2 3188G>A mutation (R1063H) was first identified in 2005 in three U.S. patients with polycythemia vera. In 2016, it appeared as a compound mutation with JAK2 E816D in a patient with erythrocytosis and megakaryocyte atypia, indicating dysregulation of the JAK-STAT pathway. A 2018 Belgian-Romanian study found the mutation in 14 JAK2-V617F+ patients, mostly with essential thrombocythemia, suggesting inheritance in some cases. The mutation was also reported in a 2019 German patient with triple-negative myelofibrosis and in a 2023 Brazilian patient with essential thrombocythemia. A 2025 analysis identified 2042 carriers, while 2017 and 2020 studies noted its presence in individuals with idiopathic venous thrombosis and cryptogenic stroke. ClinVar classified R1063H as benign with 9 submissions.
Despite the plethora of reports on these two mutations, particularly in conjunction with the canonical ones, the concomitant presence of these two germline variations in patients with myeloproliferative diseases, remains largely anecdotal. This report might suggest further investigation to elucidate the potential implications of these variations in the pathogenetic mechanisms of patients lacking canonical mutations.

MONOCYTE DISTRIBUTION WIDTH (MDW) IN EARLY DIAGNOSIS OF SEPSIS

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Introduction: MDW measures the volumetric distribution width of monocytes, reflecting monocytic anisocytosis, and is detected using advanced hematological analyzers. Different studies have shown that an increased MDW value is associated with a higher risk of sepsis and that its combination with clinical parameters (such as qSOFA) and other biomarkers (CRP, PCT) can enhance diagnostic sensitivity and risk stratification capacity. Other advantages are its ease of measurement, its high negative predictive value (NPV) and the absence of correlations with demographic factors such as age, sex, or surgical conditions.
Rationale: Sepsis is a complex and potentially life-threatening syndrome which can lead to death. Early diagnosis is crucial to improving prognosis and reducing hospital management costs. For these reasons we will set up a prospective study in ED of Policlinico Universitario A. Gemelli on the role of monocyte distribution width (MDW) as a diagnostic biomarker for sepsis, highlighting its advantages, limitations, and potential clinical applications.
Metods: We will enroll patients over 18 years who are able to give informed consent. Patients with a suspected clinical condition will be asked for CBC (containing MDW). A cutoff value of 20 will be used to indicate sepsis positivity, as supported by most studies.
Expected Results: The primary endpoint is based on evaluating the diagnostic performance of MDW, while the secondary endpoints involve comparison with other markers such as PCT and PSP. Finally, we may repeat MDW measurements to assess its utility in guiding antibiotic therapy management.

ROLE OF PRESEPSIN IN MULTIMARKERS APPROACH FOR EARLY DIAGNOSIS OF SEPSIS

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Introduction: Sepsis is an exaggerated inflammatory response to infection, requiring early and accurate treatment. However, its diagnosis is challenging due to varied clinical presentations. A prospective study on Presepsin was conducted in the ED of Policlinico Agostino Gemelli. Presepsin (sCD14-ST) is a fragment of soluble CD14 released into the bloodstream by monocytes in response to infection.
Materials and methods: Patients over 18 years who were able to sign the informed consent were enrolled thanks to a venous blood sample in EDTA. We enrolled 216 patients from the emergency room, who were suspected of having sepsis.
Results: We classified patients In 86 with positive results in blood cultures in which 89,5% had psp >165 and 65,1% with pct> 0,5. On the other side we designated 130 patients with negative results in blood cultures whose 36 with sepsis diagnosis. In this group 94,4% had psp>165 and 86,1% pct>0,5. Regardless of blood cultures, biomarkers appear to be effective in identifying sepsis. Additionally, In the remaining 94 patients: 14 were true negatives with PSP < 165 and PCT < 0.5; 36 had PSP > 165 and PCT > 0.5 with sepsis diagnosis in ward; 45 patients had one of the two markers below the negative cutoff but the other one above. This is due to the different kinetics of the markers. These 45 patients had an evolving infectious condition.
Conclusions: Our study demonstrated higher sensitivity of presepsin. Finally, our evidence also suggests the complementarity of the two markers in the diagnosis of sepsis due to their high negative predictive value.

MULTIMARKERS APPROACH IN CHEST PAIN MANAGEMENT: THE PROMISING ROLE OF SUPAR AND SST2

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Introduction: Chest pain is a frequent cause of admission to the Emergency Department (ED). Troponin measurement (0-1h) and ECG tracing represent the gold standard for acute coronary syndrome (ACS) diagnosis. However, new biomarkers showed a promising role to predict cardiovascular risk. The aim of this study is to evaluate the introduction of a multimarkers approach in patients presented with chest pain in ED, focusing on their prognostic role in-

tegrated with the results of the second/third level tests subsequently performed.
Methods: This is a retrospective, single-center study, involving 158 patients (69 female and 89 male), older than 18 years, admitted to the ED of the "Policlinico A.Gemelli Hospital" with typical chest pain between July 2021 and April 2024. Exclusion criteria were pregnancy, dispnea, cardiopalm, inability to express an informed consent.
Data related to second/third level tests were collected in an Excel-database. A statistical analysis was conducted. Seven groups were identified, and a frequency analysis has been performed. Furthermore, a dedicated test was used to detect the eventual statistical relevance of the extrapolated data.
Results: Patients have been grouped in 7 categories based on the troponin value (positive, intermediated, negative), suPAR (> or < 2.9 ng/ml) and sST2 (> or < di 24.45 ng/ml). Our preliminary data suggest that increased sST2 and suPAR correlate with ischemic cardiac findings in second/third-line testing.
Conclusions: In the ED, the multimarkers approach could result in a quick discharge with a safe and rapid rule out or a prompt admission for patients who deserve investigation.

HORTON'S ARTERITIS COMPLICATED BY OPTIC NERVE ISCHEMIA IN A FEMALE PATIENT

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Introduction: Giant cell arteritis (GCA) is the most common large-vessel vasculitis in North America and Western Europe. It typically affects individuals over the age of 50 and primarily involves large vessels, particularly the aorta and its major branches.
The pathophysiology remains non completely understood, but it is believed that dendritic cells in the adventitia activate Th1, Th17, and Th21 lymphocytes, leading to the production of cytokines such as IFN-γ, IL-17, and IL-21. Among Caucasians, individuals carrying the HLA-DRB1*04 allele have an increased risk of developing the disease and its complications.
The clinical onset can be acute or insidious. Typical symptoms include headache, scalp tenderness (often preceding the headache by weeks) and jaw claudication. Systemic symptoms are also common: general malaise, fatigue, anorexia, weight loss, muscle stiffness and low-grade fever.
On physical examination, the temporal artery may be painful and appear dilated, nodular or indurated.
Affected individuals have increased risk of complications such as vision loss (in about 30% of cases, and permanent in 10–15% of them), myocardial infarction, cerebrovascular events, limb ischemia, aneurysms and dissections. GCA should be considered a medical emergency, prompt diagnosis and treatment are important to prevent irreversible sequelae.
The diagnostic work-up includes laboratory tests, with typically elevated ESR and CRP levels, and sometimes mild anemia or elevated liver enzymes. Temporal artery biopsy remains the gold standard for diagnosis and should be performed within two weeks of treatment initiation, taking a sample of adequate size. Histological findings typically include granulomatous inflammation with multinucleated giant cells near a disrupted internal elastic lamina or panarteritis with lymphocyte and macrophage infiltration.
Alternative diagnostic tools include ultrasound, CT, MRI, and FDG-PET, all recognized by the 2022 EULAR/ACR GCA classification criteria.
First-line treatment involves high-dose corticosteroids. Steroid-sparing agents such as methotrexate or tocilizumab may be considered as alternatives.
Case report: A 75-year-old woman presented with sudden-onset vision loss in the right eye. She also reported a pulsating bilateral temporal headache (more pronounced on the left), radiating to the jaw and face, with poor response to NSAIDs.
Past medical history included type 2 diabetes mellitus, coronary artery disease, arterial hypertension, episodes of paroxysmal supraventricular tachycardia and atrial fibrillation, mild-to-moderate mitral insufficiency, polymyalgia rheumatica, surgically treated breast cancer, previous dorsal basal cell carcinoma and allergy to quinolones. Her medications included apixaban 5 mg BID, atenolol 75 mg, flecainide 100 mg BID, metformin 1000 mg TID, and simvastatin 40 mg.
On physical examination, the left temporal artery was tortuous, swollen, pulsatile and indurated; the right temporal artery was also tortuous with slightly increased consistency.
Laboratory tests showed elevated CRP levels.
Suspecting anterior ischemic optic neuropathy secondary to GCA, high-dose intravenous corticosteroid therapy with Solumedrol 500 mg/day was initiated, followed by a gradual tapering regimen.
CT angiography of the supra-aortic vessels revealed: "distal wall irregularities of the right common carotid artery extending to the proximal segment of the external carotid… no evidence of intracranial aneurysms."
Visual field testing confirmed optic nerve ischemia.
A right superficial temporal artery biopsy confirmed the diagnosis of giant cell arteritis.
Discussion and conclusions: This case presents a clinical picture highly suggestive of giant cell arteritis, with typical clinical and laboratory features: sudden vision loss, pulsatile headache, poor response to NSAIDs and elevated CRP levels. These findings constitute a medical emergency that requires immediate therapeutic intervention—even before histological confirmation—to prevent irreversible visual loss and other complications.
First-line treatment involves high-dose corticosteroids (prednisone 1 mg/kg/day or equivalent), followed by gradual tapering based on clinical response and normalization of inflammatory markers.
Given the complexity of the patient's clinical picture, early introduction of steroid-sparing agents, particularly tocilizumab, should be considered. Tocilizumab has demonstrated efficacy in reducing relapses and enabling faster steroid tapering.
The diagnostic work-up should include, in addition to temporal artery biopsy, vascular imaging (ultrasound, CT angiography, MR angiography, or PET) to assess large vessel involvement, particularly the aorta and its main branches.
Close follow-up is essential to monitor treatment efficacy, potential steroid-related side effects, and the emergence of long-term vascular complications.

SEX-SPECIFIC DIFFERENCES IN HYPERTENSIVE URGENCIES

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Introduction: Within the spectrum of acute blood pressure (BP) disorders, hypertensive urgencies (HU) are characterized by the absence of acute hypertension-mediated organ damage (HMOD) and represent a common cause of Emergency Department (ED) admission. The impact of sex on clinical presentation, BP control, and HMOD is currently unknown.
OBJECTIVES. The aim of this study was to define sex-related differences in clinical presentation, BP control and HMOD prevalence, among individuals with HU.
Methods: In this prospective multicenter study, symptomatic patients with BP ≥180/110 mmHg admitted to six Italian EDs were enrolled and managed based on clinical presentation. Subsequently, they were evaluated at a Hypertension Centre for BP control and subclinical HMOD, within 72 hours.
Results: The study included 257 patients, with 52% women. The mean age was 59.7±14 years, with women significantly older than men (62.4±15 vs. 56.8±13 years; p = 0.002). Men were more often active smokers and showed higher rates of diabetes and obesity. They also exhibited higher diastolic BP at both ED admission and discharge, as well as elevated systolic and diastolic BP at the 72-hour follow-up. Male sex emerged as an independent predictor of both increased risk of HMOD, irrespective of the target organ, and poorer BP control 72 hours after ED discharge.
Conclusion: Men with HU exhibited higher BP values and poorer BP control at 72 hours compared to women. They also had a higher prevalence and greater severity of HMOD.

A RARE CASE OF ALLOPURINOL-INDUCED TOXIC EPIDERMAL NECROLYSIS

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Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are rare and severe mucocutaneous disorders that affect skin, oral mucosa, eyes, esophagus, mouth, pharynx, larynx and genitals. Causes include drugs, radiation therapy, infectious agents and immunization. They seem to be variants of the same disease with differing severities and are classified based on body surface area (BSA) involved: SJS<10%, SJS/TEN Overlap 10–30%, TEN>30%. We

present a case of a 72 years old female who has been under medication with allopurinol on medical advice. After 4 days of treatment, she had prodromal signs: malaise, rash, myalgia, fatigue, anorexia. After another 5 days she discontinued therapy with allopurinol due to the appearance of cutaneous lesions with burning and itching sensation, fever, pharyngodynia and dysphagia. For the persistence of symptoms, after 18 days, the patient got admitted in the Department of Internal Medicine of Catanzaro. She started developing clinical presentations after being treated with allopurinol, giving us a clue about allopurinol-induced TEN. On taking history, she didn't have such manifestations before, her family members didn't have any such problems, neither did she have any known autoimmune disease, allergy history, or active malignancy, nor did she have any significant drug history except antihypertensive medications. On clinical examination, multiple lesions were present which were hyperpigmented and reddish-purple target macules and papules over her face, trunk, back and upper limbs with involvement of > 30% BSA. The rash was erythematous with the presence of blisters and necrotic core along with the presence of the Nikolsky sign. In the oral cavity, there was hemorrhagic crusty erosion of the mucosa of lips and tip of the nose and also a whitish lesion over the dorsum of the tongue. Ocular involvement was represented by conjunctivitis. At the time of admission her vital signs were within normal range. On laboratory tests: Haemoglobin (Hb) 12.8 g/dl (Female: 12–16 g/dl), C reactive protein (CRP) 125 mg/l (Reference range: 0–5), Fibrinogen 572 mg/dL (Reference range: 200-400 mg/dL), Ferritin 820 ng/mL (Reference range: 15-150 ng/mL), Serum uric acid was 4.5 mg/dl (Reference range: 2.4-5.7 mg/dl). Other parameters were in the normal range. A peripheral intravenous line has been placed in areas of uninvolved skin. The patient underwent consultation with an ophthalmologist that highlighted conjunctival hyperemia, lid congestion and margin ulceration, trichiasis, peri-ocular discharge and crusting. Management of the patient was done with Methylprednisolone 40 mg/die intravenous for 10 days, Omeprazole 20 mg/die intravenous, administration of fluids through saline solution, irrigation of the eyes every hour, mouth washes frequently and application of a spray. Ocular involvement was treated with topical corticosteroids and tear substitutes. Concerning therapeutic drug monitoring and periodically improvement of the patient's health condition, she was discharged after 16 days of hospital stay with the recovery of skin and dysphagia. Laboratory tests at the discharged: Haemoglobin (Hb) 12.9 g/dl (Female: 12–16 g/dl), C reactive protein (CRP) 37 mg/l (Reference range: 0–5), Fibrinogen 380 mg/dL (Reference range: 200-400 mg/dL), Ferritin 420 ng/mL (Reference range: 15-150 ng/mL), Serum uric acid was 4.3 mg/dl (Reference range: 2.4-5.7 mg/dl). Differentiation of adverse skin reactions from skin disorders can be difficult. The most common drug reactions include penicillin in antibiotics, carbamazepine in antiepileptics and allopurinol. Clinical presentation may show around 4-28 days after administration of the drug. In our case, the patient was under medication with allopurinol for 9 days after which cutaneous manifestations were seen. Timely discontinuation of the culprit drug is the most important action to reduce morbidity. Attention to airway, hemodynamic stability, wound care and pain alleviation measures are required. Medical therapy includes corticosteroids, cyclosporine, intravenous immunoglobulin (IVIG), and TNF-α inhibitors. If not treated timely, SJS and TEN can result in fatal, life-threatening conditions. Improved clinical treatment and care have decreased the morbidity and mortality of SJS and TEN. Prompt recognition of the disease and cure of the patient by competent staff contribute to the successful treatment of these patients.

Fig. 1. Characteristic erythema and its extent on the day of admission to hospital

Fig. 2. Characteristic erythema and its extent after 10 days in the hospital

Fig. 3. Patient during the discharged

SEVERE OSTEOPOROSIS MIMICKING DIFFUSE SPINAL METASTASES ON MRI

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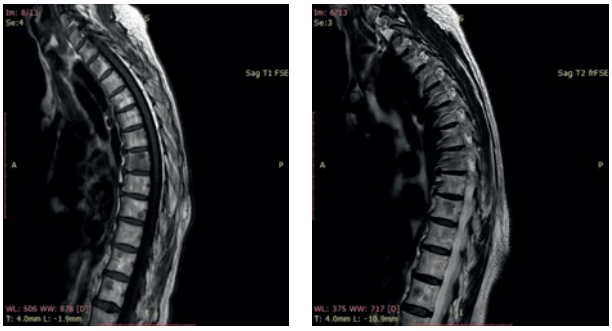
Introduction: Osteoporosis, characterized by reduced bone mass, is common but its presentation can be ambiguous. While MRI is sensitive for vertebral abnormalities, including metastases, certain patterns in severe osteoporosis involving microfractures or marrow changes can mimic neoplastic infiltration. We present a case where severe osteoporosis led to initial MRI findings highly suggestive of diffuse spinal metastases.
Case presentation: A 78-year-old female underwent a dorso-lumbar MRI following symptoms later attributed to Herpes Zoster. The scan revealed multiple vertebral body and posterior element anomalies with subtle T1/T2 hypointensity and STIR hyperintensity, along with a D7 wedge deformity. The reporting radiologist suspected diffuse spinal metastases. Laboratory tests (including tumor markers and bone metabolism markers) were unremarkable, with a bone scintigraphy showing only degenerative changes, negative contrast-enhanced CT scans of the neck/thorax/abdomen (noting only diffuse osteorarefaction), and a negative PET-CT scan. Bone densitometry (DXA) confirmed severe osteoporosis (Lumbar spine T-score: -3.4).
Discussion: This case highlights a significant diagnostic pitfall where severe osteoporosis presented with MRI findings suggestive of diffuse malignancy. The initial MRI report prompted an extensive lab and radiological workup, which turned out negative for neoplastic disease. This underscores that severe osteoporosis can cause diffuse vertebral signal abnormalities on MRI. Clinicians and radiologists must consider osteoporosis in the differential diagnosis of such findings, especially in elderly patients, to avoid misdiagnosis and unnecessary invasive procedures.



INTRAVITREAL TREATMENT WITH FARICIMAB IN PATIENTS WITH AGE-RELATED MACULAR DEGENERATION

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Background and aims: Age-related macular degeneration (AMD) is a multifactorial disorder that affects the macula leading to progressive visual loss. In developed countries AMD represents one of the primary causes of blindness among adults over the age of 60.
Faricimab is an intraocular treatment that neutralizes both the Vascular Endothelial Growth Factor A (VEGF) and Angiopoietin 2 thus stabilizing ocular vasculature ameliorating disease development and anatomical and clinical outcomes potentially for longer.
Intravitreal injection of VEGF inhibitors, has been associated with arterial thromboembolic events such as myocardial infarction and cerebrovascular accidents. Suggesting systemic adverse effects of these drugs.
Notably, numerous studies demonstrated that platelets are the main contributors to serum VEGF, which stimulates the formation of newest blood vessels. Different anti-VEGF treatments, such as bevacizumab, can be internalized by platelets, leading to an increased exposure to these treatments after platelet activation.
Cyclooxygenase 1 (COX-1) catalyses the production of a wide range of molecules, among these, thromboxane and prostaglandins. Moreover, persistent platelet activation and hyperreactivity are associated with thromboxane biosynthesis in several clinical settings.
There are conflicting reports in the literature indicating a possible correlation between COX-1 and VEGF. Most evidence demonstrated that, when COX-1 is highly expressed, we assist to a concomitant neovascularization generated by VEGF promoting pathological exudates in AMD and DME.
This study aimed at evaluating the effect of Faricimab administered in patients affected by AMD on intra-platelets levels of VEGF and COX-1.
Methods: In this study, we enrolled nine patients with AMD that underwent intravitreal treatment with Faricimab at baseline (T0) and after four months (T4).
All participants underwent clinical assessment and blood sampling. Platelets were isolated from platelet rich plasma and proteins were extracted for western blotting analysis.
Results: We observed a trend for a decrease in platelet's VEGF levels after 4 months of Faricimab treatment in all patients (p=0.063), except for two, where it increase. Similarly, COX-1 protein was reduced (p=0.031) except for the same two patients, where it increase. ΔVEGF and ΔCOX-1 (T4-T0) are directly correlated in all the patients (rho=0.734, p=0.024). Interestingly, the presence of SRPEF subretinal pigment epithelial fluid (SRPEF) was observed in these two patients, with a paradoxal increase in both platelet VEGF and COX-1.
Conclusions: Intravitreal Faricimab reduces intraplatelet levels of VEGF and COX-1 in our patient's cohort and the observed correlation between VEGF and COX-1 changes supports a potential mechanistic link between these mediators in modulating neovascularization.
Notably, patients with SRPEF – a key clinical sign for neovascular AMD – showing increased protein expression after Faricimab treatment, may represent a subgroup with suboptimal response to therapy. These findings underscore the need for larger scale studies to detect novel biomarkers of treatment response.

BACTERIAL LYSATE "LANTIGEN B" INDUCES PROLIFERATION OF B AND NK CELLS AND THE RELEASE OF RELATED CYTOKINES

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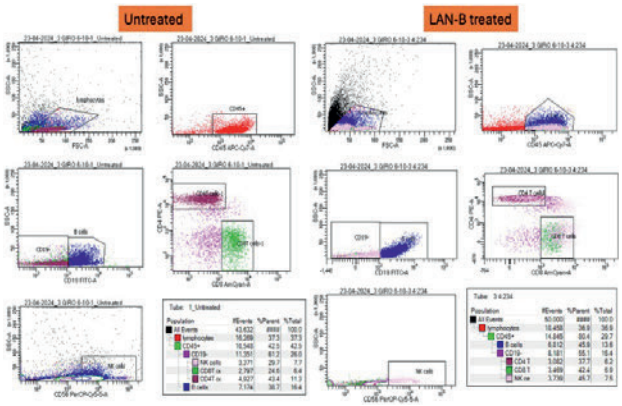
Background: Bacterial lysates (BLs) are medicines made from bacterial cells that are broken down and are intended to stimulate the immune system to recognize and fight infections. BLs are prescribed for the prevention of recurrent respiratory tract infections (RTIs) and, in general, almost all performed studies show that the number of RTIs and their severity decrease in BL-pretreated patients, without relevant side effects. Lantigen B (Lan-B), among all the commercially available lysates is one of the most interesting. Being administered sublingually, can directly stimulate the immune cells in the site of infections as demonstrated by numerous clinical trials.
Objectives: The present study aimed at exploring and evaluating the ability of Lan-B to influence the proportion of various lymphocyte subpopulations and to modulate the release of selected cytokines that play a pivotal role in determining immune reactions. Also, this work was focused on evaluating these effects at the identical concentrations used in previous human studies.
Methods: In this observational study PBMCs, from 7 healthy human donors, were isolated, cultured and incubated with Lan-B at 199.45 AU/mL. After incubation cells were resuspended with specific antibodies for the cytofluorimetric detection of cell surface phenotype using the following markers: CD45, CD4, CD8, CD16 and CD19. Consequently, cell culture supernatants were collected for the cytofluorimetric evaluation of cytokines concentration using LEGENDplexTM Human Inflammation Panel 1 (Figure).
Results: Significant changes in the proportions of both CD19+ and CD56+ cells were observed in Lan-B stimulated cultures compared to unstimulated ones. In particular, both B (CD19+) and NK (CD19-/CD56+) cells proportion significantly increased from 18.20% in untreated vs 45.27% in Lan-B-treated PBMC cultures (p=0.005).
Changes were observed in the proportion of various CDs in untreated vs Lan-B treated PBMCs, with an increase in CD19+ and in CD56+ cells. In this case, there is also an increase in CD8+ cells. Cytokines evaluation showed that, IL-1b, IFN-g, TNF-a, IL-17 and IL-18 are significantly increased whereas MCP1 significantly decreased upon Lan-B treatment. However, a trend for an increase of IL-12-p40, even though not significant, has been observed (p=0.052).
Conclusions: This study highlighted the role of Lan-B in the modulation of the immune system by activating the innate immune system, namely NK cells, as well as the adaptive immune system, which produced considerably modified cytokines indicative of a Th1-mediated reaction. These observations can support Lan-B's proven therapeutic efficacy. Following this first investigation, the activities of Lan-B dendritic cell maturation, epithelial cells, cytotoxic lymphocytes, and the immune response's specificity will need future investigations.



HEMOCHROMATOSIS: AN UNDETECTABLE CAUSE FOR AN "IDIOPATHIC" CEREBROSPINAL FLUID HYPOTHENSION SYNDROME?

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Since 2015, a 61-year-old male patient had experienced recurrent episodes of objective vertigo associated with prodromal nausea, vomiting, and diaphoresis, leading to a diagnosis of Ménière's disease managed with betahistine. Brain MRI performed at that time was unremarkable. In October 2024, the patient was urgently admitted for sudden onset of orthostatic, pressure-like headache unresponsive to NSAIDs. Neurological examination revealed bradypsychia, broad-based gait, hypoacusis, mild nuchal rigidity, and bilateral difficulty with finger-to-nose testing with eyes closed. Emergency blood tests were unremarkable, with normal electrolytes and negative neoplastic, viral, and autoimmune markers. Brain MRI showed bilateral subdural fluid collections, mild cerebellar tonsillar descent, and collapsed lateral ventricles suggestive of cerebrospinal fluid (CSF) hypotension. Spinal MRI identified a right-sided C5-C6 schwannoma causing bone erosion. The patient received supportive care with rehydration, paracetamol/caffeine combination, and enforced Trendelenburg positioning, without clinical improvement. A CT myelogram did not demonstrate any CSF-venous fistulas. Electromyography revealed mild, chronic neurogenic changes involving bilateral C7 and C8-T1 myotomes, and mild C5-C6 involvement. A lumbar epidural blood patch at L2-L3 was ineffective, while a cervical epidural blood patch at C7-T1 performed one week later resulted in symptom resolution.

In November 2024, the patient was readmitted with recurrent orthostatic headache, brief episodes of aphasia and dysarthria, intractable hiccups, and bradyphrenia. No apraxia or agnosia was observed. Emergency blood tests showed mild anemia and elevated serum ferritin (608 ng/mL) and fibrinogen levels. Cranial CT confirmed the persistence of bilateral subdural collections with subacute/chronic features and areas of recent bleeding. EEG revealed rare, nonspecific sharp theta waves in the bitemporal regions, prompting initiation of antiepileptic prophylaxis with valproic acid, resulting in clinical improvement. Corticosteroid therapy with dexamethasone was also administered. A PET-CT scan excluded the presence of tracer-avid lesions. Due to persistently elevated iron and ferritin levels, genetic testing for hereditary hemochromatosis was performed, revealing homozygosity for the HFE H63D mutation. Genotyping for TFR2 and ferroportin mutations was negative. Organ-specific MRI (heart, liver, and pancreas) showed no structural or functional abnormalities, and chelation therapy was not indicated. In February 2025, a follow-up cranial CT performed in the absence of neurological symptoms demonstrated complete resolution of subdural collections and normalization of ventricular size. The patient discontinued all medical therapy and continued radiological and laboratory follow-up for both the schwannoma and iron metabolism monitoring.
Discussion: This case highlights a rare etiology of spontaneous intracranial hypotension (SIH) caused by a cervical schwannoma, presenting with subdural fluid collections and cerebellar tonsillar herniation. SIH is often secondary to CSF leaks, typically due to dural defects or spinal microfistulas, though in this case no fistula was detected on imaging. Schwannomas can cause erosion of surrounding osseous structures and potentially dural defects, contributing to CSF hypotension.The initial failure of lumbar epidural blood patch therapy and subsequent resolution after a cervical blood patch supports the importance of targeted intervention based on the location of the underlying pathology. Recurrent neurological symptoms and subdural collections with recent hemorrhagic features prompted further investigation, ultimately revealing a coincidental diagnosis of hereditary hemochromatosis (H63D homozygosity). While typically considered a milder form of hemochromatosis, H63D homozygosity has been associated with subtle disturbances in iron metabolism. In this case, no evidence of parenchymal iron overload was found on organ MRI, and chelation therapy was not initiated. The clinical course emphasizes the importance of comprehensive diagnostic workup in patients with SIH, including evaluation for underlying spinal pathology and secondary metabolic alterations, particularly when laboratory abnormalities persist. **Conclusions**: This case illustrates that hereditary hemochromatosis can present without markedly elevated iron parameters or gastrointestinal symptoms, and may follow a benign course managed with dietary measures alone. The acute onset of CSF hypotension with subdural hematomas initially suggested a traumatic or fistula-related cause, but imaging was negative. We hypothesize that iron accumulation in the dura, undetectable by standard imaging, could contribute to CSF leakage. This highlights the need to consider rare, often overlooked etiologies in cases labeled as "idiopathic."

IMPORTANCE OF CUTANEOUS BIOPSY FOR DETECTED ORGAN DAMAGE IN SMALL NERVE FIBERS IN PATIENTS WITH S.126.G MUTATION IN FABRY DISEASE.

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Background: Fabry disease, a rare X-linked lysosomal storage disorder, is characterized by deficient activity of the enzyme alpha-galactosidase A (GLA), leading to the accumulation of glycosphingolipids, particularly globotriaosylceramide (Gb3), in various tissues. While the disease primarily manifests with multi-systemic involvement, including renal, cardiac, neurological and cutaneous symptoms. Different mutations can impact the enzyme's activity, with effects ranging from near-normal to a complete loss of function. There are over 1,000 known variants of the GLA gene, but not all of them cause Fabry disease, depending on how much enzyme activity is preserved. Deciding when to start treatment, as well as the frequency and scope of clinical monitoring, can be complex, especially for those carrying variants of unknown significance (VUS). Clinical phenotypes are divided in two main classes, classic or non-classic, based on clinical and biochemical findings. Non-classic FD is usually recognized as late-onset forms with oligosymptomatic phenotype. In the group of the non-classic FD, special attention should be given to patients carrying the c.376A > G (p.Ser126Gly) mutation.
The p.S126G variant is a common example of a VUS, with a prevalence of 0.06% in the general population. In clinical practice, key tests for Fabry disease include measuring GLA enzyme activity and plasma levels of lyso-globotriaosylceramide (lyso-Gb3), which is a deacylated form of Gb3. However, there is a lack of basic research on whether VUS like p.S126G impact GLA enzyme activity and cause cellular accumulation of Gb3, leaving gaps in our understanding of their clinical relevance. Some authors have noted an accumulation in the endoplasmic reticulum, leading to inducing with reduced trafficking to the lysosome. These data strongly suggest that p.Ser126Gly could trigger a pathogenetic mechanism different from the classic and well assessed increased turnover with loss of described for other . This mechanism appears to be primarily associated with a negative gain of function, characterized by ER retention and UPR activation, which could cause irreversible cell damage through inflammation and/or apoptosis.
Aims: Our group aims to investigate the possible existence of small fiber neuropathy by conducting and subsequently analyzing skin biopsies from patients with a "benign" mutation of the GLA gene, as indicated in the literature. We will enroll patients with normal GLA enzyme activity, without GB3 accumulation, but exhibiting neurological symptoms not attributable to other causes. The debate on whether treatment should be initiated for these patients is still ongoing, and additional studies are certainly needed to clarify the nature of this mutation.
Methods: In all our patients, we will collect samples with three mm punch from proximal (thigh: 15 cm above the patella) and distal (leg: 10 cm above the lateral malleolus) hairy skin sites.The samples will be fixed in 4% formaldehyde vials, and then stored in a PBS+sucrose solution at 4°C in the refrigerator. Refrigerated samples will be inviated at at IRCCS Institute of Neurological Sciences of Bologna. Samples will be analyzed using immunofluorescence and electron microscopy.
Results: expected: Until now, scientific evidence of clinical presentation linked with this mutation has been controversial. Through immunofluorescence and electron microscopy, we will assess the extent of the reduction in small nerve fiber representation and any potential accumulation of Gb3. Using a minimally invasive approach like skin biopsy, as opposed to renal or cardiac biopsies, we hope to add data to the existing literature that might help us understand when to start treatment in patients with variants currently considered benign, and potentially extend the study to other variants recognized as VUS.

NOT ONLY HCV: CRYOGLOBULINEMIC VASCULITIS IN AN HBV-POSITIVE PATIENT AND DOAC TREATMENT

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Case presentation: A 81-year-old female patient presented with dyspnea and swelling to her lower extremities to her cardiologist. Previous medical history included chronic kidney disease, dyslipidemia, and knee replacement surgery. She was newly diagnosed with heart failure with reduced ejection fraction (HFrEF, EF 30–35%) and atrial fibrillation, for which therapy with furosemide, beta-blockers, and edoxaban was initiated. Around two weeks later, she developed erythematous cutaneous lesions on her lower extremities, treated with prednisolone 25 mg daily. Due to the worsening of skin wounds and dyspnea, she was admitted to the Emergency department where bilateral pleural effusion was detected on chest X Ray, atrial fibrillation with rapid ventricular response (180/min), Ejection fraction (EF) of 25%, and acute renal dysfunction (eGFR 18 ml/min) were also diagnosed. Upon transfer to our Unit, physical examination showed purpuric dermatitis on her upper limbs, while the lower extremities were edematous with similar purpura complicated by necrotic lesions and serous bullae. Blood count showed mild microcytic anemia, leukocytosis predominantly neutrophilic, ProBNP 19.235 pg/mL (n.v. <166), CRP 237.5 mg/L (n.v. <3.4), PCT 1.22 ng/mL (n.v. <0.05), urinalysis demonstrated microscopic hematuria and proteinuria (1.1 g/24 hours). Blood cultures detected Staphylococcus aureus bacteremia thus piperacillin/tazobactam and daptomycin were initiated as part of a targeted antibiotic regimen. The acute worsening of heart failure and kidney function was primarily attributed to sepsis, indeed they both improved when the infection was resolved. After 10 days, a follow-up cardiac evaluation showed a heart rate of 80-90/min, hemodynamic stability, EF of about 37%, and eGFR 56 ml/min. Anticoagulant treatment was switched from edoxaban to enoxaparin and later to apixaban in the suspicion of edoxaban associated vasculitis. Dermatological management included zinc oxide dressings and topical corticosteroids (betamethasone). The persistence of the lesions raised concern for an underlying systemic cause for which an autoimmune panel was performed (normal RF, reduced C3, normal

C4, negative ANA, AMA, ANCA, lupus anticoagulant test, anti-dsDNA, anti-CCP, anti-MPO, anti-PR3, anti-GBM) alongside skin biopsy (inflammatory purpura) while immunological tests revealed mixed type II-cryoglobulinemia (monoclonal IgA lambda vs. polyclonal IgG). Causes of cryoglobulinemia encompass chronic hepatitis C, autoimmune diseases (e.g., Sjogren syndrome, SLE, rheumatoid arthritis), lymphoproliferative disorders and rarely hepatitis B. Accordingly, workup for secondary causes was expanded, Total-body CT excluded malignancy while additional serological tests confirmed chronic HBV infection (HBsAg+, anti-HBc IgG+, IgM−, HBV DNA +). Taken together (chronic HBV infection, proteinuria, microhematuria, presence of type II-cryoglobulinemia), these findings let us diagnose HBV-associated type II cryoglobulinemia. Anticipating a future immunosuppressive therapy for vasculitis, an infectious disease consult advised the initiation of therapy with Entecavir to manage the risk of HBV reactivation.
Discussion: HBV-associated cryoglobulinemia is an uncommon but clinically significant condition that may present with cutaneous vasculitis, renal involvement, and systemic inflammation. In our patient, sepsis from S. aureus acted as a precipitating factor for acute cardiac and renal deterioration, but persistent vasculitic skin lesions and laboratory abnormalities pointed to an additional immune-mediated process. In this case, HBV-induced type II cryoglobulinemia was deemed the most likely etiology for the vasculitis, given serological and immunological findings. Cryoglobulinemia in HBV-positive patients is less common than HCV-associated cases but poses similar therapeutic dilemmas. The need for antiviral prophylaxis before immunosuppressive therapy, given the risk of HBV reactivation, is highlighted. Finally, although edoxaban is not known for its implication in drug-induced vasculitis, the temporal association leave room for speculation on a potential contributory role.
Conclusion: This case highlights the diagnostic and therapeutic challenges of HBV-associated type II cryoglobulinemic vasculitis in an elderly patient with multiple comorbidities. The overlap between infectious, autoimmune, and cardiovascular processes requires a high index of suspicion and a multidisciplinary approach. Prompt identification and treatment of the underlying HBV infection, coupled with careful planning for immunosuppressive therapy, are essential to prevent complications and optimize outcomes.

AN UNUSUAL CASE OF MALNUTRITION: NEVER JUDGE A BOOK BY ITS COVER

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Introduction: Malnutrition represents a significant and not uncommon cause of hospital admission in internal medicine, affecting both the elderly and younger population. It represents a heterogeneous clinical condition, secondary to both organic and functional pathologies. In younger patients, malnutrition is frequently associated with psychiatric disorders and eating behaviour disturbances, rendering it a complex and multidimensional issue.
Case report: A 29-year-old woman (A.) was referred to our Internal Medicine with a diagnosis of "Malnutrition and weight loss in a patient with acute temporomandibular joint dysfunction". Her medical history revealed progressive and gradual weight loss (approximately 15 kg), dysphagia for solids, which had developed five weeks prior, and increasing anxiety. A performed MRI of the facial region revealed anterior disc displacement of the right temporomandibular joint. A psychiatric assessment led to initiation of pharmacological treatment (antipsychotics and benzodiazepines). During the permanence in emergency room, the patient also underwent the following specialist consultations: a maxillofacial evaluation, which recommended muscle relaxant therapy with no indication for surgery; a psychiatric evaluation, which confirmed home treatment, and a dental assessment, which advised cognitive behavioural therapy, physiotherapy and anti-inflammatory medication. On admission to our ward, the patient presented with severe malnutrition, marked generalised muscular hypotrophy, mild bilateral palpebral ptosis, and low mood. Vital signs and oxygen saturation were normal.
On the fifth day of hospitalisation, the patient developed acute psychomotor agitation and oxygen desaturation, with mild hypercapnia on arterial blood gas (ABG) analysis. This clinical picture recurred at 24 and 48 hours. On the third episode, the patient appeared significantly agitated, tachypnoeic, with lip cyanosis, hypophonic and weak speech, thoracoabdominal asynchrony, reduced chest wall expansion, cervical spine muscle weakness, and an inability to hold her head upright unaided. The ABG revealed severe hypercapnic respiratory acidosis (pH 7.17, pO_2 76 mmHg, pCO_2 90 mmHg, HCO_3 35 mmol/L).Based on the clinical presentation and physical findings, a myasthenic crisis was suspected. Pulmonology and intensive care evaluations were requested, and non-invasive ventilation (without supplemental oxygen) was initiated. A neurological consultation supported the suspected diagnosis. The patient was therefore transferred to the neurology department after a chest CT scan, which showed mediastinal tissue compatible with thymic residue. Subsequently transfer, the patient's clinical condition deteriorated, requiring intubation and admission to the intensive care unit, where treatment with intravenous immunoglobulins (0.4–0.6 g/kg/day for 5 days) was initiated, followed by corticosteroids and anticholinesterase therapy. Serum autoantibody testing confirmed the presence of AChR antibodies (AChR-Abs). With progressive clinical improvement, the patient was extubated and transferred back to the neurology ward. After optimisation of medical therapy and further confirmatory investigations, she was discharged with the diagnosis of "Generalised AChR-positive Myasthenia Gravis, MGFA Class V, in a patient with probable thymic disease". Following discharge, the patient underwent robotic thymectomy, resulting in further symptom improvement and weight recovery. She is currently undergoing regular outpatient follow-up at our hospital's regional reference centre for myasthenia.
Conclusions: Myasthenia Gravis (MG) is a rare neuromuscular disorder caused by autoantibodies targeting postsynaptic membrane proteins (AChR-Abs), leading to a reduction in functional acetylcholine receptors and progressively worsening muscle weakness, potentially involving the respiratory muscles. Timely diagnosis and early initiation of therapy are crucial for improving quality of life. The case of this patient, admitted for malnutrition initially presumed to be of psychogenic origin, shows the importance of a thorough, generalist approach in internal medicine. A critical and holistic evaluation of symptoms and signs, placed at the heart of an accurate differential diagnostic process, can lead to early — even specialist — diagnoses, sometimes preceding laboratory or instrumental confirmation.

USE OF SODIUM GLUCOSE COTRANSPORTER-2 IN TRANSTYRETIN AMYLOID CARDIOMIOPATHY: A SYSTEMATIC REVIEW AND META-ANALYSIS.

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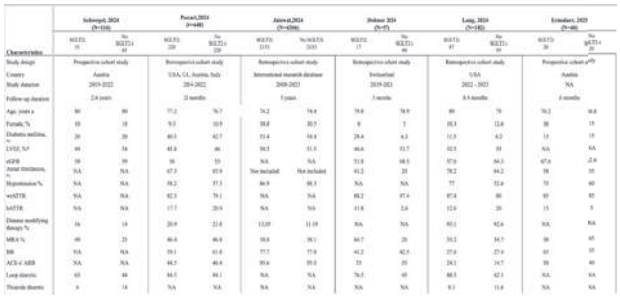
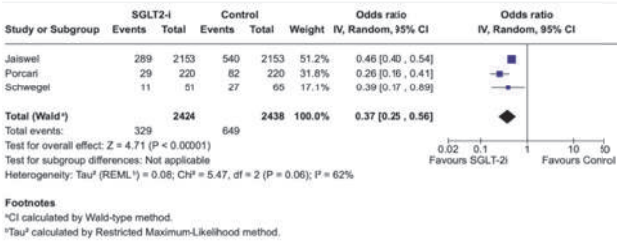
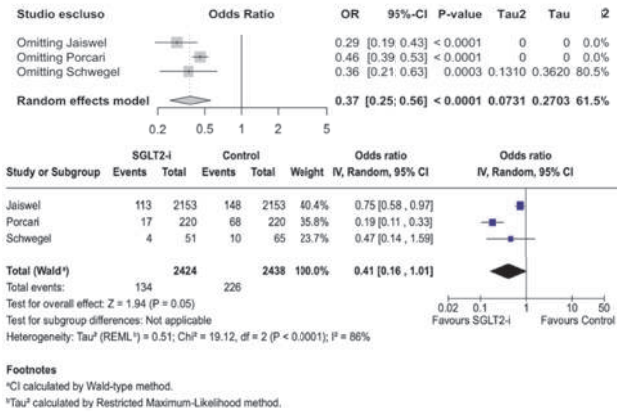
Background: Amyloid transthyretin cardiomyopathy (ATTR-CM) is an infiltrative disease characterized by deposition of misfolded transthyretin fibrils in the myocardium leading to higher risk of death, heart failure (HF) and major adverse cardiac events (MACE). Sodium-glucose cotransporter-2 inhibitors (SGLT2-i) have shown a significant cardiovascular benefits in patients with heart failure. However the potential and beneficial effects of this class of medication in ATTR-CM is unknown and needs further investigation.
Methods: We searched PubMed, EMBASE, and Cochrane Central for studies comparing SGLT2-i with control in patients with diagnosis of ATTR-CM. Outcomes of interest were overall mortality, MACE, HF-related events, change in eGFR and NT-proBNP. Statistical analysis was performed using RevMan 5.4 and R studio 2024.12.1. Heterogeneity was assessed with I2 statistics.
Results: We included in our meta-analysis 6 studies with a total of 5141

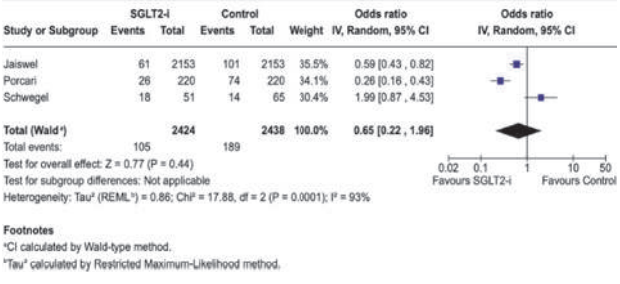
patients, with 2548 patients under SGLT2-i medication. Baseline characteristics of the studies are summarized in Table 1. Mean follow up of the studies was from 3 months to 3 years. Mean age of the patients in SGLT2i group and control were respectively 76.04 and 75.03 years. Measure of association used were risk ratio (OR) for dichotomous outcomes and mean difference (MD) with 95% confidence interval (CI). We found a statistically significant difference in mortality (OR 0.37; 0.25-0.56 CI 95%; p <0.00001; I2=62%) (Figure 1A) with substantial heterogeneity across the studies included. We conducted a leave-one-out analysis that shows consistency of the results (Figure 1B). There was no difference between two groups for MACE (OR 0.41; 0.16, 1.01 CI 95%, p 0.05; I2=86%) ,HF events (OR 0.65; 0.22, 1.96 CI 95%; p 0.44; I2= 93%) as Figure 2A-2B shows. Furthermore change in NT-proBNP favors SGLT2-i group among groups (WMD -571.26 pg/mL;-968.30,-174,22 CI 95%; p 0.005; I2=43%) (Figure 3). We found no substantial effect on change in eGFR between groups (WMD 3.23 ml/min/1.73 mq; -2.28, 8.75 CI 95%;p=0.25; I2=94%) (Figure 4)

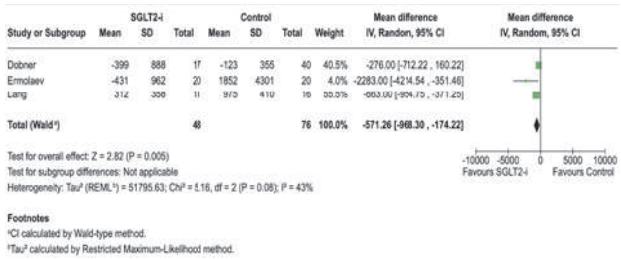
Conclusion: The results of this systematic review and meta-analysis including over 5000 patients suggest that SGLT2-i may reduce overall mortality in ATTR-CM with an associated reduction of NT-proBNP. No difference in major adverse cardiac events, heart-failure related events and change in eGFR was observed in the study.

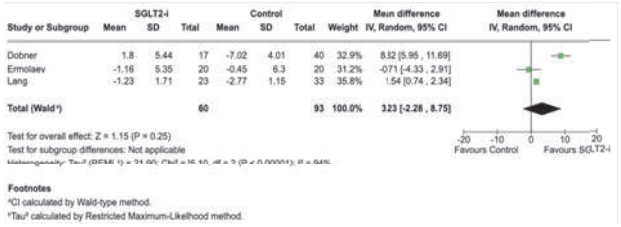












PLATELET ACTIVATION IN DECOMPENSATED CIRRHOSIS: EFFECTS OF SHORT-TERM RIFAXIMIN THERAPY – A PILOT STUDY

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Introduction: The concept of "rebalanced hemostasis" has improved the understanding of the coexistence of bleeding and thrombotic events in patients with cirrhosis, reshaping its clinical management. This balance, which includes changes of platelet function, is easily disrupted by inflammation, often driven by bacterial translocation from the gut. The possibility of modulating platelet activity through non-absorbable antibiotics remains unexplored.
Methods: To characterize the platelet phenotype and activation in patients with decompensated cirrhosis and to explore the effect of short-term rifaximin therapy on platelet function and systemic inflammation, a two-phase study was performed. First phase was a cross-sectional analysis comparing patients with decompensated cirrhosis (i.e., Child-Pugh, CP, classes B and C) with age- and sex-matched controls. Platelet phenotyping was performed via flow cytometry using 13 surface markers. Soluble TLT-1 (sTLT-1), serum LPS, inflammatory cytokines, and neutrophil extracellular traps (NETs) markers (MPO-DNA complexes) were quantified. In the second interventional phase, patients with cirrhosis were randomized to receive either rifaximin 550 mg BID or placebo for 14 days. Primary outcome was the post-treatment change in LPS and safety events during treatment were monitored...
Results: Twenty-one patients with decompensated cirrhosis (mean age 59±9 years; 65% male sex, 70% alcohol etiology; mean CP and MELD scores, 7.7±2.2 and 13.7±3.1 respectively) were matched with 16 controls. Patients with cirrhosis displayed higher LPS and inflammatory cytokines (specifically, IL-1β, IL-6, IL-18, IL-23) levels, alongside increased levels of NETs than controls. Platelets from patients with cirrhosis showed significantly lower surface expression of the platelet-specific receptor TLT-1 and higher levels of cleaved sTLT-1 in plasma, indicating ongoing platelet activation in vivo. In the interventional phase, rifaximin did not significantly reduce LPS, inflammatory cytokines, and NETsosis. No post-treatment changes in platelet activation were observed.
Conclusion: Patients with decompensated cirrhosis exhibit a distinct activation state of platelets associated with low grade systemic inflammation and NETosis. Short-term rifaximin failed to reverse these changes, suggesting that longer or combined interventions targeting LPS and NETsosis may be required to rescue platelet dysfunction.

CHOLANGITIS IN A PATIENT AFFECTED BY CROHN DISEASE: A NOT OBVIOUS INTERPRETATION

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Crohn's Disease (CD) is a chronic inflammatory bowel disease that may present with extraintestinal manifestations, including hepatic involvement. Liver abnormalities in patients with Crohn's Disease can include autoimmune hepatitis (AIH), primary sclerosing cholangitis (PSC), and infectious cholangitis. A differential diagnosis among these conditions is essential for appropriate therapeutic management and crucial for accurate prognostic assessment.
We present the case of a 21-year-old man with hypoplasia of the right sigmoid vein and ATM syndrome responsible for previous migraine episodes and a family history of thrombophilia (prothrombin mutation) and gastrointestinal tract neoplasms.
In April 2021, he was hospitalized due to progressive general malaise, diffuse abdominal pain, and elevated liver cytolysis and cholestasis parameters. Laboratory investigations led to a diagnosis of **autoimmune hepatitis** due to positive ANA, ASMA, and increased IgG levels.
Treatment was initiated with **Prednisone 50 mg/day**, which was gradually tapered to 7.5 mg/day, but disease activity resumed.
In December 2021, an abdominal MRI with contrast revealed a diffusely heterogeneous liver, focal thrombosis of a segmental branch of the middle hepatic vein, prominence of the biliary tree with signs of peribiliary inflammation, and ectasia of the cystic duct. **Ursodeoxycholic acid** was introduced at a dose of 300 mg, one tablet three times a day.Due to persistent elevation of cytolysis and cholestasis markers, a **percutaneous liver biopsy** was performed, showing histological features compatible with either primary or secondary cholangitis.
Approximately two years after the initial diagnosis of autoimmune hepatitis/sclerosing cholangitis, the patient presented again with abdominal pain and altered bowel habits. A **colonoscopy** revealed extensive inflammatory bowel disease (pancolitis), most likely **Crohn's Disease**, for which **Mesalazine** therapy was started, with partial improvement.Since August 2023, **Azathioprine 150 mg/day** was added, and **Prednisone (Deltacortene)** was reduced to 5 mg/day, while ursodeoxycholic acid was continued at 300 mg three times a day. Upon second-opinion evaluation at our Center, a **re-examination of the liver biopsy** by our Pathology Department showed intrahepatic bile duct damage with nonspecific features. A repeat MRI approximately three years later from the first one showed no progression of biliary disease and no evidence of hepatic vein thrombosis. These findings, together with the segmental involvement pattern, excluded PSC and suggested that the MRI findings were the result of **infectious cholangitis**, likely indicative early on of a gastrointestinal disorder associated with increased intestinal mucosal permeability and dysbiosis.
The probable **infectious episode** may have triggered thrombosis due to local activation of the coagulation cascade, facilitated by **heterozygosity for the prothrombin gene mutation**.Biliary infections in patients with IBD may present with symptoms indistinguishable from primary sclerosing cholangitis, making differential diagnosis challenging. It is essential to consider **infectious cholangitis**, particularly in the presence of predisposing factors such as immunosuppressive therapy.Literature documents that patients with IBD—especially those on immunosuppressants—have an increased risk of **hepatobiliary infections**, including **bacterial infectious cholangitis**, caused by translocation of pathogenic or opportunistic microorganisms through the intestinal mucosa and reaching the liver via the portal vein. These infections may **mimic PSC both radiologically and clinically**, but generally have a **more favorable prognosis** and a **segmental distribution** of intrahepatic bile duct abnormalities.

EFFECTS OF LIFESTYLE REVISION AND METFORMIN ON THE PLASMA LIPIDOME OF PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD): A PILOT STUDY

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a leading global cause of chronic liver disease and an independent risk factor for cardiovascular disease (CVD). Systemic metabolic unbalances, rewired lipid fluxes, and accumulation of toxic lipid species can lead to hepatic lipotoxicity and progression of the disease towards steatohepatitis (MASH), liver cirrhosis and hepatocellular carcinoma. Currently, there are no pharmacological treatments specifically approved for MASLD in Europe, and most of the clinical trials focus on patients with moderate/advanced fibrosis. Lifestyle modifications (particularly diet and exercise), along with medications that reduce body weight and improve insulin sensitivity, have demonstrated beneficial effects on MASLD outcomes. Metformin is a well-established insulin sensitizer; however, it has minimal impact on body weight when used alone, and its effectiveness in MASLD progression remains controversial and requires more investigation.
Methods: This pilot study included fourteen overweight/obese patients (10M:4F) with Metabolic Syndrome, hepatic steatosis diagnosed at ultrasound, and mild fibrosis (F0-1) at the shear wave elastography, pharmacologically naïve for metabolic treatment. At the Clinica Medica Frugoni (Policlinico di Bari), patients underwent nutritional counselling with traditional Mediterranean Diet with a reduced consumption of carbohydrates at evening, physical exercise (10,000 steps/day) and metformin (1000mg/day). Before and after 16 weeks of treatment we assessed body composition, biochemical tests, and untargeted plasma lipidomic analysis with state-of-the-art liquid chromatography–mass spectrometry.
Results: After 16 weeks of treatment, the MASLD patients showed a significant weight loss (-6%) associated to an improvement of insulin sensitivity [HOMA-IR (-40%)] and a significant reduction of hepatic fat accumulation (as predicted by the Fatty Liver Index [FLI]). Plasma lipidomics showed a significant increase of the Monounsaturated to Saturated Free Fatty Acids ratio (MUFA/SFA FFA), used as a potential proxy of FFA-mediated lipotoxicity. Moreover, the Polyunsaturated to SFA (PUFA/SFA) and MUFA/SFA Ceramides ratios were significantly increased, substantiating a less lipotoxic circulating lipidome. Lastly, the reduction of SFA Ceramides positively correlated with the improvement in FLI.
Conclusions: This pilot study suggests that the combined intervention of lifestyle revision and metformin might improve cardiometabolic health by positively rewiring the plasma lipidome of patients with early-stage MASLD. Given that elevated Saturated Ceramides and reduced PUFA FFA have been associated to insulin resistance and MASLD progression, the rewiring of FFA/Ceramides composition might suggest a reduced lipotoxicity burden of MASLD. We are currently enrolling additional patients and conducting analyses on isolated lipoprotein fractions (VLDL, LDL, HDL) to further explore the biological significance of these observations.

ASSOCIATION BETWEEN C-REACTIVE PROTEIN/TRIGLYCERIDES INDEX AND CLINICAL OUTCOMES IN HOSPITALIZED ELDERLY PATIENTS

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Background and Aim: The C-reactive protein/triglyceride (CRP/TG) index has emerged as a potential marker of metabolic inflammation. However, its prognostic value in non-critically ill hospitalized patients remains poorly defined. This study aimed to investigate the association between the CRP/TG index and clinical outcomes—including length of hospital stay, in-hospital mortality, and the prevalence of major comorbidities—in elderly, non-critically ill patients enrolled in the Clinical Outcomes in Hospitalized Patients Receiving Treatment at Sant'Andrea Hospital (COHORTS) study.
Methods: A total of 338 individuals (156 men, 182 women), aged 65 years or older, were included. The CRP/TG index was calculated at admission, and patients were stratified into tertiles based on index values. The Charlson Comorbidity Index (CCI) was used to assess comorbidity burden. Associations between the CRP/TG index and clinical variables were evaluated using univariate analysis. Clinical outcomes were compared across tertiles using logistic regression models adjusted for age, sex, and CCI.
Results: Patients in the highest CRP/TG tertile exhibited significantly higher levels of CRP, triglycerides, transaminases, and fasting glucose, along with lower levels of glomerular filtration rate (GFR), HDL cholesterol, and albumin compared to those in the lower tertiles. Higher CRP/TG index values were also associated with a greater prevalence of diabetes ($p = 0.005$) and a longer length of hospital stay ($p = 0.04$). After adjustment for age, sex, and CCI, a higher CRP/TG index was independently associated with an increased risk of in-hospital mortality (OR: 3.94; 95% CI: 1.53–8.91; $p = 0.01$).
Conclusion: The CRP/TG index is a simple and accessible biomarker that may help identify non-critically ill hospitalized patients at greater risk of poor clinical outcomes. Further prospective studies are warranted to validate its prognostic value in routine clinical practice.

GLUCOCORTICOID REMEDIABLE ALDOSTERONISM: LONG TERM FOLLOW-UP, A CASE REPORT

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Familial hyperaldosteronism type 1, also known as glucocorticoid-remediable aldosteronism (GRA), is an autosomal dominant form of primary aldosteronism (PA), caused by unequal crossing-over between the 11-beta-hydroxylase and the aldosterone-synthase genes. The hybrid gene encodes the 5'-ACTH-responsive regulatory sequences and the aldosterone synthase gene sequences and leads to ACTH-dependent production of aldosterone.
Here we present a case of a 61-year-old GRA woman, treated with a low dose of dexamethasone (0,75 mg/day), referred to our hospital for therapy re-evaluation. During the follow-up, she developed a headache and tachycardia with a progressive increase in BP values. Therefore, dexamethasone was initially increased to 1 mg/day in addition to bisoprolol 1,25 mg bid. Despite an optimal biochemical control of PA, she gradually gained weight (64>79 kg), showing cushingoid features with parallel BP worsening. Because of steroid overtreatment suspicion, dexamethasone was reduced (dexamethasone 1 > 0,5 mg) with only partial improvement on BP profiles and no improvements on iatrogenic Cushing.
Given the poor control of BP, the causes of worsening hypertension were re-investigated: the laboratory findings (normal ARR, non-inhibited renin, normal serum potassium levels) showed a correct suppression of the hybrid gene activity. A possible role of the concurrent SNRI therapy (venlafaxine) was supposed. Therefore, it was stopped and substituted with duloxetine. Furthermore, the iatrogenic Cushing syndrome, with relevant central obesity and increased BMI, was considered. Therefore, steroid therapy was further reduced (0,2 mg), a low sodium- and low-fat diet was prescribed and antihypertensive medication dosage was increased, with subsequent gradual weight loss (79>64 kg) and BP normalization.
In patients with GRA hypertension is often severe; the first line treatment is represented by exogenous corticosteroids, which are effective at maintaining prolonged ACTH suppression at the lowest possible dose; despite a suppression of the pathological gene, other factors can lead to hypertension and require specific treatment.

PLASMAPHERESIS: IN THE MANAGEMENT OF COMPLEX THROMBOPHILIA

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A 49-year-old male presented with acral lesions at the level of the 4th finger of the right hand. Previous medical history included kidney transplant due to complicated diabetes mellitus type I and retinopathy since he was 11. Liver fibrosis associated with portal thrombosis and cavernoma. Thalassemic trait. Thrombophilia due to mutation of factors VII, IX, and X. In 2021, the patient developed multiple episodes of necrotic cutaneous lesion of the first finger of the left foot, necessitating amputation of the tip of the finger and revascularization, while in 2022, the same lesion developed on the opposite foot, which was surgically treated with partial resolution, and a recurrent lesion appeared on his second tip of finger of the same right foot, requiring an intravenous infusion of autologous monocytes in April 2023. The patient was admitted to our ward for the resurgence of another lesion of the 4th distal phalange of the right hand. Upon physical examination, additional ulcerations were discovered on the index and 2nd finger of the left hand. Blood work revealed Creatinine 1.47mg/mL (n.v. 0.67 – 1.17), eGFR 55 ml/min (n.v. >90), Lipoprotein a 49 mg/dL (n.v. <30), hyperhomocysteinemia 23.7 umol/L (n.v. 3.2 – 10.7). To investigate the reasons behind the recurrence as in the case of vasculitis, we performed a complete autoimmune panel (normal RF, reduced C3, normal C4, negative ANA, AMA, ANCA, anti-dsDNA, anti-CCP, lupus anticoagulant tes**t),** additional serological tests that excluded HBV and HCV infection. The coagulation test, which exhibited a decrease in plasminogen activator inhibitor-1 (PAI) and an increase in IX and VIII factors, supported the initial suspicion of thrombophilia. Genetical test with real time PCR showed homozygous genotype of the MTHR C677T. The capillaroscopy demonstrated nonspecific alteration but concluded for diabetic micro-angiopathy. Considering the blood work, instrumental and previous patient history (recent admission to a nephrological ward in December 2023 for nephrotic syndrome, and a renal biopsy revealed focal segmental glomerulosclerosis and diabetes glomerulopathy class III), a nephrological consult was requested and plasmapheresis was advised to treat the microcirculation disorders.
Discussion: Thrombophilia is a condition that makes blood more likely to form clots, which can lead to several complications. This condition results from an imbalance in blood-clotting factors, increasing the risk of thrombosis (blood clots in blood vessels). It can be hereditary or acquired due to cancer, surgery or pregnancy. The most common complications include pulmonary embolism, renal failure and cardiovascular disease. The patient showed clinical improvement after undergoing the first plasmapheresis session, it could be associated with the blood removal of procoagulant molecules. Plasmapheresis leads to the elimination of tumor necrosis factor (TNF), lipoprotein-a (Lpa) and the reduction of coagulation factors, fibrinogen and von Wilibran factor resulting in improved clinical outcomes. Although PAI decrease is associated with hemorrhagic diatesis in our patient thrombophilic disorders occurred, this could be explained by a more complex procoagulant microenvironment rather than the lack of singular factor. The MTHFR 667C>T contributes to an increase cardiovascular risk by the enhancing endothelial oxidative damage and shifting the environment toward a prothrombotic state. Following discharge, folate supplements were added to domiciliary medication to minimize hyperhomocysteinemia. Maintaining terminal parts of body warmer was another advice given to the patient to promote blood circulation by stimulating vasodilatation and so reducing necrosis of tips. In addition to clopidogrel/acetylsalicylic acid, cilostazol was added to domiciliary therapy to minimize thrombotic issues, along with mycophenolate and tacrolimus were confirmed as immunosuppressive medication.
Conclusion: This case highlights the multifactorial nature of thrombophilia in a complex patient with diabetic microangiopathy, genetic predisposition, and post-transplant status. The integration of nephrological, vascular, and hematological assessments was essential for identifying the underlying pathophysiological mechanisms driving recurrent acral ischemic lesions. Plasmapheresis proved to be a valuable therapeutic option, likely through the reduction of circulating procoagulant and proinflammatory mediators, with associated clinical benefit. The presence of homozygous MTHFR C677T mutation and elevated homocysteine levels further supported the need for adjunctive metabolic correction and antiplatelet therapy. This case underscores the importance of a personalized, multidisciplinary approach in managing thrombotic disorders with atypical presentations. Future efforts should focus on pre- and post-apheresis biomarker monitoring to better understand the pathogenesis of thrombophilia and optimize individualized treatment strategies.

DEALING WITH THE UNTHINKABLE: DEATH FROM SYSTEMIC TUBERCULAR INFECTION STILL HAPPENS IN XXI CENTURY DEVELOPED COUNTRIES

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Background: Bacillus Calmette-Guérin (BCG), a live attenuated strain of Mycobacterium bovis, is mainly used as a vaccine against tuberculosis and as an intravesical treatment for non-muscle invasive urothelial bladder carcinoma. Intravesical instillation is generally well tolerated, with transient symptoms linked to hypersensitivity reactions. Infectious complications are uncommon and typically occur when the urothelial barrier is compromised. Local infections affect the genitourinary tract. Systemic disease occurs when BCG accesses the bloodstream and spreads to other organs. Despite often presenting as an early-onset infection (within 3 months of BCG instillation), it can also occur months to years later. One-third of BCG infections present as disseminated disease, in the form of sepsis, miliary disease, or fever associated with organ involvement. Histopathology may show noncaseating granulomas, often without necrosis.
Case report: Our patient is a 74-year-old Caucasian male with a history of polycystic kidney and liver disease, chronic kidney disease (serum creatinine 2 mg/dL) and high-grade urothelial carcinoma of the bladder. He underwent transurethral resection of bladder tumor (TURBT), followed by periodic intravesical BCG instillations from November 2020 to March 2024.
Following the final instillation he developed fever (up to 39°C) and fatigue, managed at home with cefixime and ibuprofen. Laboratory testing revealed elevated liver enzymes (AST 292 U/L, ALT 320 U/L, GGT 465 U/L, ALP 700 U/L, total/direct bilirubin 3,57/2,97 mg/dL) and serum creatinine (3,62 mg/dL). An abdomen ultrasound and MRI were inconclusive. A liver biopsy was performed, with histological evidence of interface and lobular hepatitis, and non-necrotic epithelioid granulomas. Ziehl-Neelsen staining was negative. While chronic hepatitis induced by toxic and iatrogenic damage was the most likely scenario, further tests were needed to rule out BCG dissemination.
He was admitted to the Infectious Diseases Unit in May 2024. During hospitalization, sputum analysis via polymerase chain reaction (PCR) and cultures was negative for tubercular infection. Serology for HIV, HBV, HCV, Coxiella burnetii, Brucella sp. and Quantiferon were negative as well. A high-resolution chest CT scan showed pulmonary fibrosis and emphysema, a few non-specific micronodules, but no evidence of an infectious process. With these findings

both BCG dissemination and sarcoidosis were considered unlikely. Liver function tests normalized and the patient self-discharged, with pneumological and hepatological follow-up recommendations.
In January 2025 the patient was admitted to the Gastroenterology Unit because of a new increase in liver tests (AST 771 U/L, ALT 567 U/L, GGT 150 U/L), associated with fatigue, general malaise, anaemia, and weight loss. Before admission, an abdomen ultrasound showed an enlarged spleen, but no acute hepatic alteration.
Further blood screenings yielded negative results for several infectious disease (Quantiferon included) and autoimmunity antibodies.As for haematological tests, Beta-2 microglobulin was elevated (34.300 mg/L). A bone marrow biopsy was then performed, and non-necrotic, noncaseating granulomas were found again. Ziehl-Nielsen staining was still negative. PET imaging showed no FDG uptake in the lungs and lymphnodes, therefore ruling out sarcoidosis a second time. Given the finding of granulomas in two separate organs, both primitive hepatological and haematological diseases were ruled out. After clinical stabilization, the patient was discharged.
He later came to our attention in March 2025, after a transfer from the Neurosurgery Unit, where he was admitted for a traumatic subarachnoid haemorrhage.Despite stable CT imaging, he began deteriorating physically and neurologically (at transfer AST 228 U/L, ALT 468 U/L, GGT 233 U/L, creatinine 4,17 mg/dL).
Cerebrospinal fluid test, brain MRI and EEG were inconclusive.Serology for parasitic infections (Leishmania included) was negative. Whipple's disease was excluded after further analysis of prior bone marrow samples. PCR performed on gastric secretum showed no trace of Koch's bacillum.
Despite being ruled out twice, we believed BCG dissemination was the correct diagnosis. A liver biopsy was repeated, with specific request for mycobacterial PCR test and cultures (previously omitted). PCR confirmed an active mycobacterial infection. Antitubercular therapy (Ethambutol, Levofloxacin, Linezolid, Terizodone) was started, with dosing tailored to the patient's renal and liver function.
Unfortunately, the patient's conditions had worsened. He developed multiorgan failure and died a week after starting therapy.
Conclusion: BCG infection can be difficult to diagnose due to low sensitivity of standard diagnostic tools. Granulomas may be present but typically lack caseous necrosis, and Koch's bacillum is often not identified in histological examinations.
In case of suspected BCG dissemination, even with initial negative results (such as Ziehl-Neelsen staining), microbiological testing in tissue sampling is essential. Simultaneous exclusion of other potential causes, both infectious and non-infectious, remains crucial.

BURNING CLUES: AN ASTROCYTOMA'S RARE SYSTEMIC BETRAYAL

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We present the case of a 60-year-old man with a history of heavy smoking and longstanding vegan diet. The patient was diagnosed in November 2023 with IDH1-mutant astrocytoma (WHO grade 4) after presenting with acute-onset right hemiparesis. Initial neuroimaging revealed a 4.5 cm left frontoparietal mass with intratumoral hemorrhage, for which he underwent craniotomy with subtotal resection. Post-operative and serial surveillance MRIs through July 2024 demonstrated stable residual enhancement without evidence of disease progression. Nevertheless, the patient declined the recommended adjuvant treatment, opting instead for alternative medicine. The patient underwent two Ayurvedic treatment cycles in India (March and October 2024), during which he received unspecified herbal therapies and discontinued all conventional medications. Notably, these trips were undertaken without appropriate preventive measures - he received neither recommended vaccinations nor malaria prophylaxis.
During his second Ayurvedic cycle, the patient developed persistent high-grade fever, migratory large joint polyarthralgia and a peritrochanteric erythematous rash. Two courses of empirical doxycycline provided only transient symptom improvement. Initial testing for malaria (negative) and dengue was conducted in India, however, the patient left the hospital before the results of dengue testing were made available. By November 2024, he manifested progressive pancytopenia (Hb 6.9 g/dL, WBC $2.1\times10^3/\mu L$, platelets $89\times10^3/\mu L$) and markedly elevated inflammatory markers (CRP 258 mg/L, ferritin 1,845 ng/mL), prompting hospitalization.
The diagnostic evaluation proved particularly challenging given the patient's recent travel to endemic regions and systemic inflammatory presentation. Given the high suspicion for infection, an extensive microbiological workup was performed, all resulting negative, including: viral serologies (HIV, EBV, CMV, dengue, Zika, West Nile virus), bacterial studies (standard and prolonged-incubation blood cultures, Coxiella, Brucella, Borrelia, Bartonella, and Rickettsia species), parasitic evaluations (malaria smears during febrile episodes, Leishmania, Toxoplasma, and stool parasitological/cultural examination), and mycobacterial screening . To note that, while initial dengue IgM serology from India was reported as positive, confirmatory testing at our institution suggested cross-reactivity, likely attributable to prior chikungunya exposure rather than acute dengue infection. Cross-sectional imaging also proved non-diagnostic as the brain MRI showed stable disease, while whole-body PET-CT demonstrated diffuse moderate bone marrow hypermetabolism abdominal and CT revealed only nonspecific splenic hypodensities and mild retroperitoneal lymphadenopathy.
As the clinical course evolved, the patient's fever gradually subsided and he was discharged home with a diagnosis of fever of unknown origin (FUO), with close outpatient follow-up arranged. The follow up hematologic assessment revealed ongoing low-grade evening fevers, anemia, and markedly elevated but stable LDH (1,152 U/L). A bone marrow evaluation was recommended at this time, but the patient deferred invasive testing.
Afterwards, following two emergency department visits for recurrent low-grade fever, debilitating fatigue, and progressive bone pain, each visit requiring blood transfusions, the patient consented to bone marrow biopsy. It was performed in December 2024 and showed infiltration by large, pleomorphic cells expressing S100, SOX10, and CD56, with immunoprofile identical to the primary brain tumor, confirming metastatic astrocytoma. Given the diagnosis, the multidisciplinary board recommended transition to palliative care with symptomatic management and regular transfusion support. However, the patient demonstrated limited adherence to conventional medical follow-up and was ultimately lost to further surveillance.
This bone marrow metastasis represents an exceptional occurrence as gliomas rarely metastasize systemically (<2% of cases), with most series reporting <1.5% extracranial spread and given that the bone marrow involvement is particularly uncommon, with <30 documented cases worldwide. To note that, the IDH1-mutant status makes this dissemination biologically surprising, as these tumors typically show less aggressive behaviour than grade IV IDH-wildtype glioblastoma (median survival 24-36 vs 12-15 months with treatment). While is usually spread locally (80%) or via CSF (15%), this case highlights that extracranial metastasis - though rare - should be considered in patients with systemic symptoms.
Conclusions: This case illustrates the profound diagnostic challenges posed by rare metastatic patterns of CNS malignancies, where systemic symptoms may initially mimic more common infectious or inflammatory conditions. It also serves as a reminder that even IDH-mutant gliomas - typically showing more indolent behaviour - can exceptionally demonstrate aggressive systemic dissemination, with bone marrow involvement representing an extraordinarily rare phenomenon.

BEHÇET'S DISEASE OR MYCOPLASMA PNEUMONIAE INDUCED RASH AND MUCOSITIS (MIRM) A POSSIBLE OVERLAP DIFFICULT TO DECODE.

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Background: La malattia di Behçet è una rara vasculite cronica multisistemica recidivante le cui manifestazioni più frequenti comprendono aftosi orale e genitale, coinvolgimento oculare (uveite), lesioni cutanee pustolo-papulari. Complicanze più gravi includono trombosi venose ed arteriose, coinvolgimento del sistema nervoso (neuro Behçet), del tratto gastro-enterico e dei reni.
Il Mycoplasma Pneumoniae è un batterio responsabile di circa il 10 % delle polmoniti acquisite in comunità. Oltre il distretto respiratorio può essere causa di manifestazioni extra – polmonari quali: pericardite, artrite, trombosi, anemia emolitica da agglutinine fredde e coinvolgimento muco-cutaneo. Recentemente è stata descritta una manifestazione muco-cutanea associata all'infezione da Mycoplasma Pneumoniae nota come MIRM (Mycoplasma pneumoniae – Induced Rash and Mucositis).
Caso clinico: Uomo di 41 anni giungeva in P.S. per febbre, tosse produttiva, comparsa di aftosi orale e genitale, iperemia congiuntivale e malessere generale. In anamnesi patologica remota: asma bronchiale ed assunzione da circa un anno di corticosteroidi a seguito di precedente ricovero per febbre ed aftosi oro-esofagea.
Gli esami ematochimici dimostravano l'aumento degli indici di flogosi: PCR 69.8 mg/L, le emocolture risultavano negative per batteri e miceti. La TC del torace evidenziava addensamento parenchimale del lobo inferiore sinistro e al biofire (pannello polmoniti) positività per Mycoplasma pneumoniae (il paziente riferiva recente ricovero del figlio in ambito pediatrico per polmonite da Mycoplasma Pneumoniae). Negativa sierologia per: HCV, HBV, HIV, LUE, Epstein Barr, citomegalovirus, herpes simplex 1 e 2, morbillo, varicella zooster,

toxoplasma, rosolia, parvovirus. Negativa la ricerca genetica dell'allele HLA B51. La valutazione oftalmologica confermava coinvolgimento congiuntivale bilaterale.
Il quadro clinico, nonostante terapia antibiotica sistemica con ceftriaxone e claritromicina e steroidea ad alte dosi si complicava con la comparsa di lesioni crostose perioculari e lesioni a coccarda inizialmente al tronco e successivamente ubiquitarie.
Dopo 23 giorni di terapia cortisonica si assisteva ad un netto miglioramento della sintomatologia a carico della cute e delle mucose.
Conclusioni: La malattia di Behçet e la MIRM sono due condizioni cliniche con simili manifestazioni ma differente fisiopatologia e prognosi. La sovrapposizione clinica tra queste due patologie può rendere la diagnosi differenziale complessa ed influenzare l'approccio terapeutico. La storia clinica del paziente la ricorrenza degli episodi di aftosi orali ed il raggiungimento del punteggio nei criteri ICBD (International Criteria for Behçet Disease) del 2013 ha permesso di porre diagnosi di Malattia di Behçet ma non è possibile escludere la sovrapposizione dell'infezione da Mycoplasma Pneumoniae nelle manifestazioni muco - cutanee ed oculari.

A DIAGNOSTIC ODYSSEY: A CRYPTOGENIC STROKE AT THE CROSSROADS OF INFLAMMATION, EMBOLISM, AND HYPOPERFUSION, THREE POSSIBLE MECHANISMS FOR MULTIPLE STROKES

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Stroke remains one of the leading causes of disability and mortality worldwide. While its most common etiologies — cardioembolism, large vessel atherosclerosis, and small vessel disease — are well established, there are clinical scenarios where stroke emerges as the visible tip of a far more intricate and hidden pathophysiological iceberg. In such cases, the real challenge lies not only in treating the event, but in unveiling its origin. Here we described the case of a patient whose stroke defied the usual patterns.
A 75-year-old woman, with a medical history of arterial hypertension and a recent diagnosis of polymyalgia rheumatica under corticosteroid therapy, presented to the Emergency Department of our hospital reporting colicky abdominal pain localized in the mesogastric region, associated with seven episodes of gastric-content vomiting and three episodes of diarrhea. She denied fever. Shortly thereafter, the patient experienced the sudden onset of weakness in her right hand.
Transferred to our Internal Medicine Unit, the clinical scenario was complex: asymmetric bilateral upper limb weakness, with both proximal and distal involvement, in the absence of a clear territorial distribution.
Initial CT scans were negative, but brain MRI unveiled the unexpected: multiple bilateral ischemic lesions, predominating in the watershed areas of both hemispheres — a radiological footprint often suggesting cerebral hypoperfusion. What could have triggered such a multifocal ischemic insult?
The diagnostic journey unfolded like a medical investigation through overlapping clues.
The potential cardioembolic etiology was initially investigated through 24-hour Holter ECG monitoring and transthoracic echocardiography, both of which yielded negative results. Subsequently, a transcranial color-coded Doppler ultrasound revealed the presence of a latent right-to-left shunt, likely of mild extent, documented by the passage of two microembolic signals within the left middle cerebral artery during Valsalva maneuver. This finding was further confirmed by transesophageal echocardiography, which demonstrated the presence of a patent foramen ovale (PFO) of mild-to-moderate size. In this context, the coexistence of a PFO and deep vein thrombosis could physiopathologically explain the cerebral lesions. However, the cardioembolic mechanism appeared only partially consistent with the clinical picture, given the absence of involvement of the middle cerebral artery or another large intracranial artery
During hospitalization, considering the recent diagnosis of polymyalgia rheumatica, a Doppler ultrasound of the temporal artery was performed in suspicion of Giant Cell Arteritis (GCA). The examination was positive, showing the presence of the "halo sign," a highly suggestive finding indicative of active GCA. PET imaging disclosed intense vascular inflammation along the axillary arteries and the aortic arch, suggesting a state of systemic vasculitis that possibly could have rapresented a possible basis of the current multiple stroke pathogenesis too.
Given the clinical picture, characterized at home by multiple episodes of vomiting and diarrhea, likely resulting in hypotension and consequent cerebral hypoperfusion, along with the instrumental findings showing multiple synchronous and bilateral ischemic areas involving different vascular territories — both cortical and subcortical — as well as the watershed zones between the anterior and posterior cerebral arteries, a hemodynamic mechanism cannot be excluded in the pathogenesis of the observed ischemic lesions, consistent with so-called "watershed infarcts". This hypothesis appears further supported when considering the possible coexistence of arteriolosclerosis (in a patient with longstanding hypertension) or of an inflammatory vasculitis-related stenosis (in a patient with giant cell arteritis) affecting the vessels supplying the involved territories.
Thus, three possible stroke mechanisms emerged: embolic, inflammatory, and hemodynamic. None could fully explain the event alone; all were plausibly contributing.
Faced with this multifactorial and elusive pathogenesis, the stroke was classified as cryptogenic (TOAST type 5) — the only category capable of encompassing such clinical complexity.
This case tells a story of uncertainty, where Medicine transcends protocols and enters the realm of reasoning, intuition, and integrative thinking. It teaches us that stroke is not always what it seems — and that sometimes, behind a small neurological deficit, lies a vast and silent battle between vessels, inflammation, and hemodynamics.
A battle that only curiosity, perseverance, and a holistic approach can hope to illuminate.

BASELINE LIVER ELASTOGRAPHY AND ITS LONGITUDINAL CHANGES PREDICT LIVER RELATED OUTCOMES IN PATIENTS WITH METABOLIC DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE (MASLD)

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Background: and Aims: Liver fibrosis is the primary prognostic factor in MASLD. Liver biopsy is the gold standard for staging fibrosis, although it is invasive and expensive procedure. Currently, non-invasive methods are available to stratify the degree of fibrosis.
The aim of this study is to validate liver stiffness as a prognostic factor both at baseline and in its variation over time during follow-up.
Method: This is a retrospective single-center cohort study including 389 patients who underwent at least two Fibroscan liver stiffness measurements, with a minimum 6-month interval between scans, from January 2011 to December 2023. They were stratified into 3 risk groups according to Baseline liver stiffness measurements (LSM) (<10, 10-20, >20 kPa). Primary outcome was a composite of Liver Related Events (LRE), death or liver transplantation. Kaplan-Meier curves were generated for time to primary outcome stratified by Baseline LSM and Δ% Fibroscan categories (worsening: LSM increase >20%, stable, improved: LSM decrease >20%). Multivariable Cox regression analysis, adjusted for age, gender, BMI and type 2 diabetes, was used to assess the association of baseline LSM and Δ% fibroscan with primary outcome event. Cumulative incidence curves and incidence rates have been assessed and compared for each risk subgroup.
Results: During a median follow-up of 28 months (IQR 14.4 – 43.4), 29 (7.5%) patients experienced the composite primary endpoint. These patients were older and had a higher LSM at baseline (median 23.3 vs 6.2 kPa, p <0.01) and higher Δ% fibroscan (16.9% vs -3.5%, p <0.01) than patients who did not experienced a liver related events (LRE).

Baseline LSM show a good predictive performance for the composite endpoint events with an AUC of 0.897 (95% CI 0.845 – 0.948). Compared to patients with an LSM <10, patients with LSM between 10 and 20 kPa had a 9.7 fold higher risk for the primary outcome (HR 9.7 [2.05 – 45.79], p ≤0.01) and those with LSM>20 had a 55.6-fold higher risk (HR 55.63 [12.15 – 254.74], p ≤0.01). Median time between baseline and follow-up LSM was 12.2 months (IQR 7-21 months). Multivariate Cox regression analysis revealed a significantly lower risk of developing LRE for high-risk patients who showed LSM longitudinal improvements (Δ%LSM decrease >20%) compared to patients with stable or worsened one (HR 0.16, 95%CI 0.04 – 0.68, p=0.01). It also revealed a significantly higher risk of developing LRE in intermediate-risk patients who showed worsening longitudinal changes (Δ%LSM increase > 20%) of Fibroscan results (HR 6.66, 95%CI 1.69 – 26.23, p<0.01) compared with patients with improved or stable LSM. Interestingly, intermediate-risk patients who show a significant LSM improvement (Δ%LSM decrease >20%) did not experience any LRE in our cohort.
Conclusion: Our study strengthens the use of LSM both at baseline and during follow up as reliable prognostic factors in MASLD able to identify the subgroups of patients with MASLD at risk of LREs. In patients with intermediate or high risk of events at baseline, elastography surveillance should be encouraged.

ACUTE DIARRHEA IN A TERTIARY EMERGENCY DEPARTMENT: FROM READMISSION DETERMINANTS TO ANTIBIOTIC PRESCRIPTION

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Acute diarrhea represents a major public health issue, and the management of adult patients admitted to the emergency department (ED) for this problem remains challenging. In a retrospective analysis of over 20,000 patients who visited our tertiary-center ED for acute diarrhea between 2015 and 2022 and were subsequently discharged home, we found that age > 65 years, symptom onset > 24 hours before ED admission, refusal of hospitalization, and a history of chronic renal and liver diseases were independently associated with ED readmission for abdominal symptoms within 7 days. Specifically, in younger patients (aged 18 to 65 years), the presence of specific comorbidities (dementia, liver, and renal disease) significantly impacted ED readmission, while fever and altered serum creatinine levels were the main determinants in older patients (aged > 65 years). Antibiotics were prescribed in approximately 25% of patients, even if the etiology of diarrhea (viral or bacterial) was usually unavailable. Consistent with international guidelines, fluoroquinolones were the most frequently prescribed class, showing an inverse correlation with ED readmission. β-lactams and probiotics were also commonly prescribed; the latter were independently correlated with ED readmission in the elderly group. Although are study presents some intrinsic limitations, first of all its retrospective nature or the fact that we only analyzed records of discharged patients, resulting in possible analysis bias, mainly in the older population, which, due to comorbidities and the possibility of developing complications, is hospitalized more often, what emerges is the need of a comprehensive approach. This approach, including a detailed clinical history and laboratory and comorbidity assessment can support physicians in the management of different age subgroups of adults admitted to the ED for acute diarrhea.

THE ROLE OF DIABETES MELLITUS ON DELIRIUM ONSET: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Il delirium può svilupparsi in associazione ad una malattia cardiovascolare o cerebrovascolare sottostante e complicare un ricovero ospedaliero su tre, rappresentando un' importante problematica per i sistemi sanitari. Ciononostante, non è stata spiegata una chiara relazione tra l'insorgenza di delirium e il diabete mellito. Lo scopo di questo studio è stato quello di esplorare l'associazione tra il diabete mellito e il delirium, attraverso i seguenti obiettivi: a) valutare l'incidenza di delirium tra i pazienti affetti da diabete mellito, b) definire il rischio di insorgenza di delirium nei pazienti con diabete mellito, c) studiare il ruolo dei farmaci antidiabetici sull'insorgenza di delirium.
Metodi: È stata condotta una ricerca sulle principali banche dati biomediche quali: MEDLINE, Scopus e Web of Science fino a dicembre 2024. Sono stati selezionati gli studi che riportavano l'incidenza di delirium nei pazienti diabetici, i dati rilevanti sulla relazione tra il delirium e il diabete mellito e quelli riguardanti il ruolo dei farmaci antidiabetici sull'insorgenza di delirium.
Risultati: È stato identificato un numero totale di soggetti affetti da diabete mellito pari a 124356. L'incidenza ponderata del delirium è risultata essere pari al 30.2% (IC 95% 26,7-33,7 I2=99,6%). L'odds ratio (OR) aggregato corretto per lo sviluppo del delirium è risultato essere di: 1.59 (IC 95% 1,44-1,75 I2=88,9%). La somministrazione intra nasale di insulina rispetto al placebo è stata caratterizzata da un rischio relativo (RR) di 0,34 (IC 95% 0,23-0,52). L'utilizzo di metformina rispetto al suo non utilizzo nei pazienti diabetici è stato caratterizzato da un RR più basso per il delirium: RR aggregato = 0,71 (IC 95% 0,59-0,85 I2=84,8%).
Conclusioni: L'incidenza di delirium nei pazienti affetti da diabete mellito è di circa 30%. Il diabete mellito si associa ad un rischio più elevato di insorgenza di delirium. L'utilizzo cronico di metformina e l'uso di insulina intra nasale sono utili nella prevenzione di delirium.

IMMUNO-INFLAMMATORY PROFILE AND SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) IN PATIENTS WITH ACUTE ISCHEMIC STROKE: A PROSPECTIVE STUDY OF THE RELATIONSHIP BETWEEN GENETIC, ACUTE PHASE CYTOKINE LEVELS AND STROKE PROGNOSIS

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Background: The genetic basis of complex diseases like ischemic stroke probably consists of several predisposing risk factors, including genes involved in inflammation and thrombotic pathways. Genetics contribute significantly to stroke risk through several mechanisms: some genetic polymorphisms have been associated with the risk of stroke. However, the individual contribution of such polymorphisms is considered modest. Furthermore, since most ischemic strokes are due to thrombotic or thromboembolic occlusion, it is realistic to believe that there are polymorphisms in the genes that encode for factors involved in the coagulation cascade, in particular in maintaining the balance between fibrinolysis and thrombosis, that play a pathogenic role.
Aim of the study: This study aimed to evaluate:
- the frequency of some single-nucleotide polymorphisms (SNPs) of genes encoding pro-inflammatory cytokines and coagulation factors in stroke patients;
- the relationship between each identified SNP and TOAST stroke subtype (pathophysiological classification system of ischaemic stroke);
- the recurrence of major vascular events (new ischemic stroke, acute myocardial infarction and death for vascular causes);
- the relationship between the serum levels of the cytokines and the diagnostic subtype of ischemic stroke.
Materials and methods: All patients over 18 years old admitted for acute ischemic stroke in the period between 2011 and 2021 were prospectively enrolled. We collected blood samples within 72 hours of the onset of signs/symptoms referable to ischemic stroke. We performed genetic analysis for each patient to assess various genetic polymorphisms and laboratory analysis of serum cytokine levels at different collection times (T0, T1 and T2). We searched for the most important SNPs in the genes of the tested inflammatory cytokines, factors involved in platelet activation and the coagulation cascade such as TPA, PAI-1, PTSG-2, MMP-2, and MMP-9.
Results: We enrolled 624 subjects in this prospective observational study, including 429 patients with ischemic stroke and 195 patients without stroke. Compared with the controls, patients with acute ischaemic stroke had a significantly higher frequency of diabetes (55% vs 30%), hypertension (56% vs 25%), atrial fibrillation (40% vs 2%), previous stroke (52% vs. 8%), transient ischaemic attack (TIA) (42% vs. 12%), silent ischaemic brain injury (64% vs. 0.5%), carotid stenosis (68% vs. 0.5%), white matter changes or white matter hyperintensity lesions (WMHLs) (51% vs. 0.5%), and left ventricular hypertrophy (39% vs. 16%). Moreover, patients with ischaemic stroke showed significantly higher mean glucose blood levels (149.9 ± 73.8 mg/dL vs. 106.2 ± 22.6 mg/dL),

total cholesterol (184.3 ± 38.9 mg/dL vs 144.4 ± 38.2 mg/dL), LDL-cholesterol (110.1 ± 45.3 mg/dL vs 45.8 ± 21.1 mg/dL), and triglycerides (156.6 ± 104.7 mg/dL vs 77.9 ± 29.7 mg/dL), with statistical significance. Among patients with ischemic stroke, 47% had a large artery atherosclerosis stroke (LAAS), 27% had a lacunar stroke (LAC), and 26% had a cardioembolic stroke (CEI). Regarding the immunoinflammatory variables, patients with CEI showed significantly higher levels of blood glucose and all the cytokines analysed (IL-10, TNF-alpha, IL-1, and IL-6) compared to patients with LAC or LAAS. This result, in agreement with another study, further supports the hypothesis that inflammation plays an essential role in the pathogenesis of ischaemic stroke, but also suggests the possibility of a peculiar immunoinflammatory pattern for each stroke subtype. The marked inflammatory background that characterises the CEI subtype agrees with that described in previous reports, indicating the higher severity of this subtype. Multiple regression analysis revealed elevated IL-10, TNF-alpha, IL-6, and IL-1beta values are associated with LAAS and CEI subtypes, respectively. Furthermore, IL-10 levels were lower in patients who developed stroke during follow-up, whereas TNF-alpha and IL-1 levels were significantly higher in patients with recurrent stroke at follow-up. From the analysis of the distribution of the genotypic frequencies of the polymorphisms analysed, a statistically significant difference emerged between the cases and the controls for all the polymorphisms in the genes that encode for pro-inflammatory cytokines, for TPA, PAI-1, and PTSG-2.
Conclusions: In conclusion, our work emphasises the role of the inflammatory microenvironment in cerebral vascular disease, that ischemic stroke is a macrocosm that contains within it different entities with a different immune-inflammatory profile, and that, depending on this factor, the probability of having a different prognosis changes in relation to the subtype. The complexity of the ischaemic risk profile does not depend only on the classic risk factors, but it also seems to depend on specific SNPs that contribute to the genesis of the vascular event by unbalancing the difficult counterbalance between pro-thrombotic and antithrombotic factors.

THE IMPACT OF NOACS VS. VKAS ON ABSOLUTE AND RELATIVE COGNITIVE FUNCTION DECLINE OVER TIME: A MACHINE LEARNING APPROACH

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Background: Atrial fibrillation (AF) is the most common arrhythmia in adults, with incidence increasing with age. Cognitive impairment (CoI) and dementia share risk factors with AF. Meta-analyses indicate that AF increases the risk of CoI by 2.4-fold and 1.4-fold in patients with and without prior stroke, respectively. Thromboembolic events contribute to CoI, highlighting the importance of anticoagulant therapy (OAT). Non-vitamin K antagonist oral anticoagulants (NOACs) have a better safety profile than vitamin K antagonists (VKAs), but evidence of a cognitive benefit remains inconclusive.
Aims: This multicenter prospective cohort study evaluates the impact of NOACs versus VKAs on cognitive decline in elderly AF patients, using a Machine Learning approach.
Methods: Between 2008 and 2022, AF outpatients were enrolled at the Geriatrics Department, "Magna Graecia" University of Catanzaro, and the ProMISE Department, University of Palermo, Italy. Stroke and bleeding risks were assessed, and cognitive function was evaluated via the Mini-Mental State Examination (MMSE). A Random Forest Classifier predicted cognitive decline based on clinical and demographic features.
Results: At baseline, 58% of patients had normal MMSE scores, 18% were borderline, and 24% had mild impairment. NOAC users were younger (74±5 vs. 77±6 years, p<0.001) and had a lower BMI (29±5 vs. 30±3, p=0.002). The predicted probability of cognitive decline was significantly higher for VKA users (0.5027) versus NOAC users (0.2473, p<0.001).
Conclusion: NOAC use is associated with a lower predicted probability of cognitive decline, suggesting potential cognitive benefits over VKAs.

NOVEL BIOMARKERS IN ACUTE KIDNEY INJURY: THEIR ROLE IN THE DIAGNOSIS OF KIDNEY DYSFUNCTION AND ETIOLOGY DEFINITION, THEIR POTENTIAL AS PREDICTIVE MARKERS OF STRUCTURAL RENAL DAMAGE SEVERITY

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Background: Acute kidney injury (AKI) is a life-threatening condition, whose early diagnosis is crucial. The most commonly used method to evaluate renal function is the glomerular filtration rate (eGFR). The detection of new circulating molecules has taken hold for the early identification of kidney damage.
Methods: In this prospective observational study, 57 patients with AKI and 23 patients without acute renal damage were consecutively enrolled; urinary and serum concentrations of L-FABP, CYR61, TIMP-2, IGFBP-7, PENK, and KIM-1 were obtained in all patients.
Results: Patients with AKI showed significantly higher median urinary levels of NGAL [13.3 pg/mL (5.2-10.7) vs 6.4 pg/mL (3.2- 10.6); p=0.009], IGFBP7 [453 pg/mL (210-2108) vs 221 pg/mL (103-337); p=0.011], and TIMP-2 X IGFBP7 [812 pg/mL (284-3288) vs 306 pg/mL (73-1058); p=0.044] compared to the control group, with statistical significance. The patients comprised 20 females and 37 males, with a mean age of 75 (74.2±7.9). They were divided into two subgroups based on the aetiology of the kidney damage: 33 patients were diagnosed with prerenal AKI, and 24 patients with renal AKI. Patients with a renal AKI in comparison with ones with a prerenal etiology showed significantly higher serum levels of FABP1 [8.0 pg/mL (2.9-59) vs 3.0 pg/mL (2.1-6.4); p=0.047)], Cyr61 [203 pg/mL (59-493) vs 94 pg/mL (44-200); p=0.030], NGAL [18 pg/mL (12-22) vs 9.8 pg/mL (4-16); p=0.011], IGFBP7 [1714 pg/mL (350-2367) vs 234 pg/mL (128-626); p=0.001)], and [TIMP-2 x IGFBP-7] [2684 pg/mL (784-9288) vs 360 pg/mL (177-1261); p=0.002)]. However, only IGFBP-7 and FABP1 levels have maintained a statistical association with the AKI aetiology at the multinomial regression analysis. Furthermore, we have tried to associate the values of these markers with an improving or worsening as changes of creatinine serum values, defining two variables: delta creatinine 1, which refers to the entity of the renal damage through the evaluation of the difference between the creatinine at admission and the basal value previous the kidney injury, and the delta creatinine 2, defined by the difference between the creatinine value at the admission and the value at the discharge. We have found a significant correlation using the correlation Spearman's test, between the urinary values of FABP1 (p= 0.006), TIMP-2 (p= 0.040) and the serum concentrations of KIM-1 (p=0.048), with a higher value of the delta creatinine 1, underlining a greater worsening of the creatinine at the admission compared with the basal values and so a more severe harming of the renal function. A statistically significant correlation was found between KIM-1 and the positive value of the delta creatinine 2, stressing the degree of the improvement of the renal function defined as the entity of the reduction of the creatinine values at the discharge compared with the admission values. Moreover, we performed a ROC (receiver operating characteristics) curve for IGFBP7 that identifies an area under the curve (AUC) of 0.756 with p<0.001 and that can thus be considered a statistically significant predictor of etiologic diagnosis - prerenal or renal - of AKI.
Discussion: We have found that concentrations of NGAL, IGFBP7 and TIMP-2 X IGFBP7 were statistically higher in patients with AKI compared to controls, underlying the potential use of these markers for the detection of renal injury, as demonstrated in previous studies. In the group of patients with AKI, we found a statistically significant difference between prerenal and renal AKI in terms of FABP1, Cyr61, NGAL, IGFBP7, and TIMP-2 X IGFBP7 concentrations. In the multinomial regression analysis, only IGFBP-7 and FABP1 levels maintained a statistical association with the AKI aetiology. The use of the ROC curve allowed us to graphically report that IGFBP7 plays a role in the etiologic diagnosis of AKI because it directs the diagnostic pathway of patients with acute kidney damage. Furthermore, our study has found an association between some of these biomarkers and creatinine variations, defined as delta creatinine 1 and delta creatinine 2. In particular, urinary FABP1, TIMP-2, and serum KIM-1 levels were associated with a greater worsening of renal function. Patients affected by AKI with higher serum creatinine values at admission, which differed more from the basal values, had higher concentrations of FABP-1 and TIMP-2 in the urine and KIM-1 in the serum, supporting a possible role of these proteins in defining the severity of renal injury. We have found higher concentrations of KIM-1 in the serum of patients with a greater reduction of the creatinine values compared with the time of the acute damage. Thus, it may be related to defining the severity of the renal injury but also to a higher probability of recovery from renal dysfunction.
Conclusions: These results gain relevance in clinical practice: patients with kidney damage should not all be considered the same at the time of first contact with the physician, and therapy for them should not always be the same.

NON-INVASIVE EVALUATION OF LIVER STEATOSIS: THE POTENTIAL ROLE OF ULTRASOUND-DERIVED FAT FRACTION

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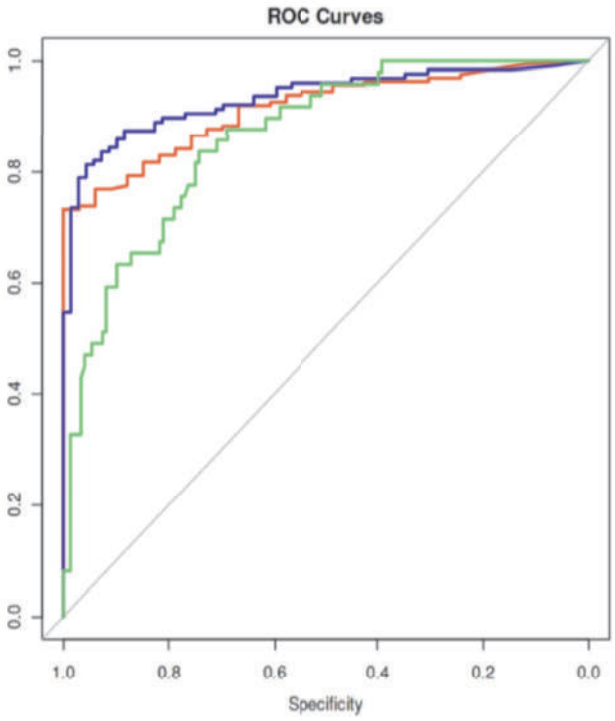
Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is defined by the presence of hepatic steatosis detected either through imaging or biopsy, along with at least one of the following five cardiometabolic risk factors: 1) body max index (BMI) ≥ 25 kg/m2 (≥ 23 kg/m2 in Asians) or waist circumference > 94 cm in men, > 80 cm in women, or adjusted for ethnicity; 2) fasting serum glucose ≥ 100 mg/dL (≥ 5.6 mmol/L) or 2- hour post-load glucose level ≥ 140 mg/dL (≥ 7.8 mmol/L) or HbA1c ≥ 5.7% or on specific drug treatment; 3) blood pressure ≥ 130/85 mmHg or specific drug treatment; 4) plasma triglycerides ≥ 150 mg/dL (≥ 1.70 mmol/L) or specific drug treatment; 5) plasma HDL cholesterol < 40 mg/dL (< 1.0 mmol/L) for men and < 50 mg/dL (< 1.3 mmol/L) for women or specific drug treatment. MASLD affects nearly 25-30% of the global adult population and has shown a notable increase in prevalence over recent decades. Liver steatosis is one of the main causes of liver disease with several clinical implications, such as steatohepatitis, liver cirrhosis, and hepatocellular carcinoma. Liver biopsy is considered the gold standard for diagnosing liver steatosis, as it allows for grading steatosis and staging fibrosis in the histological sample. However, its invasiveness, limited patient acceptability, sampling variability and high cost make it unsuitable for routine clinical practice. For this reason, the development of non-invasive techniques for the early diagnosis of MASLD and the subsequent assessment of the response to the interventions is crucial.
Aim: This study aims to evaluate the accuracy of ultrasound-derived fat fraction (UDFF) in a population of patients with moderate to morbid obesity.
Method: A total of 95 obese patients were evaluated for liver steatosis with ultrasound visual assessment and UDFF measure using the Samsung RS85 Prestige system. Therefore, the patients were classified in four groups based on visual assessment of steatosis (absent, mild, moderate, severe). For each group distribution of UDFF has been evaluated and one-way ANOVA and post-hoc comparisons were performed to identify significant differences between the groups. Receiver Operating Characteristic (ROC) curves were generated the Youden Index was then utilized to identify the optimal cut-off points for the UDFF within each group.
Results: This retrospective study evaluated a total of 95 patients. According to inclusion criteria, 84 patients were included (51 females, 33 males) with a mean age of 45.6 years (SD 12.5, range: 17-71 years). The population exhibited a higher prevalence of class II and III obesity (respectively 27 and 54 patients), with a mean BMI of 42.9 kg/m2 (SD 6.5, median 41.7 kg/m2). A significant proportion of patients had prevalent comorbidities: 39.3% had type 2 diabetes, 35.7% had hypertension, and 16.7% had both. Dyslipidemia, defined as elevated LDL cholesterol levels (above 100 mg/dl for low-to-moderate cardiovascular risk and above 70 mg/dl for high or very high risk), was present in 76.2% of the cohort. Among these patients, 16 showed no evidence of steatosis (S0) on liver ultrasound; 6 patients had mild steatosis (S1), 39 had moderate steatosis (S2), 23 had severe steatosis (S3). No statistically significant differences were found between the four groups regarding the degree of fibrosis measured by 2DS Shear-Waves elastography. Significant differences in mean UDFF values were observed across the four steatosis severity groups (ANOVA, $p < 0.001$). Post-hoc analysis revealed significant pairwise differences between all groups. Mean UDFF values increased progressively across the severity spectrum, with Group 1 (No steatosis) exhibiting the lowest mean (5.33 ± 2.00, 95% CI: 4.26-6.40), followed by Group 2 (Mild steatosis) (9.08 ± 2.19, 95% CI: 6.79-11.37), Group 3 (Moderate steatosis) (14.19 ± 4.89, 95% CI: 12.60-15.78), and Group 4 (Severe steatosis) exhibiting the highest mean (21.36 ± 5.28, 95% CI: 19.08-23.64). Based on the ROC curves (Figure 5) and the Youden index, we propose the following cut-off values for classifying steatosis severity.
Conclusions: Our findings suggest that UDFF may offer a valuable tool for objectively quantifying liver fat content with a more easily comparable parameter, improving the accuracy of steatosis grading and follow-up.



INFLAMMATORY ACTIVATION, EPIGENETIC SIGNATURE AND MORPHO-STRUCTURAL ALTERATION IN A COHORT OF PATIENTS WITH CHRONIC HEART FAILURE AND PERMANENT ATRIAL FIBRILLATION: A CROSS-SECTIONAL STUDY

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Background: Atrial fibrillation (AF) is a complex disorder involving inflammatory, morpho-structural, and genetic factors. Emerging evidence suggests inflammation plays a pivotal role in AF initiation, maintenance, and outcomes.
Methods: We conducted a cross-sectional case-control study to assess whether, among patients with chronic heart failure (CHF) and permanent AF, serum inflammatory cytokines, metabolic parameters, epigenetic factors, and echocardiographic markers of structural remodeling are interrelated. Eighty-two consecutive CHF patients with permanent AF and 82 CHF patients with sinus rhythm and no AF history were enrolled from the Internal Medicine and Stroke Care Unit at "P. Giaccone" Hospital, Palermo, between January 2020 and May 2022.
Results: AF patients were older and exhibited higher left atrial volume index (LAVI), reduced left atrial (LA) strain, increased relative wall thickness (RWT), and lower ejection fraction (EF%). Renal markers, including estimated glomerular filtration rate (eGFR) and microalbuminuria, were significantly different. Inflammatory markers such as C-reactive protein (CRP), interleukin 6 (IL-6), interleukin 8 (IL-8), and NT-proBNP were elevated in the AF group. Multivariable logistic regression identified LAVI, LA strain, microalbuminuria, albumin/creatinine ratio (ACr), and protein/creatinine ratio (PCr) as independent predictors of AF. Correlation analyses demonstrated strong associations between echocardiographic, inflammatory, and renal parameters. No significant differences in circulating miRNAs were observed.
Conclusions: These findings highlight the intricate interconnection between atrial remodeling, renal dysfunction, and systemic inflammation in AF pathogenesis. A better understanding of these mechanisms may inform future risk stratification strategies and support the development of more effective, targeted therapies in patients with CHF.

BILATERAL OPTIC NEURITIS AND HYPOVISION IN A PATIENT WITH CARDIOVASCULAR COMORBIDITIES: SYPHILIS OR HORTON'S ARTERITIS? A COMPLEX CLINICAL CASE

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La perdita del visus improvvisa bilaterale è un'emergenza clinica che impone una rapida diagnosi differenziale. Sebbene l'arterite di Horton sia una delle principali cause in età avanzata, è fondamentale non trascurare eziologie infettive, paraneoplastiche o autoimmuni, specialmente in contesti clinici complessi.
Paziente di 68 anni, con storia di ipertensione, fibrillazione atriale in terapia anticoagulante, dislipidemia, sindrome di Raynaud, psoriasi e fumatore attivo, si presentava presso il Pronto Soccorso per calo del visus bilaterale ingravescente (sinistra > destra) da circa due settimane. In Area di Emergenza agli esami ematochimici evidenza leucocitosi neutrofila associato ad incremento degli indici di flogosi (VES e PCR)marcatamente elevati.
In Area di Emergenza eseguiva dapprima TC Encefalo e successiva integrazione con RM Encefalo con studio angio che ha escluso la presenza di lesiosi parenchimali ischemiche e/o emorragiche. In anamnesi: episodio pregresso di neurite ottica destra (ottobre 2024) per cui eseguiva valutazione oculistica con diagnosi di neurite ottica ischemica anteriore e trattata con terapia steroidea con discreto beneficio.
All'ingresso, il paziente si presentava vigile,collaborante,orientato nello spazio-tempo e sul se, eupnoico a riposo ed in aria ambiente,apiretico; esame obiettivo neurologico nella norma eccetto per presenza di marcato ipovisus bilaterale (sinistra>destra) ed all'esame obiettivo presenza di onicogrifosi alle mani e alopecia occipitale a "morso di tarma" e perdita del terzo esterno delle sopracciglia (segno di Hertoghe). Iniziava terapia con metilprednisolone ad alte dosi, con parziale miglioramento oculare e riduzione degli indici di flogosi.
Al fine di confermare o escludere l'eziologia autoimmune, venivano richiesti dosaggio di autoanticorpi (ANA,ENA,ANCA) ed eseguita biopsia dell'arteria temporale , entrambi con esito negativo.
Sospettando una eventuale eziologia infettiva/parainfettiva, sono stati indagati i possibili agenti determinanti un possibile coinvolgimento encefalico/oculare, e richieste numerose indagini microbiologiche tra cui sierologia per virus epatotropi maggiori (HBV e HCV) e minori (CMV, EBV,HSV),Borrelia B., Quantiferon TB Gold, Leptospira, Lyme, HIV, Ryckettisia Conorii, ed infine sierologia per Treponema pallidum IgG e IgM risultata positiva, successivamente confermata al test sierologico di II livello (VDRL e TPHA). Sulla scorta di tali reperti, veniva eseguita puntura lombare con prelievo di LCR con riscontro di lieve leucorrachia, lieve glicorachia ed ricerca immunoglobuline IgG di T.Pallidum tramite immunoblot con esito positivo, seppur a basso titolo. Posta dunque diagnosi di neurosifilie, veniva introdotta terapia antibiotica con Ceftriaxone con beneficio.
Infine per escludere una genesi paraneoplastica, è stata eseguita TC TB c/s m.d.c. che ha escluso la presenza di lesioni eteroplastiche.
Ulteriori accertamenti (potenziali evocati visivi) documentavano sofferenza bilaterale delle vie ottiche in assenza di ulteriori reperti significativi come danni retinici, uveite e/ o segno di Argyll-Robertson. A completamento, veniva eseguito screening dell'assetto glicometabolico con riscontro di valori di emoglobina glicata indicativi di diabete mellito (HbA1c 7,3%, insulina e C-peptide ridotti).
Il caso ha posto una sfida diagnostica rilevante. L'iniziale sospetto di arterite temporale è stato ridimensionato dalla negatività della biopsia e dalla contemporanea evidenza sierologica per Treponema Pallidum. La compromissione visiva potrebbe essere attribuita a un meccanismo multifattoriale: ischemia vasculitica, neuroinfiammazione da sifilide, immunosoppressione da steroidi e dismetabolismo.
La neurosifilide è una grave complicanza della sifilide che può svilupparsi a uno stadio precoce (< ¹ anno) o tardivo (> ¹ anno). Nella sifilide, con l'invasione del SNC e la neurosifilide che ne consegue può essere suddivisa in early (¹, ² anni dopo l'infezione primaria) o late (vari anni dopo l'infezione primaria). L'infezione early può essere asintomatica o presentarsi con le classiche caratteristiche della meningite (cefalea, fotofobia, meningismo) fino a neuropatia del nervo ottico e acustico comportando deficit visivi o uditivi.L'infezione tardiva è caratterizzata da paralisi generalizzata(progressiva demenza, sindromi psichiatriche, disartria) e dalla tabe dorsale, come esiti di una reazione meningea cronica alla invasione del treponema con un danno simil vasculitico delle arterie cerebrali di piccolo-medio calibro determinando ictus, paralisi dei nervi cranici e diverse forme di mielopatia. La diagnosi di neurite ottica bilaterale impone un approccio differenziale ampio e multidisciplinare. Questo caso evidenzia l'importanza di indagare anche eziologie infettive come la sifilide, ancora oggi causa sottovalutata di neurosintomi in età avanzata. La tempestiva identificazione e il trattamento multidirezionale hanno permesso un miglioramento clinico e laboratoristico significativo.

HUMAN METAPNEUMOVIRUS IN ADULTS: A RETROSPECTIVE OBSERVATIONAL STUDY AT ASST GRANDE OSPEDALE METROPOLITANO NIGUARDA

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Introduction: Human metapneumovirus (hMPV) is a respiratory virus from the Pneumoviridae family, first described in 2001 in the Netherlands. Initially identified as pathogen of children, it is now considered ubiquitous and a major cause of respiratory infections also in frail adults, including the elderly and immunocompromised. While infections are often mild in healthy adults, hMPV can have a significant impact on morbidity and, occasionally, mortality. Following the COVID-19 pandemic, the virus's incidence nearly doubled, accounting for up to 8.8% of all respiratory virus tests in Italy. No vaccines are currently available and treatment is supportive.
Objectives:
Primary: to describe demographic and clinical characteristics, comorbidities, disease severity, treatments, and outcomes in hospitalized adult patients with hMPV.
Secondary: to identify potential risk factors for poor outcomes (non-invasive ventilation, ICU admission, invasive ventilation, mortality).
Methods: This retrospective, single-center observational study was conducted at "Grande Ospedale Metropolitano Niguarda" (Milan) between January 2023 and April 2024. Adult patients (≥18 years) hospitalized in medical wards with a positive multiplex RT-PCR for hMPV were included. Demographic, clinical, and outcome data were collected retrospectively.
Results: Among 3020 respiratory viral tests, 753 (24.9%) were positive; 85 for hMPV (11.2%). After exclusions, 49 patients were analyzed.
Mean age was 70.2 years and 73.5% were aged ≥65. Nearly all patients (95.9%) had at least one comorbidity, most commonly hypertension (55.1%), diabetes (42.9%), and immunosuppression (34.7%). Cardiovascular (46.9%) and respiratory (38.8%) conditions were most prevalent. 28.6% were current or former smokers. Median Charlson Comorbidity Index was 5, corresponding to a 10-year survival of 21%.
Diagnoses included pneumonia (49%), acute bronchitis (24.5%), and COPD exacerbation (16.3%). 71.4% required oxygen therapy. ICU admission occurred in 4.1%, and 18.4% were admitted to a high-dependency unit. A composite outcome (ICU or intermediate care) was observed in 20.4%. No intubations; one death was recorded, unrelated to hMPV.
Risk factors for pneumonia included active smoking (RR 2.3) and interstitial lung disease (RR 1.8). COPD exacerbation was associated with home oxygen therapy (RR 6.8). The composite outcome was significantly associated with pre-existing respiratory disease (RR 14.2), COPD (RR 8.1), long-term oxygen therapy (RR 7.5), connective tissue disease (RR 5.9), and interstitial lung disease (RR 3.8). Pneumonia (RR 9.4), COPD exacerbation (RR 7.7), and viral coinfection (RR 3.8) were also linked to worse outcomes.
Conclusions: hMPV is responsible for around 11% of respiratory viral infections in hospitalized adults. It affects mainly elderly patients with multiple comorbidities, especially cardiovascular and respiratory. Clinical outcomes are often severe, with pneumonia in nearly half the cases and respiratory failure in over 70%. Risk of clinical deterioration is significantly associated with pre-existing respiratory conditions.

ALL THAT IS GOLD DOES NOT GLITTER: THE CASE OF A LARGE HEMATOMA-LIKE ABDOMINAL ABSCESS

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A94-years-old female patient came to our attention during an outpatient visit for general malaise and a persistent swelling of the entire right side of the

abdomen starting one month before. Clinical history was unremarkable, save for atrial fibrillation treated with dabigatran. A prior abdominal CT scan revealed a hematoma of the right external abdominal oblique muscle, without acute bleeding. Anticoagulation was not stopped owing to high thromboembolic risk (CHA_2DS_2-VA score =4), favouring clinical surveillance. At ultrasound examination, a corpuscular mass was detected, occupying the entirety of the right paracolic gutter, while a second CT scan revealed the presence of a large gallstone (43mm) and signs of emphysematous cholecystitis. The gallbladder showed no clear separation from the right colic flexure and was encapsulated within a larger13x10x21cm mass occupying the entirety of the right abdominal wall. Due to the high surgical risk, a percutaneous drainage of the abscess was performed (10F drain), with removal of ~350ml of stercoraceous exudate. Microbiological cultures were not conclusive for any specific pathogen. As surgical risks far outweighed the possible benefits, the patient was treated with piperacillin/tazobactam4,5g QID for fifteen days and discharged upon normalization of serum inflammation markers. Acute cholecystitis can progress to gallbladder empyema, a clinical picture requiring a time-sensitive, multi-disciplinary approach based on antibiotics treatment, surgical aspiration, up to cholecystectomy. Left untreated, the condition quickly evolves into life-threatening septic shock. Bile statis caused by impacted and obstructing gallstones creates an ideal medium for pathogens, chiefly Clostridia, Klebsiella and E. coli, leading to an empyema in5-15% of calculus cholecystitis. Mortality is noticeably higher in the elderly and in patients affected by diabetes and immunodeficiency. Clinical presentation mimics acute cholecystitis, with tenderness of the right hypochondrium and a positive Murphy's sign, leading into fever, tachycardia, and septic shock in case of perforation. Ultrasonography shows pericholecystic oedema and gallstones, along with fluid collections along the paracolic gutter, whereas CT scans can contribute to cases where the window is either inadequate or does not allow an accurate characterisation of the entire empyema. First-line treatment focuses on broad spectrum antibiotics, intravenous fluids and cholecystectomy, along with abscess drainage, ideally within48-72hours.

In the clinical case presented, the afebrile presentation with mild or absent right upper quadrant pain was unusual. Nevertheless, symptoms can be misleading and not directly correlate with disease severity or progression towards systemic sepsis. Furthermore, the preexisting haematoma acted as both a risk factor and a locus minoris resistentiae forthe development of empyema. An internist must be aware of atypical manifestations associated with gallstone disease, cholecystitis and empyema, especially in elderly people, in order to plan a prompt combined approach to initial workup and follow-up combining accurate history taking and physical examination with ultrasonography.

MEDITERRANEAN DIET AND HYPERTENSION: RELATIONSHIP BETWEEN ADHERENCE TO A MEDITERRANEAN DIET AND ARTERIAL HYPERTENSION

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Background: and aims: No study has examined the relationship between the presence of hypertension and the Mediterranean diet (MeDi) concerning other cardiometabolic risk factors. We conducted a retrospective study to evaluate the presence of lower adherence to the Mediterranean diet in hypertensive subjects and analyze the correlation between adherence to the Mediterranean Diet and other cardiovascular risk factors.

Materials and methods: We analyzed the records and collected the data of the patients admitted to our Internal Medicine ward from 2010 to 2020 with a discharge diagnosis of metabolic syndrome according to the NCEP ATP-III criteria. We divided patients in two groups: hypertensive and no hypertensive. The Mediterranean Diet Score was used to evaluate the consumption and frequency of the foods characterizing a Mediterranean-type diet.

Results: Hypertensive patients were older (73 ± 11.5 vs. 57.2 ± 5.7; $p < 0.0005$) and had a higher mean BMI (29.9 ± 5.2 vs. 25 ± 2.4, $p < 0.0005$) compared to control group. The degree of adherence to the Mediterranean diet, evaluated by the Mediterranean diet score (MDS), was significantly higher in the control group than in the hypertensive group (3.8 ± 1.6 vs 6.9 ± 1.5; $p < 0.0005$). Various comorbidities were more prevalent in hypertensives, such as type 2 diabetes mellitus, heart failure, ischemic heart disease, and chronic renal failure. Lower adherence to the Mediterranean diet was significantly associated with an increased prevalence of dyslipidemia, cardiovascular diseases, chronic renal insufficiency, and PAD/carotid atherosclerosis, and significantly worse lipid profiles.

Conclusion: Our findings show that a lower adherence to a Mediterranean Diet Style is associated with a worse cardiovascular risk factor profile in hypertensive patients. Thus, Mediterranean diet adherence in hypertensive subjects is associated with a wider cardiometabolic scenario.

STEROID-SENSITIVE NEUROINFLAMMATION IN 2 SIBLINGS WITH AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME

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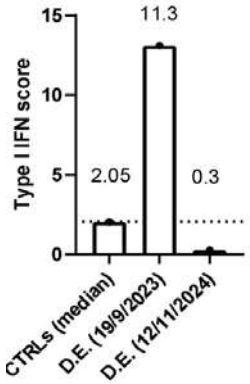
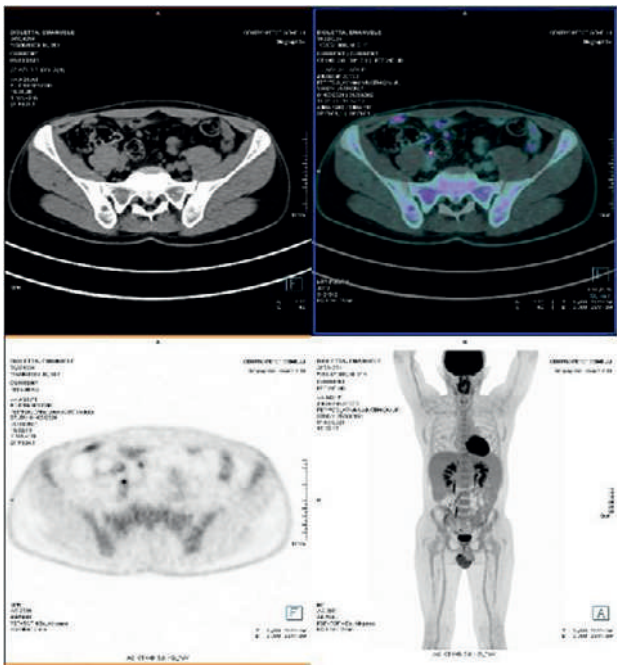
Introduction: Autoimmune lymphoproliferative syndrome (ALPS) is characterized by defective lymphocyte homeostasis due to failure of Fas-mediated apoptosis: genetic variants leading to defects in the classic Fas-Fas ligand (FasL) pathway result in abnormal lymphocyte survival and cause both non-infectious chronic lymphoproliferation and autoimmune phenomena. Although neurologic manifestations have been rarely reported in ALPS, no psychiatric features have ever been described.

Case report: A 35-year-old man was hospitalized for focal seizures, cognitive decline, hallucinations and delusions. Since the age of 2 years, he suffered from recurrent fevers, arthralgia, oral ulcers, pharyngodynia, hepatosplenomegaly and persistent elevation of inflammatory markers without cytopenia. At 29 years, because of severe abdominal pain and fever, a colchicine trial was tried without benefit. The NGS panel for autoinflammatory syndromes was negative.

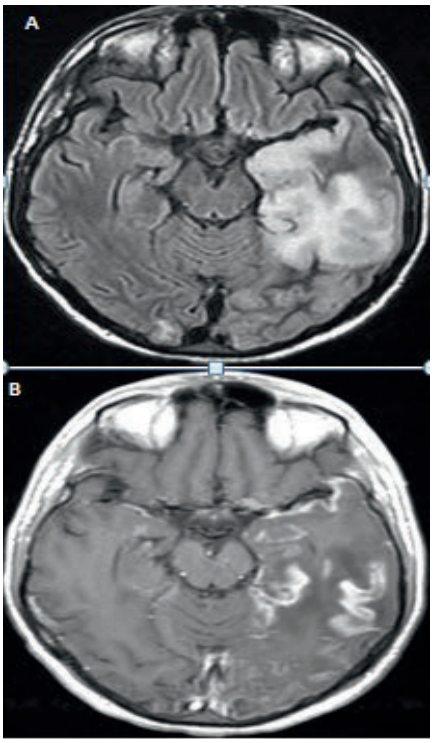


The interferon (IFN) signature demonstrated high type I IFN levels (11%; n.v. <2) (fig. 1).

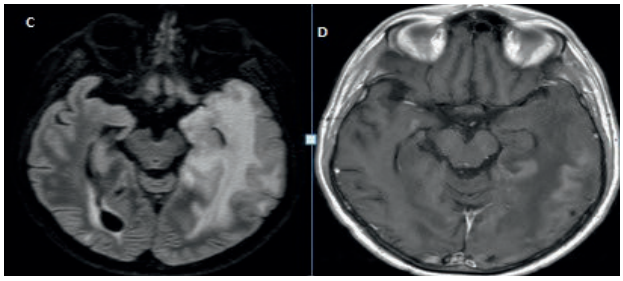
The total body 18FDG PET-CT scan showed multiple lymphnodes involvement and confirmed hepato- and splenomegaly (Fig.2).



At 32 years an **increased number of double negative lymphocytes** was found (11%) with **Fas receptor assay after exposure to specific FasL antibodies showing 93% survival**, which led to a diagnosis of ALPS. At the age of 34 years, he presented new onset of focal epilepsy with secondary generalization. EEG showed left-sided irritative anomalies and brain MRI detected right parieto-occipital oedema with T2/FLAIR hyperintensity and gyral and hippocampal contrast enhancement. Levetiracetam was started but, one month later, progressive cognitive decline with suicidal ideation emerged. A diagnosis of psychosis was established, requiring a combination of valproate, aripiprazole and haloperidol with poor benefit. Left homonymous hemianopsia and occasional transitory phosphenes were also referred. One year later, at 35 years, the patient presented confusion with worsening cognitive/motor slowness and apathy; brain MRI showed T2/FLAIR hyperintensity of the left cerebral cortex with extension to the temporal lobe, insular region, external capsule, occipital regions and gyral/hippocampal contrast enhancement (fig.3)



The cerebrospinal fluid analysis revealed increased protein and IgG levels thus showing blood brain barrier damage. A tissue-based assay demonstrated liquor immunoreactivity against rat brain tissue, but no specific neuronal antibody was ever accordingly detected. The patient did not present other signs of systemic involvement consistent with a mitochondrial disorder, as demonstrated by negative lactate levels on both serum and cerebrospinal fluid and the muscle biopsy. Quantiferon test, autoantibodies panel and thrombophilia screening were negative. A total body CT scan excluded any neoplasm. A 5-day intravenous high-dose methylprednisolone treatment was started, leading to rapid benefit of cognitive/psychiatric symptoms and brain oedema improvement on subsequent MRI (fig. 4).



The patient's sister, 20 years earlier, presented similar features. Her symptoms started at the age of 10 years with recurrent fevers, persistent elevation of inflammatory markers, hepatosplenomegaly, hypergammaglobulinemia, epileptic encephalopathy, and slowly progressive cognitive decline. Psychiatric symptoms with motor dysfunction were noted at around 30 years. The patient died at 36 years due to infectious complications secondary to steroid adverse effects and prolonged immobilization.

Conclusion: This report shows that an extensive autoimmune neurological involvement resulting in psychosis, epileptogenic encephalopathy, motor and visual involvement (with consistent radiological images) may be present in ALPS syndrome, without detecting any known anti-neuronal antibodies thus defining a neurological autoinflammatory phenotype. The clinical exome testing is currently ongoing to assess the different ALPS genes potentially involved in such

Acknowledgments: We acknowledge: the patient, his family and the Italian Association of Periodic Fevers (AIFP).

MEDITERRANEAN DIET EFFECTS ON VASCULAR HEALTH AND SERUM LEVELS OF ADIPOKINES AND CERAMIDES

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Background: A randomized clinical trial to evaluate the effect of a Mediterranean-style diet on vascular health indices such as endothelial function indices, serum lipid and ceramide plasma and some adipokine serum levels. We recruited all consecutive patients at high risk of cardiovascular diseases admitted to the Internal Medicine and Stroke Care ward at the University Hospital of Palermo between September 2017 and December 2020.

Materials and methods: The enrolled subjects, after the evaluation of the degree of adherence to a dietary regimen of the Mediterranean-style diet, were randomised to a Mediterranean Diet (group A) assessing the adherence to a Mediterranean-style diet at each follow up visit (every three months) for the entire duration of the study (twelve months) and to a Low-fat diet (group B) with a dietary "counselling" starting every three months for the entire duration of the study (twelve months).The aims of the study were to evaluate: the effects of adherence to Mediterranean Diet on some surrogate markers of vascular damage, such as endothelial function measured by means of the reactive hyperaemia index (RHI) and augmentation index (AIX), at the 6-(T1) and 12-month (T2) follow-ups; the effects of adherence to Mediterranean Diet on the lipidaemic profile and on serum levels of ceramides at T1 and T2 follow-ups; the effects of adherence to Mediterranean Diet on serum levels of visfatin, adiponectin and resistin at the 6- and 12-month follow-ups.

Results: A total of 101 patients were randomised to a Mediterranean Diet style and 52 control subjects were randomised to a low-fat diet with a dietary "counselling". At the six-month follow-up (T1), subjects in the Mediterranean Diet group showed significantly lower mean serum total cholesterol levels, and sig-

nificantly higher increase in reactive hyperaemia index (RHI) values compared to the low-fat diet group. Patients in the Mediterranean Diet group also showed lower serum levels of resistin and visfatin at the six-month follow-up compared to the control group, as well as higher values of adiponectin, lower values of C24:0, higher values of C22:0 and higher values of the C24:0/C16:0 ratio. At the twelve-month follow-up (T2), subjects in the Mediterranean Diet group showed lower serum total cholesterol levels and lower serum LDL cholesterol levels than those in the control group. At the twelve-month follow-up, we also observed a further significant increase in the mean RHI in the Mediterranean Diet group, lower serum levels of resistin and visfatin, lower values of C24:0 and of C:18:0,and higher values of the C24:0/C16:0 ratio.
Discussion: The findings of our current study offer a further possible explanation with regard to the beneficial effects of a higher degree of adherence to a Mediterranean-style diet on multiple cardiovascular risk factors and the underlying mechanisms of atherosclerosis. Moreover, these findings provide an additional plausible interpretation of the results from observational and cohort studies linking high adherence to a Mediterranean-style diet with lower total mortality and a decrease in cardiovascular events and cardiovascular mortality.

UNMASKING LATENT AUTOIMMUNE DIABETES IN ADULTS: A CASE REPORT OF EARLY-ONSET INSULIN DEPENDENCE IN A 57-YEAR-OLD PATIENT

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Introduction: Latent Autoimmune Diabetes in Adults (LADA) is a form of autoimmune diabetes that typically manifests after age 30 and is often misclassified as type 2 diabetes mellitus (T2DM) due to its insidious onset and transient response to oral hypoglycemic agents [1]. Unlike classic type 1 diabetes, LADA evolves more slowly and patients are not insulin-dependent at diagnosis, yet they test positive for pancreatic islet autoantibodies—most commonly anti-GAD, and less frequently anti-IA2, anti-insulin, or anti-ZnT8 [2].
Epidemiological studies estimate that 2–12% of adult-onset diabetes cases may in fact be LADA, with variation based on ethnicity and diagnostic criteria used [3]. The clinical course is heterogeneous, often leading to delayed diagnosis and suboptimal treatment. Importantly, early identification of LADA is critical, as insulin therapy may preserve residual β-cell function and delay disease progression [1]. Furthermore, LADA patients often present with a personal or familial history of autoimmune diseases, such as autoimmune thyroiditis, which can be a useful diagnostic clue [4].
In this case report, we describe the diagnostic process of a patient initially considered to have type 2 diabetes but subsequently diagnosed with LADA, highlighting the clinical features, laboratory findings, and importance of a tailored therapeutic approach.
Case Description: We report the case of a 57-year-old man with a recent diagnosis of diabetes mellitus in September 2024, presenting with an HbA1c of 14.1%. His medical history includes Hashimoto's thyroiditis, hypertension, and a family history of autoimmune diseases (systemic lupus erythematosus SLE). The patient exhibited symptomatic hypoglycemia and occasional postprandial hyperglycemia despite lifestyle modifications. Laboratory investigations revealed low C-peptide (0.7 ng/ml), positive anti-GAD (267.33 IU/mL), anti-insulin (9.67 IU/mL), anti-ZnT8 (229.33 U/mL), and anti-islet cell (73.4 COI) antibodies, confirming an autoimmune etiology. Given the presence of multiple islet autoantibodies and the clinical course, a diagnosis of LADA was established. The patient was initiated on a basal-bolus insulin regimen with Degludec and Aspart fast acting, leading to improved glycemic control. Additional findings included mild hepatic steatosis and non-hemodynamically significant carotid atherosclerosis.
Conclusion: This case underscores the importance of considering LADA in adults presenting with new-onset diabetes, especially in the presence of autoimmune markers and absence of metabolic syndrome features. Early detection through autoantibody screening allows for timely initiation of insulin therapy, which may preserve residual β-cell function and reduce the risk of complications. Clinicians should maintain a high index of suspicion for LADA to ensure accurate diagnosis and optimal management.
References:
Diabetes
J Clin Endocrinol Metab
Diabetes Metab Res Rev
Diabetologia

NON-INVASIVE ASSESSMENT OF LIVER HISTOLOGY IN MASLD USING MULTIPARAMETRIC ULTRASOUND

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Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) is an increasingly prevalent condition and a leading cause of hepatic cirrhosis worldwide. Histological evaluation remains the reference standard for diagnosing and quantifying hepatic fat content, as well as assessing key pathological features such as inflammation and fibrosis. However, liver biopsy is invasive and unsuitable for routine clinical monitoring.
There is a growing need for non-invasive imaging techniques capable of evaluating not only hepatic steatosis, but also inflammatory activity—recognized as the primary driver of fibrogenesis and disease progression.
Multiparametric ultrasound (MPUS), which combines assessments of attenuation, stiffness, and viscosity, represents a promising tool to address this clinical gap. The aim of this study was to investigate the correlation between MPUS parameters and histological findings in a cohort of patients with MASLD.
Materials and methods: In this prospective single-center study, 42 adult patients undergoing ultrasound-guided percutaneous liver biopsy for MASLD-related indications were prospectively enrolled. A MPUS examination was performed immediately prior to biopsy.
USAT (attenuation), E (elastography), and Vi (viscosity) measurements were acquired as the mean of five acquisitions, each meeting the quality criterion of IQR/M ≤30%, in accordance with WFUMB recommendations.
Liver histology was evaluated using both the SAF score (Steatosis, Activity, Fibrosis) and the NAFLD Activity Score (NAS) to grade steatosis, inflammation, and fibrosis, and to assess overall disease activity.
Testing the non-normal distributions, continuous variables were compared using the Mann–Whitney U test or Kruskal–Wallis test, as appropriate. Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of USAT in distinguishing histological grades of steatosis. Finally, two predictive models were developed to identify significant inflammatory activity (A ≥ 2), integrating biochemical and MPUS-derived parameters.
Results: The study population included 18 males and 24 females, with a mean age of 52.9 years and a mean BMI of 30.9 kg/m². Clinical and histological characteristics are summarized in Table 1.
USAT values increased progressively with steatosis grade, ranging from 0.54 dB/cm/MHz in S0 to 0.82 in S3 ($p < 0.0001$, Figure 1), and showed a significant upward trend with both inflammatory activity ($p = 0.0068$) and fibrosis stage ($p = 0.023$). USAT demonstrated a strong correlation with the percentage of histological steatosis ($\rho = 0.86$, $p < 0.001$), and significantly differed across NAS categories ($p < 0.0001$), with notably higher values in patients with NAS ≥5 (0.79 ± 0.08) compared to those with NAS ≤2 (0.55 ± 0.06). In contrast, E and Vi did not show significant associations with fibrosis or inflammatory activity, respectively.
ROC curve analysis confirmed the diagnostic value of USAT for steatosis grading. Discriminative performance was limited between S0 and S1 (AUC = 0.62), reflecting modest ability to detect early steatosis. However, accuracy improved with increasing severity: AUC reached 0.81 for S1 vs S2 and 0.76 for S2 vs S3, indicating good diagnostic performance. The best results were obtained when distinguishing mild from moderate-to-severe steatosis (S01 vs S23), with an AUC of 0.85, sensitivity of 86.7%, and specificity of 80.0% at a cut-off of 0.79 dB/cm/MHz.
A machine learning model combining USAT and liver stiffness (E) with serum liver enzymes (AST, ALT, and gGT), identified as relevant predictors of inflammation, enhanced the detection of significant inflammatory activity (A ≥ 2) compared to the model based solely on biochemical markers. The combined model achieved an AUC of 0.89 and an accuracy of 85.0%.
Conclusion: USAT is a reliable, non-invasive tool for assessing hepatic steatosis in MASLD, demonstrating strong correlations with histological fat content. Moreover, the progressive increase in USAT values with higher inflammatory grades suggests a link between fat accumulation and inflammation severity. Notably, combining MPUS parameters with biochemical markers enhanced the predictive accuracy for steatohepatitis. These findings support the inclusion of USAT in multiparametric models for comprehensive, non-invasive characterization of MASLD, warranting further validation in larger, multicenter cohorts.

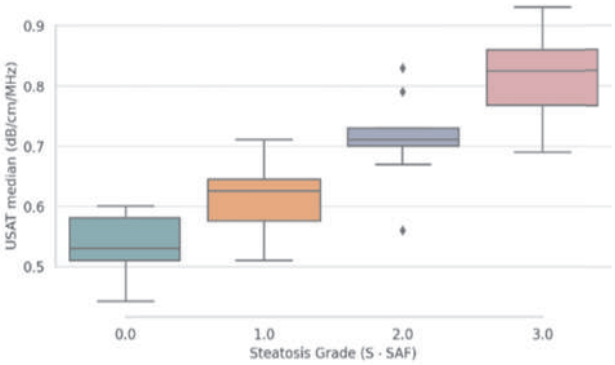

Figure 1. distribution of USAT by steatosis degree

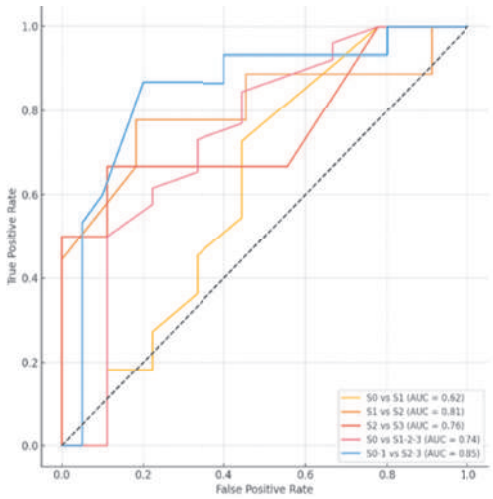

Figure 2. ROC curve analysis of USAT in distinguishing steatosis grades

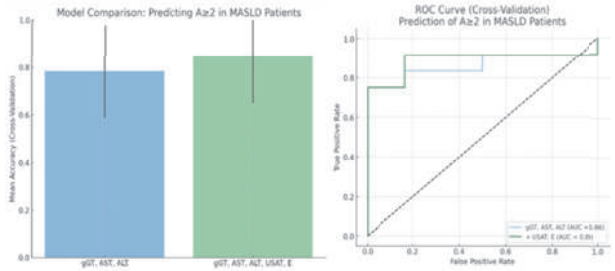

Figure 3. Predictive performance of two models for identifying significant histological inflammation

Table 1. demographic, clinical and histological features of patients.

N of patients	**42**
M/F	18/24
Age, y (SD)	52.9 (12.3)
BMI, kg/m2 (SD)	30.9 (7.1)
Laboratories (SD)	
- **AST, U/L**	34 (21.1)
- **ALT, U/L**	40.9 (33.9)
- **GGT, U/L**	64.6 (124.8)
- **FA, U/L**	73.3 (20.9)
- **Creat mg/dl**	0.7 (0.2)
- **Alb, g/dl**	39.7 (3.4)
- **INR,**	0.98 (0.07)
- **PLT, 10^3/µL**	214 (59)
US steatosis	
- **Absent**	19
- **Mild**	9
- **Moderate**	10
- **Severe**	4
SAF*	
- **S 0/1/2/3**	9/12/9/6
- **A 0/1/2/3/4**	5/8/14/6/3
- **F 0/1/2/3/4**	6/21/5/4
NAS**	
- **≤ 2**	11
- **3-4**	17
- **≥ 5**	9

*missed in 6 patients, **missed in 5 patients.

THIS DAMN FEVER

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A Challenging Case of Fever of Unknown Origin:
Diagnostic Workup and Final Diagnosis of T-Cell Lymphoma

Introduction: Fever of unknown origin (FUO) is defined as a body temperature ≥38.3°C lasting for more than 3 weeks, without diagnosis after 3 days of hospital investigation or multiple outpatient evaluations. FUO can result from infections, malignancies, autoimmune conditions, or other rare causes. The diagnostic process often requires extensive and systematic evaluation. We report a complex case of FUO that led to the unexpected diagnosis of T-cell lymphoma.

Case presentation: A 51-year-old woman presented with persistent fever (>38°C) for approximately one month, accompanied by asthenia and night sweats. She reported a mild rash on her back and chest. A privately obtained CT scan revealed hepatosplenomegaly and abdominal effusions. Her medical history included selective IgA deficiency, stage 2b chronic kidney disease (post-ureteral surgery), breast implants, atrophic gastritis (H. pylori eradicated), and a remote anaphylactic reaction to azithromycin. She was a smoker (35 pack-years), with no recent travel, animal contact, or known infectious exposures.

Physical Examination: The patient was alert and hemodynamically stable, with a temperature of 37.9°C. Mild rash was noted on the chest and trunk. Cardiac, respiratory, and abdominal examinations were unremarkable except for hepatosplenomegaly and fine crackles at the right lung base. Lymphadenopathy and peripheral stigmata of endocarditis were absent.

Diagnostic Workup: Laboratory tests revealed pancytopenia, elevated CRP (56 mg/L), ESR (43 mm/h), ferritin, D-dimer. Infectious screening, including blood/urine cultures, viral serologies (HIV, hepatitis, TORCH), and specific tests for atypical infections (Brucella, Leishmania, TB, beta-D-glucan) were negative. Autoimmune panel (ANA, ENA, RA test, C3/C4) was unremarkable. Tumor markers (TPA, CA 19.9, beta-2 microglobulin) were mildly elevated. Imaging (PET/CT) showed diffuse mild splenic uptake. Hematologic evaluation included negative JAK2, BCR-ABL, MPL, and calreticulin mutation tests. Peripheral smear was negative. Bone marrow biopsy was performed.

Differential Diagnosis: Given persistent fever and systemic signs, differential diagnosis included infections, autoimmune diseases, and hematologic malignancies. The exclusion of infectious and autoimmune etiologies, along with persistent inflammatory markers and PET/CT findings, shifted focus toward a lymphoproliferative process.

Final Diagnosis and Outcome: The patient was discharged with suspected lymphoproliferative disease and referred to hematology. Bone marrow biopsy, confirmed by a second opinion center, established the diagnosis of T-cell lymphoma. The patient is currently undergoing corticosteroid therapy.

Conclusion: This case highlights the diagnostic complexity of FUO and the importance of a structured and multidisciplinary approach. T-cell lymphoma, though rare, should be considered in prolonged febrile syndromes when initial workup is inconclusive.

PERSISTENT HYPERFERRITINEMIA AND ADDISON'S DISEASE: PARANEOPLASTIC SYNDROME AS A HIDDEN CULPRIT?

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Case presentation: A 70-year-old men with a history of arterial hypertension and dyslipidemia presented with progressive fatigue, insomnia, and weight loss over one year. Laboratory findings showed persistent hyperferritinemia (December 2023: 1720 ng/mL; August 2024: 1857 ng/mL; September 2024: 1763 ng/mL; December 2024: 1550 ng/mL; January 2025: 4152 ng/mL) with normal transferrin saturation and negative HFE gene testing. Given the patient's symptoms, hormonal tests were performed during therapy with Prednisone 1 mg, showing: Cortisol 84 µg/L (n.v. 48–195 µg/L), ACTH 130 pg/mL (n.v. 7.2–63.3 pg/mL), Renin 230 mU/L (n.v. 4.2–59.7 mU/L). Corticosteroid therapy was then suspended for five days to allow an ACTH stimulation test, which confirmed primary adrenal insufficiency (T0: Cortisol 114 µg/L; T30: 140 µg/L; T60: 151 µg/L; elevated ACTH and renin). Further investigation excluded drug-induced adrenal insufficiency, as none of the medications used by the patient were associated with adrenal dysfunction. Autoimmune causes were also ruled out with negative adrenal-specific antibodies, including anti-21 hydroxylase. The patient was started on corticosteroid replacement therapy with hydrocortisone 37.5 mg daily, leading to improvement in fatigue and overall well-being. To investigate whether the adrenal dysfunction could be due to iron infiltration in the context of a non-HFE hemochromatosis, an abdominal MRI was performed. No evidence of iron deposition in the adrenal glands was found; however, a pulmonary nodule in the posterior basal segment of the right lower lobe was detected, and subsequently confirmed by chest CT. The discovery of the pulmonary nodule raised suspicion for a paraneoplastic syndrome contributing to both hyperferritinemia and elevated ESR (70 mm/h – n.v. <15 mm/h) and Addison's disease. A multidisciplinary approach was initiated, including follow-up with endocrinology, thoracic surgery, and oncology teams for further evaluation of the pulmonary nodule. Ferritin levels remained elevated, consistent with an inflammatory or paraneoplastic process.
Discussion: This case illustrates the diagnostic complexity of primary adrenal insufficiency in the setting of unexplained hyperferritinemia. Although primary adrenal insufficiency is typically autoimmune, rare causes such as iron deposition must be considered when metabolic workups are negative. Hyperferritinemia is often linked to iron overload or chronic inflammation and is recognized as a marker of both inflammation and neoplastic activity, with ferritin acting as an acute-phase reactant. Tumor-associated hyperferritinemia is well documented in hematologic malignancies and lung cancer, making the pulmonary nodule a critical point for further investigation. The exclusion of iron overload and autoimmune causes shifts the diagnostic focus toward malignancy-associated inflammatory activity. In our patient with referred weight loss and fatigue, the absence of adrenal antibodies and of iron overload in the adrenal glands, as well as the presence of a suspicious pulmonary nodule, suggested a paraneoplastic process.
Conclusions: This report explores the diagnostic complexity of hyperferritinemia and adrenal insufficiency in the setting of a suspicious pulmonary nodule. This case highlights the importance of a thorough search for secondary causes of hyperferritinemia, especially when linked to endocrine dysfunction.

HBV REACTIVATION INITIATED BY EPSTEIN-BARR VIRUS INFECTION IN PATIENT WITH CLL AND RHEUMATOID ARTHRITIS: A CASE REPORT

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Introduction: It is estimate that 257 million worldwide are chronically infected with HBV. Among them only 36 million are aware of their carrier status and 6-8 million are receiving antiviral therapy. The natural course of HBV infection is influenced by the dynamic interaction between host's immune status and viral replication. HBV's genome persists despite the host immune response in the form of covalently closed circular DNA (cccDNA) and integrated DNA.
Epstein-Barr virus, also known as human herpesvirus type 4, is a ubiquitous oncogenic DNA virus belonging to the gamma-herpesvirus family. It is estimated that 90-95% of the world's population has been infected with this virus. EBV is transmitted primarily through saliva. Primary infection is often asymptomatic and occurs at a young age in developing countries and at an older age in more industrialized countries. EBV infects the epithelial cells of the oropharynx, where it can replicate and subsequently infect B lymphocytes in the oral cavity. Like other herpesviruses, EBV can persist in a permanent latent state in the human host, in an episomal form within B cells.
Case presentation: We describe the case of an 82-year-old Caucasian woman affected by chronic lymphocytic leukemia and rheumatoid arthritis, under treatment with methylprednisolone 4 mg per day. She worked as an auxiliary in hospital, and in 2018 she had documented complete seroconversion of previous undatable HBV infection (HBsAg negative, HBs-Ab and HBc-Ab positive).
The patient reported having suffered asthenia for two months and recently nausea and dark urine. She also presented blood test results showing alteration of functional hepatic parameters, HBs-Ab negative (7,52 mlU/mL), HBe-Ab borderline and both HBsAg and HBeAg positive and a recent ultrasound displaying heterogeneous liver parenchyma.
At the admission in our hospital, she presented with jaundice and, furthermore her laboratory tests showed hyperbilirubinemia (total bilirubin 7,54, conjugated bilirubin 6,68 mg/dL), elevated transaminases (ALT 498 UI/L, AST 871 UI/L) with an AST/ALT ratio greater than 1. Virological tests confirmed HBeAg and HBsAg, positivity for HBc IgM Ab and high levels of HBV-DNA (311.000 UI/L). The other hepatitis markers, such as anti-HAV, anti-HCV, anti-HDV and autoimmune panel (ANA, ENA, LKM, ASMA) were negative.Based on evidence of HBV reactivation hepatitis and considering the further increase in functional hepatic parameters, antiviral therapy with entecavir 0.5 mg daily was started.
At the same time, the TORCH panel was also requested. The results showed positivity for EBV-VCA IgM and IgG, EBV-EBNA IgG borderline and the quantification of the EBV-DNA was 1000 copies/mL. After two weeks of entecavir therapy virological test showed a significant reduction of HBV-DNA (14.300 copy/mL) and EBV-DNA undetectable.
With entecavir therapy we had achieved progressive remission both clinical and laboratorial of the acute hepatitis.At 1-month post-hospital admission the HBV-DNA was 910 U/mL, total bilirubin was 2,49 mg/dL and liver cytolysis markers were practically normalized (AST 41 U/L, ALT 36 U/L).
Discussion: HBV reactivation is a relatively common condition that can be prevented with antiviral prophylaxis. It can occur in the context of immunosuppression (solid organ or bone marrow transplantation, high-dose corticosteroid therapy, treatment with anti-CD20 or anti-TNF-α agents) or viral infections such as advanced HIV infection, or co-infections such as HCV or, in rarer cases, especially in immunocompromised patients, SARS-CoV2 and some Herpesviruses such as CMV.
Epstein-Barr virus can alter the host's immune system by inducing the expansion of cells involved in humoral immunity and suppressing helper T lymphocytes. T-helper cells are crucial for regulating cytotoxic lymphocytes, which are essential for controlling latent HBV infection and for activating B cells, which are responsible for the production of anti-HBs antibodies. For this reason, EBV infection could contribute to HBV reactivation.
Conclusions: These findings support the hypothesis of a EBV infection that may have triggered a reactivation of HBV.Just another case of hepatitis B virus (HBV) reactivation triggered by Epstein-Barr virus infection has been reported in literature. In our case, a woman without a history of previous HBV reactivation and on the same therapeutic regimen for years -no variation of corticosteroid dosage or introduction of new immunosuppressive agents-developed an acute EBV infection and subsequently HBV reactivation.
Considering all this, although it is a rare condition, EBV infection should be considered among the causes of HBV reactivation.

LOW T3 SYNDROME IN AN ONCOLOGIC PATIENT WITH SEVERE SEPSIS

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The euthyroid sick syndrome is a condition characterized by altered thyroid hormone levels in the absence of true primary thyroid dysfunction.
It is commonly observed in patients with severe systemic illnesses such as sepsis, trauma, surgical interventions, advanced neoplasms, heart failure, and late-stage chronic inflammatory diseases. This condition is often mistakenly treated with L-thyroxine replacement therapy.
A 68-year-old Caucasian woman was admitted to our attention in critical clinical condition. The patient had severely dyspnea and complained of significant asthenia and marked weight loss. She reported a previous hospitalization for cholecystectomy. She was a smoker. Her medical history was negative for

thyroid disorders. Laboratory and culture tests revealed a severe septic state with marked neutrophilic leukocytosis, elevated C-reactive protein, and increased procalcitonin levels. Imaging studies showed a pulmonary nodular lesion that was biopsied and diagnosed as advanced-stage lung adenocarcinoma. The patient exhibited low T3 levels, normal T4, and borderline low TSH levels.
Low T3 syndrome is frequently observed in oncologic patients, particularly in advanced stages of disease. In these individuals, increased levels of pro-inflammatory cytokines can impair the peripheral conversion of thyroxine (T4) to triiodothyronine (T3), along with a concurrent rise in reverse T3 (rT3), a biologically inactive form. Chemotherapy, radiotherapy, and immunotherapy can also alter the hypothalamic-pituitary-thyroid axis and peripheral deiodinase activity. Low thyroid hormone levels is considered an unfavorable prognostic indicator in neoplastic conditions.
The hormonal profile observed in our patient was therefore consistent with Euthyroid Sick Syndrome. The absence of typical hypothyroid symptoms, the lack of thyroid morphological abnormalities on ultrasound and the presence of systemic disease support this diagnosis and help exclude the possibility of primary hypothyroidism.
Differentiating this syndrome from overt hypothyroidism requires careful clinical evaluation within the context of a significant acute or chronic illness. It is crucial to recognize this condition to avoid inappropriate use of levothyroxine replacement therapy, which has not shown any proven benefit in such contexts.

ADIPO-NEUROINFLAMMATION, COGNITIVE IMPAIRMENT AND SURROGATE MARKERS OF CARDIOVASCULAR RISK IN A POPULATION OF PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD): A CROSS-SECTIONAL STUDY.

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Background: Non-alcoholic fatty liver disease (NAFLD) is the outbreak of the 21st century, with an increasing epidemiological burden and a natural history that can result in liver cirrhosis and hepatocellular carcinoma. Over the years, NAFLD has become the so-called 'hepatic manifestation' of the metabolic syndrome, as the factors contributing to its pathogenesis include impairments in metabolism, among which insulin resistance is predominant. To date, there are no trials that have assayed markers of adipo-neuro-inflammation (lipocalin-2 – LCN2) and tried to find associations between these markers and the overall cardiovascular risk of patients with NAFLD through surrogate markers such as endothelial dysfunction, intima-media thickness of supra-aortic vessels, left ventricular mechano-energetic efficiency – MME - and with indicators of cognitive impairment by means of the mini mental state examination - MMSE.
Matherial and methods: In this cross-sectional study, between December 2022 and June 2023, we enrolled a group of 40 patients with a recent diagnosis of NAFLD, afferent to the Internal Medicine and stroke care ward of the Policlinico Paolo Giaccone Hospital of Palermo, and a group of 40 controls, who had no current or previous diagnosis of NAFLD. All subjects underwent anamnestic collection, serological sampling for the assay of Lipocalin-2, assessment of cognitive status by MMSE, assessment of endothelial function through reactive hyperemia index (RHI) using Endopat2000 device, evaluation of intima-media thickness on vascular ultrasound, and assessment of MEE on echocardiography.
Results: The ANOVA analysis showed that between patients with NAFLD and controls, the intergroup difference in terms of heart rate, body weight, BMI, BSA, HbA1C, echocardiographic variables (IVST, LVPWT, FE%, LAVI, E/A), MMEE, MMSE, RHI, and LCN-2 was statistically significant. We also found that patients with NAFLD were more affected by hypertension, dyslipidaemia, and diabetes mellitus than controls. In contrast, we found no statistically significant differences between patients with NAFLD and controls with regard to the intima-media thickness of the carotids. In the multinomial logistic regression analysis of the variables found to be significant in the univariate analysis, we found a statistically significant association between NAFLD and high BMI values (p=0.000). Concerning endothelial dysfunction and markers of adipo-neuro-inflammation, in a multinomial logistic regression model where we included RHI, LCN2 and MMSE as continuous independent variables, a statistically significant association emerged between NAFLD and endothelial dysfunction (RHI, p=0.011) and between NAFLD and increased serum lipocalin-2 (LCN2, p=0.003). About the cognitive impairment, in a multinomial logistic regression model that included MMSE and LCN2 as continuous independent variables, we found a statistically significant association between NAFLD and lower MMSE values (p=0.027) and between NAFLD and higher serum LCN2 levels (p=0.000). We found no confirmation on multinomial logistic regression analysis of the association between NAFLD and reduced MMEE, which was statistically significant on univariate analysis. Speaking about the comorbidities, analysing logistic regression analysis, the diseases with which NAFLD was statistically significantly associated on univariate analysis, a statistically significant association emerged and was confirmed with diabetes mellitus (p=0.029) and metformin use (p=0.005). We also performed a ROC curve to assess the predictive value of RHI regarding NAFLD. We found that, with an area under the curve (AUC) of 0.826 and a statistical significance p=0.000, RHI can serve as a marker of endothelial dysfunction and thus as an indirect indicator of cardiovascular risk in patients with NAFLD.
Discussion: There is a statistically significant association with low levels of RHI, low MMSE scores and high serum levels of LCN2, thus reaffirming, as mentioned earlier, that patients with NAFLD, compared to controls, have a more pronounced endothelial dysfunction and a worse cognitive performance. Thinking about the dysmetabolic nature of NAFLD, these data allow us to agree with what has been found in the other trials previously, namely that there would be an adipo-neurovascular axis of NAFLD, dependent on the proinflammatory activity of lipocalin 2 that originates in the setting of a dysregulation of metabolism and has repercussions on vascular and cerebral health. In light of this, we performed a ROC curve, as mentioned above, that shows RHI as a reliable indicator of vascular damage in patients with NAFLD, most likely linked to the microenvironment of inflammation, attributable to the imbalance between proconstrictive and dilating factors. If, therefore, the vascular health in these patients is altered, the function of the endothelial cell compromised for all the reasons we have discussed, it is quite plausible to understand the repercussions on the overall cardio- and cerebrovascular risk, on vascular health leading to earlier cognitive impairment and an increased likelihood of cardio- and cerebrovascular events.

AUTOIMMUNE CYTOPENIAS IN COMMON VARIABLE IMMUNODEFICIENCY

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Background: Common variable immunodeficiency (CVID) is the most common symptomatic antibody deficiency in adults, characterized by heterogeneous genetic, immunological, and clinical phenotypes with immune dysregulation, autoimmunity and lymphoproliferation. A significant proportion have autoimmune cytopenias, such as sudden-onset immune thrombocytopenia, hemolytic anemia, or both (Evans syndrome), or less commonly, neutropenia, as the only manifestation of the immune defect. Often the autommune cytopenia is the presenting symptom of CVID and it is often not recognised causing delay and severe complications in these patients.
Aim: This study aims to describe the autoimmune cytopenias complication in a cohort of adults with CVID.
Patients & Methods: We enrolled 85 adults consecutively diagnosed for CVID at our ERN-RITA Centre for Inborn Errors of Immunity in Milan, Italy. All the patients met the ESID criteria for CVID diagnosis and were started with replacement therapy with immunoglobulins. Their documentation and data were revised and analysed. The autoimmune cytopenias and hematological complication, their therapies and outomes are described.
Results: In this study, 85 CVID adult patients were analyzed. Of these, 29 (34%) were CVID who presented only infections (uCVID) and 56 (66%) were CVID with complex phenotypes (CVIDc). Among these 56 CVIDc, 19 (22.4% of the oveall CVID) patients had had 1 or more episodes of immune thrombocytopenia (14 ITP), hemolytic anemia (4 AIHA), and/or neutropenia (N=3), one had TTP. ITP occurred in half of these patients as part of Evans syndrome, having had 1 or more concomitant or usually separate episodes of AIHA (N = 4 patients). Fewer had neutropenia (N = 3), two patients had also AIHA+ITP and one had only ITP. All the patients were treated according to guidelines and recovered. All received high dose of intravenous immunoglobulins, steroids, some rituximab and some rTPO. Nine of the patients had ITP as onset of CVID, but CVID diagnosis was done several years after when they presented other organs complications. Genetical analysis of the overall CVID patients showed that variations on causative genes of CVID immunedysregulation and B- T-cells interactions, as NFKB1 or 2, CTLA4 gene, were more frequent in the CVIDc patients with hematological complications than in the other CVIDc or uCVID patients. TNFRSF13B/TACI gene variations were more common among CVIDc than uCVID patients.

Among the overall 19 CVIDc patients with hematological complications, seven had lymphoma (1 Burkitt EBV+, 3 Non-Hodgkin, 2 Hodgkin EBV+, 2 CD8+ lymphoma). Two patients who had lymphoma had had Evans syndrome (one ITP+AIHA, one ITP+neutropenia+AIHA). All the patients were diagnosed for CVID when had lymphoma. They all, except the two patients with CD8+ lymphoma, recovered from lymphoma and are in complete remission.
Conclusion: Autoimmune cytopenia is frequent among CVID patients, especially in those with complex phenotypes. The autoimmune conditions are concurrently or later associated with additional inflammatory features, such as interstitial lung disease (GLILD) or liver or gastrointestinal complications. Because of the high morbidity and mortality of these conditions, especially if not promptly recognized, CVID patients should be managed at the referral Centre for adults with primary immunodeficiencies.

VEXAS SYNDROME IN A PATIENT WITH MYELODYSPLASTIC FEATURES AND SYSTEMIC INFLAMMATION

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Introduction: VEXAS (Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic) syndrome is a monogenic disorder stemming from a somatic mutation in the UBA1 gene. It is characterized by a constellation of systemic inflammatory and autoimmune manifestations alongside hematological abnormalities, predominantly myelodysplastic syndromes (MDS).
Case report: M.N. is a 68-year-old man from Philippines with a medical history of chronic ischemic heart disease and type 2 diabetes mellitus, complicated by severe sensorimotor axonal polyneuropathy. Since early 2024, he experienced a progressive deterioration of performance status, which led to two prior hospitalizations during which a diagnosis of MDS was established, along with recurrent infectious complications.
He presented to the Emergency Department with a two day history of hyporexia, back pain, diffuse arthralgias, altered mental status, and fever. On admission, laboratory analysis revealed systemic inflammation (elevated C-reactive protein and hyperferritinemia >1600 ng/mL), alongside pancytopenia necessitating transfusions of packed red blood cells, a double IgG monoclonal gammopathy and severe acute kidney injury (creatinine 4.0 mg/dL), resulting in anasarca in the context of severe non-nephrotic hypoalbuminemia.
Given the patient's history of recurrent infections empirical broad-spectrum antibiotics were introduced. Comprehensive microbiological analyses [encompassing cultures, respiratory viral and fungal panels, polymerase chain reaction for Epstein-Barr virus, cytomegalovirus, parvovirus B19, human immunodeficiency virus, hepatitis B virus, and hepatitis C virus and serological testing for Mycobacterium tuberculosis, Leishmania, and Strongyloides stercoralis] yielded negative results.
In light of the pancytopenia, renal impairment, and persistent inflammation, autoimmune and vasculitic processes were also considered. A thorough immunological workup, including antinuclear antibodies, extractable nuclear antigens, antineutrophil cytoplasmic antibodies, anti-glomerular basement membrane antibodies, anti-smooth muscle antibodies, anti-gliadin antibodies, anti-β2 glycoprotein I antibodies, rheumatoid factor, and complement levels, returned negative. Urinalysis ruled out glomerulonephritis.
The profound hypoalbuminemia, anasarca, and detection of a biclonal gammopathy raised suspicion for systemic amyloidosis. However, both periumbilical fat pad biopsy with Congo red staining and urine immunofixation were negative.
A positron emission tomography/computed tomography scan demonstrated increased uptake of fluorodeoxyglucose in the bone marrow and splenomegaly, consistent with marrow hyperactivity in the context of the diagnosed MDS. Bone marrow aspiration revealed multilineage dysplasia along with cytoplasmic vacuolization in approximately 6% of myeloid precursors. These findings strongly suggested the possibility of VEXAS syndrome. Pending molecular confirmation, empirical corticosteroid therapy (methylprednisolone 40 mg/day) was initiated, resulting in a rapid clinical and biochemical improvement, including normalization of mental status, decline in inflammatory markers, improved renal function, and increased serum albumin levels, supporting the autoinflammatory nature of the condition.
Concurrently, genetic analysis for UBA1 mutations was performed on DNA extracted from the bone marrow aspirate and confirmed the presence of a pathogenic variant, establishing the diagnosis of VEXAS syndrome.
Discussion: Diagnosing VEXAS syndrome is challenging due to its clinical overlap with systemic diseases, a difficulty compounded by coexisting MDS, where shared features like cytopenias and inflammation can be misleading. In this case, initial investigations for infection and autoimmunity were negative, thus promping a re-evaluation. The key finding of cytoplasmic vacuolization in myeloid precursors, a VEXAS hallmark, in a patient with MDS and systemic inflammation, guided UBA1 genetic testing and confirmed the diagnosis (1). While corticosteroids offer initial symptom control, long-term use is limited. Emerging therapies include interleukin-1 and interleukin-6, Janus kinase inhibitors, and hypomethylating agents such as azacitidine for MDS-associated cases; stem cell transplant may be curative in select individuals. Ongoing research aims to refine VEXAS classification and develop targeted treatments.
Conclusion: This case report emphasizes the necessity of maintaining a high index of suspicion for VEXAS syndrome in older male patients presenting with unexplained systemic inflammation and cytopenias, especially when concurrent MDS is present, as it complicates both diagnosis and treatment. The presence of bone marrow vacuolization should prompt targeted UBA1 genetic testing, even without pathognomonic signs. Although corticosteroids are the initial treatment, their limitations necessitate individualized, disease-modifying strategies, underscoring the importance of increased clinical awareness for timely diagnosis and improved patient outcomes.
Bibliografia: 1. Koster M.J. et al. "VEXAS Syndrome: Clinical, Hematologic Features and a Practical Approach to Diagnosis and Management." Am.J.Hematol. 2024

SARCIRAM: A PILOT STUDY ON THE IMPACT OF HYDROXIRAM D SUPPLEMENTATION ON SARCOPENIA IN PATIENTS WITH LIVER CIRRHOSIS

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Background: & Aims: Sarcopenia is a common complication of chronic liver disease and is associated with poor prognosis and adverse outcomes. However, no specific pharmacological treatments for sarcopenia in cirrhotic patients currently exist in clinical practice. While various nutritional strategies have been investigated, comprehensive data on their quantitative and qualitative effects on muscle parameters are still lacking. Emerging evidence supports the role of branched-chain amino acids (BCAAs) and their metabolite β-hydroxy-β-methylbutyrate (HMB) in preserving and enhancing muscle mass, strength, and clinical performance. The SARCIRAM pilot trial aimed to evaluate the effects of Hydroxiram D -a supplement containing L-leucine, L-isoleucine, L-valine, calcium HMB, and vitamin D- on the
progression of sarcopenia in patients with metabolic dysfunction-associated steatotic liver disease (MASLD)-related cirrhosis.
Methods: In this single-center, open-label, randomized (1:1) pilot study, patients were assigned to receive either standard of care plus Hydroxiram D (twice daily) or only standard of care for 6 months. Eligible patients were consecutively enrolled during routine ultrasound surveillance if they were aged 18 years or older, had compensated MASLD-related cirrhosis (Child-Pugh class A), and met no exclusion criteria, which included previous episodes of decompensation, malignancies, any acute illnesses, and chronic musculoskeletal diseases. Body composition was assessed by bioelectrical impedance analysis (fat-free mass [FFM], phase angle [PA], appendicular skeletal muscle mass index [ASMM/h^2]) and ultrasound-derived indices
(quadriceps thickness index, cross-sectional rectus index, psoas height-to-width ratio, diaphragm excursion). Muscle function and performance were evaluated via handgrip strength (HGS) and 4-meter walk test (4mWT). Within-group post-treatment changes were assessed using paired-sample t-tests. Between-group differences were evaluated using ANCOVA models, adjusting for baseline values measurements.
Results: Forty patients were randomized. Of these, thirty-two completed the study and were included in the analysis. Five patients were lost to follow-up, two were excluded following a diagnosis of hepatocellular carcinoma detected at baseline ultrasound screening, and one patient was excluded as a statistical outlier due to an irreconcilable data entry error. Baseline anthropometric characteristics, age, sex, laboratory data and measured muscle parameters were comparable between groups (all $p > 0.05$). After 6 months, the adjusted mean change in FFM was −1.89 kg in the Hydroxiram group vs −2.69 kg in the control group ($p = 0.431$). The adjusted change in PA was +0.20° vs −0.34° ($p = 0.242$), and in ASMM/h^2 was −0.28 vs −0.44 kg/m^2 ($p = 0.343$), respectively. Although these differences were not statistically significant, Hydroxiram D was associated with a trend toward a smaller decline in FFM and ASMM/h^2 and an increase in PA. Notably, although between-group differences did not reach statistical significance [ΔHGS 2.36 vs. 1.8 Kg ($p = 0.7$), Δ4mWT -0.142 m\s vs -0.210 m\s ($p= 0.29$), respectively in the treated vs non-treated groups], within-group analysis showed a significant improvement in HGS in the Hydroxiram group ($p = 0.044$), and a greater decline in 4mWT in the control group ($p = 0.004$). Among ultrasound-derived indices and laboratory parameters, no statistically significant changes were observed between the groups Finally, no

safety concerns or adverse events were reported.
Conclusions: Six months of Hydroxiram D supplementation was associated with improvements in muscular strength and physical performance in patients with compensated MASLD-related cirrhosis. These data were consistent with favorable trends in nutritional status and indicators of muscle mass preservation. This pilot study supports further investigation in larger, adequately powered trials to confirm its efficacy and to assess long-term clinical and functional outcomes in patients with cirrhosis-related sarcopenia.

CHECKPOINT INHIBITOR-INDUCED LIVER INJURY (CHILI) IN PATIENTS WITH ADVANCED SKIN CANCER: A SINGLE CENTER EXPERIENCE

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Introduction: Immune checkpoint inhibitors (ICIs) are now considered the first-line treatment for advanced melanoma and non-melanoma skin cancers. One of the most commonly reported adverse events is checkpoint inhibitor-induced liver injury (ChILI), which occurs in approximately 10% of patients. For those who develop ChILI, it remains uncertain whether permanent discontinuation of the drug is necessary or if treatment can be safely resumed after a temporary pause, either with the same agent or with a different class of ICI. This report shares our center's experience with ChILI in patients receiving care for skin neoplasms at a tertiary-level facility.
Aims and methods: This study aimed to analyse the prevalence of ChILI among patients treated with ICIs for skin cancers at our center. We included retrospectively all consecutive patients admitted to our facility who received ICI therapy for advanced melanoma or non-melanoma skin cancer between June 2016 and April 2024. The diagnosis and severity of ChILI were evaluated using the CTCAE v5.0 criteria, and the type of liver injury was classified based on international guidelines. Liver function tests (LFTs) were collected at baseline, after three treatment cycles, and at the time of suspected ChILI onset. Data on ChILI management and outcomes were also collected.
Results: We enrolled 111 patients (32.4% female, median age 75 years), including 70 patients (63.1%) with advanced melanoma and 41 (36.9%) with locally advanced or metastatic cutaneous squamous cell carcinoma. Among them, 3 patients (2.7%) received first-line therapy with anti-CTLA-4, 106 (95.5%) with anti-PD-1, and 2 (1.8%) were treated with a combination of both. The median duration of therapy was 10 months (IQR 5–21). ChILI developed in 8 patients (7.2%) after a median of 14 treatment cycles (IQR 7–20). According to the CTCAE severity scale, one case was grade 2, three were grade 3, and four were grade 4. Among those who developed ChILI, 3 patients tested positive for anti-nuclear antibodies (ANA), 1 had a positive extractable nuclear antigen (ENA) test, and 2 had a known autoimmune disorder prior to initiating ICI therapy. All patients discontinued ICIs upon ChILI onset. Liver function tests normalized spontaneously in 4 patients, while 4 required corticosteroid treatment. Four patients underwent drug rechallenge, and only one of them received a new class of ICI. Regarding extrahepatic adverse events, ChILI patients more frequently exhibited diarrhea and dermatological manifestations such as papular or bullous rashes (37.5% and 50%, respectively), with a significantly higher prevalence compared to patients without ChILI (7.8% and 15.4%, respectively; $p < 0.05$). No significant differences in liver function test results were observed at baseline or after the third infusion between patients who developed ChILI and those who did not ($p > 0.05$).
Conclusions: Our study confirms the occurrence of liver toxicity associated with ICI therapy in cancer patients, with an incidence rate consistent with current international literature. The median time to ChILI onset—typically after multiple treatment cycles—supports the hypothesis of an indirect, immune-mediated mechanism rather than a direct toxic effect on the liver. Notably, we found that ChILI is often preceded by dermatological and/or gastrointestinal adverse events. Although based on a limited patient cohort, this observation may serve as an important clinical signal, helping physicians to anticipate ChILI, intervene earlier, prevent progression to more severe presentations, and initiate appropriate management promptly.

INTERSTITIAL LUNG DISEASES AS A REFLECTION OF UNKNOWN DRUG TOXICITY

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Background: interstitial lung diseases (ILDs) are a heterogeneous group of rare conditions that primarily or secondarily affect the lung interstitium.
ILDs may present in inflammatory, fibrotic, or mixed forms.
They are classified as idiopathic, autoimmune-related, exposure-related, cystic or airspace-filled, sarcoidosis-related, and others.
The exposure-related category includes drug-induced ILDs (DIILDs). Various drugs—particularly oncological, rheumatological, and antimicrobial agents—have been associated with pulmonary toxicity, although their mechanisms are often poorly understood.
Early diagnosis and treatment are critical, as some ILDs can rapidly progress to severe fibrosis and respiratory failure.
Case presentation: a 56-year-old woman was hospitalized for severe pancytopenia due to a relapse of marginal zone lymphoma (MZL).
Her medical history included a previous diagnosis of marginal/follicular lymphoma treated with six cycles of COMP chemotherapy (cyclophosphamide, oncovin/vincristine, methotrexate, and prednisone), resulting in complete remission.
During hospitalization, she received her first cycle of DHAOX chemotherapy (dexamethasone, high-dose cytarabine, and oxaliplatin). Two weeks later, she developed mild breathlessness and oxygen desaturation, without other symptoms.
A chest computed axial tomography (CT) revealed new extensive interstitial thickening, predominantly central, in the upper lobes and similar smaller changes in the lower lobes. These findings were absent on a recent CT.
All microbiological and autoimmune tests returned negative.
Bronchoalveolar lavage (BAL) confirmed the absence of infection. BAL immunophenotyping (IF) revealed a CD45+ leukocyte population consisting of 37% neutrophils and 11% lymphocytes, predominantly CD3+ with an elevated CD4/CD8 ratio (3.6). Lung biopsy was not performed due to an unfavorable risk-benefit ratio.
Based on the clinical and radiological findings and BAL results, a diagnosis of DIILD was made. High-dose steroid pulse therapy was initiated, leading to rapid clinical improvement.
Conclusion: DIILDs are diagnostically challenging, and many causative drugs remain unidentified. Their clinical presentation is often more subtle than that of infectious pneumonias. In this case, the radiological pattern—bilateral, symmetrical, central interstitial involvement—was more suggestive of a non-infectious, non-lymphomatous process.
BAL was essential for diagnosis: a predominance of CD3+ lymphocytes with an elevated CD4/CD8 ratio is typical of type IV delayed hypersensitivity reactions, a key immune-mediated mechanism in DIILDs. BAL also ruled out pulmonary lymphoma infiltration.
The patient had received a cycle of DHAOX, which includes oxaliplatin—a drug associated with DIILD. Oxaliplatin may cause oxidative stress, act as a hapten in type IV hypersensitivity reactions, and directly damage the alveolar epithelium and pulmonary capillary endothelium. These toxicities may present acutely, subacutely, or in delayed forms, and may lead to irreversible interstitial fibrosis with prolonged or repeated exposure.
Despite the diagnostic complexity, early identification of DIILD is essential to discontinue the offending drug and begin treatment promptly, thereby preventing permanent lung damage.

PNEUMOTHORAX FOLLOWING ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY: A RARE BUT CLINICALLY SIGNIFICANT COMPLICATION

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Background: Endoscopic retrograde cholangiopancreatography (ERCP) is associated with known risks such as pancreatitis, bleeding, cholangitis, and gastrointestinal perforation. Thoracic complications, including pneumothorax or pneumomediastinum, are rare and underreported, particularly in the absence of perforation.
Case presentation: We report the case of a 52-year-old Italian woman with a history of left hepatic lobectomy, segmentectomy I, and bilioenteric anastomosis for a neuroendocrine tumor of unknown primary origin. She was admitted with acute cholangitis and initially treated with percutaneous transhepatic cholangiodrainage (PTCD) and antibiotics. ERCP was subsequently performed with removal of the PTCD, biliary stone extraction using a Fogarty balloon, and biliary stenting.
Post-procedure, the patient developed acute right upper quadrant pain, thoracic back pain, and dyspnea. CT imaging revealed a right-sided pneumothorax

(1.5–2 cm) with pleural effusion, but no evidence of perforation, pneumomediastinum, or pneumoretroperitoneum. Conservative management with oxygen therapy led to complete resolution.
Discussion: The pathogenesis of isolated pneumothorax following ERCP remains unclear. Proposed mechanisms include barotrauma or translocation of insufflated air along fascial planes. Notably, our case showed no evidence of pneumomediastinum or retroperitoneal air, findings typically described in previously reported cases.
Conclusion: Though rare, isolated pneumothorax should be considered among the differential diagnoses in patients presenting with respiratory symptoms following ERCP—even in the absence of radiologic evidence of perforation. Prompt recognition and conservative management are often effective.

STEROID REFRACTORINESS OF SEVERE IMMUNE-RELATED ADVERSE EVENTS, WHAT TO DO?

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Background: immune checkpoint inhibitors (ICIs) are oncologic drugs that inhibit the regulatory molecules (CTLA-4, PD-L1, PD-1) of cytotoxic T-cells, enhancing their anti-tumour activity.
Over recent decades, ICIs have taken on an increasingly important therapeutic role in a growing number of malignancies, ranging from melanoma to early-stage breast cancer.
Along with their effectiveness, a specific group of immune-mediated toxicities has emerged, known as immune-related adverse events (irAEs). These can affect any organ, although some are more frequently involved, such as the gastrointestinal tract (GI-irAEs). These toxicities can arise at any time, even after ICIs have been discontinued. Most irAEs are moderate, reversible, and manageable; however, life-threatening cases refractory to steroid therapy may occur.
Case presentation: a 49-year-old woman was hospitalized due to vomiting and severe diarrhoea with weight loss following neoadjuvant chemotherapy with carboplatin + paclitaxel + pembrolizumab, followed by epirubicin + cyclophosphamide + pembrolizumab, for triple-negative infiltrating ductal breast cancer with lymph node involvement.
Her medical history included pulmonary and lymph node tuberculosis, paroxysmal supraventricular tachycardia, deep vein thrombosis with patent foramen ovale, bicuspid aortic valve, and prior lichen planus.
During hospitalization, reduced faecal elastase and serum amylase and lipase levels were noted. Extensive microbiological and immunological investigations were performed, all returning negative. Abdominal magnetic resonance imaging (MRI) revealed pancreatic atrophy and liver and spleen steatosis.
Colonoscopy (CS) showed no macroscopic abnormalities; however, histology revealed focal active colitis (chronic interstitial inflammation, cryptitis, regenerative epithelial changes, and mucus depletion).
Esophagogastroduodenoscopy (EGDS) showed antral gastropathy, and biopsies revealed chronic active duodenitis (mild villous atrophy, T-lymphocyte, plasma cell and neutrophil infiltrate, cryptitis, mucus depletion, and reactive-regenerative epithelium) and acute gastritis in the antral region (interstitial and intraepithelial neutrophilic infiltrate, crypt micro abscesses and cryptolysis, mucus depletion).
Pancrelipase therapy was started due to exocrine pancreatic insufficiency, and corticosteroids (1 mg/kg) were administered for gastrointestinal toxicity, with poor clinical response. Infliximab was considered as second-line therapy but was avoided due to the risk of tuberculosis reactivation. Vedolizumab was administered instead, with rapid clinical improvement.
Conclusion: irAEs represent a significant challenge in internal medicine due to their heterogeneity, the need for careful differential diagnosis, and the occurrence of steroid-refractory cases.
The mechanisms underlying steroid resistance are still unclear and may include inflammation driven by tissue-resident memory T cells and Th17 cells, established tissue damage, or cytokines not responsive to steroids (e.g., IL-6, TNF-α). In GI-irAEs, microbial dysbiosis and local immune cell activation may sustain inflammation despite systemic immunosuppression.
Currently, only a few drugs are approved for second-line treatment of steroid-refractory irAEs. Among them, infliximab (anti-TNFα) and vedolizumab (anti-α4β7 integrin) are used in GI-irAEs. Vedolizumab targets the integrin α4β7, which binds to mucosal addressin cell adhesion molecule-1 (MAdCAM-1), promoting gut-specific homing of activated T lymphocytes. Vedolizumab is an excellent therapeutic option due to its localized action in the gastrointestinal tract and its specific effect on T cells that are mainly responsible for the GI-IrAEs.

IS HORTON'S ARTERITIS ONLY TEMPORAL ARTERITIS?

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Background: giant cell arteritis (GCA), also known as Horton's disease, is the most common form of vasculitis and typically affects large vessels, particularly the temporal arteries.
Pathophysiologically, dendritic cells residing in the vascular wall release cytokines that activate CD4+ lymphocytes toward Th1 and Th17 differentiation, leading to macrophage activation. This results in both proteolytic tissue damage and pro-angiogenic intimal proliferation. Consequently, GCA is characterized by a typical non-caseating granuloma composed of CD4+ T cells and macrophages infiltrating the arterial wall.
Cranial GCA (C-GCA), large vessel GCA (LV-GCA), and polymyalgia rheumatica (PMR) are the three main clinical presentations, although overlapping forms also exist.
While C-GCA has long been recognized and studied, certain atypical forms of LV-GCA involving unusual anatomical sites remain underrecognized, potentially leading to diagnostic delays. Nevertheless, high-dose glucocorticoids should be initiated promptly to prevent irreversible damage.
Case presentation: a 64-year-old man was hospitalized with hyperpyrexia, pharyngodynia, and arthralgia persisting for one month.
His medical history included seronegative spondyloarthritis, previously treated with salazopyrin, which was discontinued due to suspected dermatological toxicity (ulcerated lesions on the lower limbs). One year prior, he had suffered a myocardial infarction, treated with coronary stenting.
During hospitalization, symptoms persisted. Laboratory tests revealed neutrophilic leukocytosis, monocytosis, mild normocytic anemia, a marked elevation of inflammatory markers, and increased C3 and C4 levels. Microbiological and autoimmune testing returned negative results.
A total body computed tomography (CT) scan showed mediastinal lymphadenopathy, prompting bronchoalveolar lavage (BAL), which identified only an Enterovirus. A needle biopsy of the mediastinal lymph nodes was inconclusive. Positron emission tomography (PET) revealed mild uptake in mediastinal lymph nodes and inflammatory uptake along the major vessels of the lower limbs. The viral infection did not appear sufficient to explain the elevated inflammatory markers and persistent symptoms over several weeks. A diagnosis of LV-GCA limited to the limb arteries (LR-GCA) was therefore suspected, and prednisone at 1 mg/kg was initiated, resulting in rapid clinical improvement. A femoral artery biopsy was not performed due to an unfavorable risk-benefit ratio.
During steroid tapering, the patient developed scapular and pelvic girdle pain and headache, necessitating an increased steroid dose and initiation of methotrexate.
Conclusion: diagnosing LV-GCA remains a significant challenge in internal medicine, as it presents as a systemic disease with often non-specific symptoms. In this case, the diagnosis was supported by three key clinical features, alongside elevated inflammatory markers: constitutional symptoms (fever), rheumatic symptoms (scapular and pelvic girdle pain), and vascular symptoms (headache). PET imaging was essential in identifying an atypical GCA location.
Although GCA typically involves the cranial vessels, it may also affect non-cranial arteries, including the ascending aorta and its major branches, and more rarely, distal vessels such as the iliac or femoral arteries (LR-GCA).
The pathophysiological mechanisms of LR-GCA appear to mirror those of cranial GCA. However, the temporal artery may contain more dendritic cells, making it more susceptible to Th1 and Th17-mediated damage. That said, a diagnostic bias favoring cranial GCA due to easier detection cannot be excluded.

EFFICACY AND SAFETY OF REDUCED-DOSE DIRECT ORAL ANTICOAGULANTS IN SEVERE HEREDITARY THROMBOPHILIA

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Background: Direct oral anticoagulants (DOACs) are established as effective treatments for venous thromboembolism (VTE) in patients with severe hereditary thrombophilia. However, the efficacy and safety of reduced-dose DOACs for long-term secondary prevention in this high-risk population

remain uncertain.
Objective: To evaluate the incidence of recurrent VTE and bleeding complications in patients with severe hereditary thrombophilia receiving reduced-dose DOACs as extended secondary prophylaxis.
Methods: In this prospective cohort study, we enrolled 192 adult patients with documented severe hereditary thrombophilia and a history of VTE between 2014 and 2022. All patients completed at least 3 months of full-dose anticoagulation, followed by a minimum of 3 months on reduced-dose DOAC therapy. Primary outcomes included VTE recurrence and bleeding events occurring during the reduced-dose phase.
Results: The cohort had a mean age of 57.5 years, and 48.5% were male. The distribution of thrombophilia types was: protein S deficiency (32%), protein C deficiency (23%), antithrombin deficiency (15%), homozygous factor V Leiden (9%), homozygous prothrombin mutation (2%), combined heterozygosity (14%), and factor V Leiden pseudo-homozygosity (5%). Patients received a mean of 20.5 months of full-dose anticoagulation followed by a mean of 50.5 months of reduced-dose therapy. During the reduced-dose period, there was one VTE recurrence (incidence rate [IR] 0.35 per 100 patient-years; 95% CI 0.018–1.76) and three non-major bleeding events (IR 1.07 per 100 patient-years; 95% CI 0.27–2.91). At the time of analysis, 36% of patients remained on full-dose anticoagulation, 26.5% had discontinued therapy after a reduced-dose phase, and 36.5% continued on reduced-dose DOACs (39 on rivaroxaban 10 mg daily and 31 on apixaban 2.5 mg twice daily).Among the entire cohort, 36% of patients continued with full-dose anticoagulation, 26.5% discontinued therapy after completing the reduced-dose period, and 36.5% are currently on reduced-dose therapy (39 receiving rivaroxaban 10 mg and 31 receiving apixaban 2.5 mg twice daily). The cumulative incidence of VTE recurrence was 1.43% (95% CI 0.25–7.65) in the reduced-dose group, 13.7% (95% CI 6.8–25.7) in those who discontinued anticoagulation (hazard ratio [HR] 22.5, 95% CI 3.69–137.4), and 1.4% (95% CI 0.25–7.55) in those continuing full-dose therapy (HR 1.97, 95% CI 0.43–9.03) (Figure 1A). The bleeding rates were 4.3% (95% CI 1.46–11.86) for the reduced-dose group and 5.63% (95% CI 2.21–13.6) for the full-dose group (HR 3.51, 95% CI 0.76–16.1) (Figure 1B).

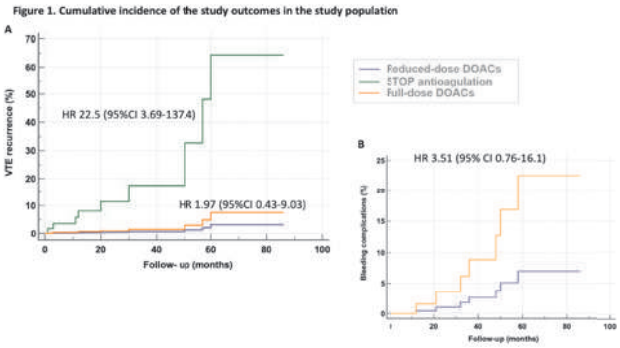

Figure 1.
1A
1B

Conclusions: Reduced-dose DOACs were associated with a significantly lower risk of VTE recurrence compared to treatment discontinuation, while maintaining a similar safety profile to full-dose anticoagulation. These findings support the use of reduced-dose DOACs as an effective and well-tolerated option for long-term secondary prevention in patients with severe hereditary thrombophilia.

TREND ANALYSIS OF TOBACCO USE PREVALENCE AND SMOKING CESSATION CENTERS FROM 2005 TO 2023 IN ITALY

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Introduction: Tobacco consumption is a modifiable behavioural risk factor for the development of Non-Communicable Diseases (NCDs) and a global public health threat. The clinical management of NCDs, also known as chronic diseases, is a critical issue, especially for internal medicine. Smoking cessation centers, known as *Centri Antifumo* in Italy, are dedicated healthcare services that offer a wide range of interventions, specific treatments and supports to assist in quitting smoking in an integrated care pathway. Given the significant health and economic burden of tobacco use, it is essential to examine temporal trends in smoking behaviours and the development of the healthcare services for tobacco dependence.
Materials and methods: Data were obtained from ISTISAN reports published by the Italian National Health Institute (ISS) and from the national surveys provided by the Italian National Institute of Statistics (ISTAT). We identified three indicators: i) *the number of smoking cessation centers in Italy*, ii) prevalence (per 100 population) of smokers aged 15 years and older, and iii) prevalence (per 100 population) of heavy smokers (≥ *20 cigarettes per day*) aged 15 years and older. In constructing datasets, we considered data from 2005 (when the Sirchia Law -which banned smoking indoors- was introduced in Italy) to 2023 (the latest data available) in the Italian population. We performed a joinpoint regression analysis for each data point, to describe temporal changes using joinpoint models, where several different lines are connected at the inflection points. We considered the year as the independent variable, while the three indicators were the dependent variables, assuming homoscedasticity. The software calculated the Annual Percentage Change (APC) and the Average Annual Percent Change (AAPC), considering them significant when *p-value* < 0.05.
Results: The resulting graphs of the output data displayed the trend changes (Figure 1). The analysis of the *number of Italian smoking cessation centers* showed two joinpoints, identifying 3 trends over the study period: the first interval showed a non-significant increase (APC = +0.18%, p>0.05), followed by a significant decrease between 2018 and 2021 (APC = –16.62%, p<0.05), and a subsequent non-significant increase (APC = +2.88%, p>0.05). Overall, there was a reduction (AAPC was = 2.55%, p<0.05).The analysis of the *prevalence of smokers aged 15 and over* identified 4 intervals and 3 joinpoints with non-significant changes: (APC = +0.34%, p>0.05); (APC = –4.38%, p>0.05); (APC = –1.04%, p>0.05); (APC = +1.50%, p>0.05). Overall, there was a decreasing trend in prevalence (AAPC was –0.73%, p<0.05). In the prevalence of heavy smokers aged 15 and over, the analysis identified 3 intervals with 2 joinpoints. A non-significant increase (APC = +1.27%, p<0.05) from 2005 to 2008 was followed by a significant decrease between 2008 and 2016 (APC = –8.54%, p<0.05). A non-significant decrease was observed from 2016 to 2023 (APC = –1.79%, p>0.05). Overall, a decreasing trend was observed with an AAPC of -4.36% (p<0.05).
Conclusions: Overall, a decreasing trend was described for all three indicators. The reduction in prevalence of smokers was important during 2005–2023. Additionally, a significant decrease in heavy smokers between 2008 and 2016 was potentially related to the implementation of the Sirchia Law and the gradual increase in the number of smoking cessation centers. Conversely, from 2018 to 2021, there was a reduction in the number of smoking cessation centers, especially during the COVID-19 pandemic.
Further studies should be conducted over longer periods of time, including regional data, to better understand the key role of appropriate healthcare services, such as *Centri Antifumo*, in reducing the burden of tobacco-related chronic diseases with a comprehensive framework. In the healthcare complexity, the trend analysis of the risk factors is crucial to examine population health needs and to address decisions and programs for promoting healthy lifestyles, contrasting substance use and providing appropriate levels of prevention for NCDs.

WHEN SOCIAL ISSUES PROLONG HOSPITAL STAYS: WHO PAYS TH E PRICE? INSIGHTS FROM A RETROSPECTIVE ANALYSIS OF AN INTERNAL MEDICINE WARD DEDICATED TO PATIENTS WITH DELAYED DISCHARGE ISSUES

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Background: Delayed discharge occurs when patients, although medically fit for discharge, remain hospitalized due to non-clinical factors. The term "bed blocker" places the burden on patients, emphasizing individual vulnerabilities such as frailty, cognitive decline, or social isolation. Conversely, the concept of delayed discharge shifts the focus to the challenges faced by the healthcare system in ensuring appropriate discharge planning and continuity of care, underlining the need for structured post-acute care programs. In Internal Medicine wards, this issue is common and multifactorial, often involving both patient-

related and organizational challenges. Delayed discharge extends hospital stays, increases healthcare costs, and exposes patients to adverse outcomes such as delirium, infections, and functional decline. According to the CO-CARED study results, in our healthcare setting over 20% of patients experiences delayed discharge for non-clinical reasons, primarily due to the need for post-discharge care facilities.

Methods: We present preliminary data from a six-month retrospective study (November 2024–April 2025) conducted at hospital San Paolo, a teaching hospital in Milan. We consecutively enrolled adult patients who had been admitted to an Internal Medicine unit dedicated to patients without ongoing clinical need for hospitalization. The unit, operating within an Internal Medicine ward was created to reduce emergency department overcrowding by providing beds for patients with delayed discharge issues. Collected data included demographics, admission reason, length of stay, and scores assessing clinical complexity (Charlson Comorbidity index, CCI), social frailty (Blaylock Risk Assessment Screening Score, BRASS) and 3-month mortality risk (BECLAP score) calculated with data available at the time of admission to the Internal Medicine ward. In case of bedridden status after hospitalization the BECLAP score was recalculated. The primary outcome was a composite of all-cause in-hospital mortality or complications (confinement to bed rest, delirium, infections, falls). Hospitalization costs were estimated based on the regional average cost per inpatient day in Internal Medicine wards, calculated from the time the patient was considered eligible for discharge until discharge or death. The time the patient was considered eligible for discharge was defined as the resolution of the primary acute issue; for patients that had been hospitalized for social reasons only, it matched the admission date.

Results: At the time of this preliminary analysis, 39 patients were eligible, 54% male, with a median age of 85 years (IQR 76–90). At admission, the median 3-month mortality risk was 27% (IQR 12–44) according to the Beclap score. The median CCI was 8 (IQR 6–11), and 46% of patients presented cognitive impairment. Notably, in 28% of cases, no acute clinical event was identified at admission, implying that hospitalization was driven by social frailty only. The mean BRASS score was 20, indicating an intermediate discharge risk. The median time between emergency department presentation and hospital admission was 2 days (IQR 1–3). Prior to transfer to the dedicated unit, patients spent a median of 13 days (IQR 7–26) in acute care wards, of which 9 days (IQR 4–16) were clinically justified. During their hospital stay the patients had a median social hospitalization of 18 days (IQR 9–32). The estimated avoidable cost per patient, calculated from the day the patient was eligible for discharge, was €11,748 (IQR €6,408–21,538). The primary outcome occurred in 25 (64%) patients. All-cause in-hospital mortality occurred in 9 (23%) patients, while 22 (56%) experienced complications: 8 (21%) experienced only one complication, whereas 13 (34%) had multiple. The most frequent complications were infections (31%), delirium (28%), and bed confinement (28%). Falls affected 5 patients; among them, 3 (60%) sustained head trauma and 1 (20%) suffered a fracture.

Conclusions: Our preliminary analysis shows that delayed discharge in frail patients is associated with high rates of complications, in-hospital mortality, and avoidable healthcare costs. Social vulnerability plays a key role in prolonging hospital stays. For internists, who often care for the most complex and frail patients, this issue reflects a broader systemic gap between acute care and long-term support. Structured discharge planning and integrated post-acute care pathways are essential to close this gap. Acute hospital wards are not suitable for managing social frailty and may contribute to adverse outcomes. A coordinated, multilevel approach is needed to ensure safe transitions and continuity of care. Importantly, many complications occurred because patients remained in Internal Medicine wards after resolution of the acute issue, highlighting the limits of acute care in these settings.

SUCCESSFUL MANAGEMENT OF THERAPEUTIC ANTICOAGULATION FOR VENOUS THROMBO-EMBOLISM IN PRIMARY IMMUNE THROMBOCYTOPENIA: A CASE SERIES

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Introduction: Primary immune thrombocytopenia (ITP) is an acquired autoimmune disease characterized by a transient or persistent reduction in the platelet count (<100×109/L) in the absence of any known condition associated with thrombocytopenia. While bleeding is the hallmark clinical manifestation of ITP, an increasing body of evidence suggests a paradoxical predisposition to thrombotic events in these patients. Venous thromboembolism (VTE), although uncommon, has been reported in both newly diagnosed and chronic ITP, and may be related to disease-specific factors such as platelet microparticles, increased platelet turnover, and the prothrombotic effects of certain treatments, including corticosteroids, intravenous immunoglobulins (IVIG), and thrombopoietin receptor agonists (TPO-RAs)1. Fostamatinib is a novel treatment for ITP, which appears to be associated with low rates of thrombosis but is characterized by a slow onset of therapeutic effect. In a multicenter, randomized, placebo-controlled trial of fostamatinib compared to placebo, the median time to response was 15 days, and 83% of patients responded within 8 weeks since treatment initiation2. Managing VTE in the context of ITP is a unique therapeutic challenge, as clinicians must balance the risk of bleeding due to low platelet counts with the potentially life-threatening consequences of thrombotic events. Here, we report two cases of young women with ITP who developed VTE and required anticoagulant therapy.

Case 1 In May 2024, a 26-year-old woman with a 2-year history of primary ITP, recently started on eltrombopag due to insufficient response to corticosteroids and IVIG, presented to the emergency department with atypical chest pain, cough, asthenia, and haemoptysis. She was taking combined oral estrogen-progestin therapy. Vital signs were stable on admission, and the platelet count was 362.000/mm^3. A CT pulmonary angiography revealed bilateral pulmonary embolism. Estrogen-progestin therapy was discontinued, and anticoagulation with low-molecular-weight heparin was initiated, followed by apixaban 5 mg twice daily after discharge. The patient was referred to the Platelet Disorders clinic of hospital San Paolo. Testing for congenital and acquired thrombophilia was negative. During follow-up, we cautiously tapered eltrombopag while continuing anticoagulation and regular blood monitoring. In November 2024, after completing a full course of anticoagulation, the platelet count was 137.000/mm^3 while on eltrombopag 125 mg/week, making further tapering difficult. Fostamatinib 100 mg twice daily was added, allowing discontinuation of eltrombopag in December 2024. After three months since eltrombopag discontinuation, we decided to stop anticoagulant therapy because the thrombotic event was interpreted as provoked by combined oral contraceptives and eltrombopag, which had both been discontinued. At her latest follow-up in February 2025, the patient was still taking fostamatinib and her platelet count is stably above 100.000/mm3.

Case 2 A 32-year-old woman with a history of primary ITP diagnosed in 2012 with two subsequent relapses treated with rituximab presented to the emergency department in late October 2024 due to the appearance of ecchymosis and petechiae. At the time, she was on combined estrogen-progestin therapy via a vaginal ring. Blood tests at arrival revealed severe thrombocytopenia (platelet count: 6.000/mm^3). She was started on high-dose dexamethasone (40 mg/day for 4 days), with a favorable initial response. After 24 hours of hospital stay she was discharged, but a few days later she returned to the emergency department due to swelling of her right leg. A venous Doppler ultrasound confirmed deep vein thrombosis (DVT) of the right popliteal vein. Her platelet count was 134.000/mm3. Anticoagulant therapy with fondaparinux 7.5 mg daily was initiated, later transitioned to apixaban 5 mg twice daily. A week later, she was referred to the Platelet Disorders clinic of hospital San Paolo. Here, she was started on fostamatinib 100 mg twice daily. Testing for congenital and acquired thrombophilia was negative. At the time of her latest follow-up in April 2025, the patient was still on anticoagulation with apixaban and on fostamatinib, with platelet counts stably above 100.000/mm3.

Conclusion: We have presented a case series of young, otherwise healthy primary ITP patients who developed VTE while on combined estrogen-progestin therapy. The first patient developed pulmonary embolism while on eltrombopag, whereas the second patient developed DVT during an acute symptomatic relapse of her ITP, managed high-dose dexamethasone. This case series offers two teachable moments: (1) it challenges the preconceived notion that ITP is solely associated with bleeding risk and that thrombocytopenia protects from thrombosis; (2) it shows that fostamatinib can be successfully used to allow for therapeutic anticoagulation despite its slow onset of therapeutic action, if introduced while safe platelet counts are maintained by other ITP treatments.

References: 1. doi:10.1016/j.ijcard.2024.132417 2. doi: 10.1002/ajh.25125

CLINICAL BURDEN OF RSV INFECTION IN ADULTS: A RETROSPECTIVE COHORT STUDY FROM A TERTIARY CARE HOSPITAL IN MILAN

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Background: Respiratory syncytial virus (RSV) is an RNA virus from the *Pneumoviridae* family, genus *Orthopneumovirus*. Historically known for its impact on pediatric populations, RSV, has recently emerged as a significant pathogen in adults. In Europe, it is responsible for approximately 158,229 adult hospitalizations per year. In Italy, RSV causes 291,000 respiratory tract infections, 26,000 hospital admissions and 1,800 deaths annually. Approximately 12% of

RSV infections require hospitalization, with 10-31% needing intensive care and an 8% in-hospital mortality rate.
To date, three vaccines have been approved for adult RSV prophylaxis: two protein-based (Arexvy and Abrysvo) and one mRNA-based (mResvia). Recommendations are currently limited to patients ≥75 years and those ≥60 with selected comorbidities. Further studies are ongoing in adults under 60 years of age, particularly those with severe comorbidities or other high-risk younger individuals.
Objectives *Primary:* To describe a cohort of patients admitted to medical and intensive care units at the Grande Ospedale Metropolitano Niguarda (Milan) with RSV-positive respiratory samples collected between January 2023 and April 2024, including demographic characteristics, comorbidities and clinical course. *Secondary:* To identify factors associated with a more severe disease course (pneumonia, respiratory failure, shock), non-invasive ventilation, ICU admission, intubation, and in-hospital mortality
Methods: This retrospective, single-center observational study included adult patients admitted to Grande Ospedale Metropolitano Niguarda between January 1st 2023 and April 30th 2024, with a positive RSV RT-PCR result from respiratory samples. Of 3020 tested samples, 753 (24.9%) were positive for viral pathogens, with 87 (11.5%) testing positive for RSV. After applying exclusion criteria, data from 59 patients were analyzed.
Results: The average age was 66.4 years, with 34 patients (57.6%) aged ≥65. Most patients (40.7%) were admitted to Internal Medicine wards. Among these, 89.8% had at least one comorbidity, and 83% had two or more. Median Charlson Comorbidity Index was 5. The most common comorbid conditions were hypertension (40.7%), COPD (32.2%), and immunosuppression (33.9%). Symptom onset ranged from 1 to 30 days. The most common symptoms were cough (55.9%), dyspnea (54.2%), and fever (42.4%). Only 6.8% were asymptomatic. Bacterial superinfection was suspected in 67.8% of cases, confirmed microbiologically in 22%.Pneumonia was radiologically diagnosed in 66.1% of patients (most with lobar and bilateral infiltrates). Complications included acute respiratory failure (40.7%), shock (8.5%), acute kidney injury (32.2%), heart failure (22%) and delirium (10.2%). Oxygen therapy was required in 54.2% cases, with 16.9% patients receiving non-invasive ventilation. Four patients (6.8%) required intubation for an average of 9 days, and nine patients (15.3%) required high-intensity care. No tracheostomies or prone cycles need were recorded.
Outcomes were favorable in most cases: 96.6% were discharged (one to Hospice), with a median hospital stay of 13 days. Two patients (3.4%) died—one in ICU from aspiration pneumonia and one in a high-intensity unit after extubation in advanced COPD.Radiologic pneumonia was significantly associated with older age (p = 0.014), cardiac failure (p = 0.012), and chronic renal disease (p = 0.022). Smoking history was significantly associated with the need for oxygen therapy (p = 0.019) and respiratory failure (p = 0.002), as was COPD (p = 0.015). Risk of requiring non-invasive ventilation was higher in patients with heart failure (p = 0.008) and COPD (p = 0.039). Among all factors, only smoking history was associated with increased risk of high-intensity care admission. No anamnestic factors were found to be correlated with the risk of intubation or death, possibly due to the small sample size.
Conclusions: RSV is an emerging pathogen among adult inpatients, particularly in Internal Medicine. It often causes significant clinical manifestations, with lower respiratory tract involvement and pneumonia being common. These complications lead to prolonged hospital stays, increased resource use, and occasionally, critical illness. Many patients experience complications such as bacterial superinfection, heart or kidney failure, and respiratory insufficiency, occasionally requiring high-intensity care or invasive ventilation. Although the registered mortality was low, the overall clinical burden of RSV in adults is significant, underscoring the need for improved prevention strategies and increased awareness.

LONGITUDINAL COAGULATION PROFILING OF INDIVIDUALS UNDERGOING GENDER-AFFIRMING HORMONE THERAPY

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Background: Transgender individuals may face an increased risk of thrombosis, potentially due to a hypercoagulable state induced by gender-affirming hormone therapy (GAHT).
Objective: To assess the longitudinal effects of GAHT on coagulation parameters, metabolic function, and erythropoiesis, and to investigate the mechanisms contributing to hypercoagulability in the transgender population.

A

Assigned Male At Birth -AMAB				
Parameter	Baseline	6 months	12 months	p for trend
Blood count				
Hb - g/dL	15.3 [15-16]	14.3 [12.6-13.9]	14.4 [14.2-15.0]	<0.01
HCT - %	45.9 [44.7-48.3]	40.4 [37.4-42.2]	42.6 [40.9-44.6]	<0.001
Erythrocytosis (HCT>48%)	14 (34%)	0	0	<0.001
Anemia (Hb<12 g/L)	1 (2.4%)	1 (2.4%)	2 (4.9%)	ns
Platelets – x 10^9/L	244 [203-276]	291 [210-349]	277 [206-369]	0.0033
Sex steroids				
Testosterone – ng/mL	5.3 [4.2-6.5]	0.2 [0.1-0.3]	0.3 [0.2-1.2]	0.006
Estradiol (E2) – ng/L	33.6 [26-35]	40.7 [34-83]	167 [51-289]	0.007
LH – U/L	5.3 [3.5-7.3]	0.2 [0.1-0.3]	0.2 [0.1-2.9]	0.0002
FSH – U/L	2.4 [1.9-3.9]	0.4 [0.35-0.6]	0.5 [0.4-1.5]	<0.001
Procoagulant factors				
Factor VIII activity - %	1[3 [97-133]	115 [98-131]	108 [92-127]	ns
Fibrinogen activity – mg/dL	323 [290-390]	318 [252-353]	307 [282-340]	Ns
Anticoagulant factors				
Protein C activity - %	100 [85-106]	93 [87-101]	101 [94-108]	ns
Protein S activity - %	109 [102-123]	123 [114-125]	128 [122-134]	0.007
Protein S free antigen - %	102 [96-115]	107 [99-115]	119 [101-121]	ns
Antithrombin - %	98 [89-102]	101 [88-119]	97 [94-109]	ns
Thromboelastometry				
CFT-INTEM - sec	89 [71-99]	177 [147-206]	59 [57-76]	0.003
MCF-INTEM – mm	61 [57-66]	62 [61-64]	63 [62-65]	ns
MCF-EXTEM – mm	65 [61-67]	63 [62-67]	66 [65-67]	ns
MCF-FIBTEM - mm	16 [12-16.5]	15 [13.5-23]	16 [15.7-20.5]	ns
Whole blood aggregometry				
TRAP – AUC	99 [94-117]	108 [87-134]	142 [133-145]	0.05
Thrombin-generation				
Peak – nM	213.6 ± 64.8	275.2 ± 51.2	281.6 ± 37.8	< 0.0001
ETP+TM – nM*min	842 ± 333	1075 ± 314	1171 ± 294	<0.0001
ETP ratio (with/without TM)	0.6 ± 0.2	0.7 ± 0.2	0.8 ± 0.1	<0.013
Iron metabolism				
Iron – umol/L	9.5 [5.9-16.4]	19.5 [11.5-20]	15.4 [11.6-19]	0.018
Transferrin saturation – %	28 [21-39]	36 [28-49]	31 [22-41]	0.011

B

Assigned Feminine At Birth -AFAB				
Parameter	Baseline	3 months	6 months	p for trend
Blood count				
Hb - g/dL	13.3 [12.8-13.5]	14 [13.5-14.5]	14.6 [14.4-14.9]	0.0006
HCT - %	40.5 [39.9-40.9]	43 [42-44.2]	44.8 [43-46.4]	<0.0001
Erythrocytosis (HCT>48%)	0	3 (4.2%)	9 (12.7%)	0.0019
Anemia (Hb<12 g/L)	10 (14%)	4 (5.6)	0	0.012
Sex steroids				
Testosterone – ng/mL	0.3 [0.24-0.39]	3 [2.5-5.2]	4.8 [2.3-14.9]	<0.0001
Estradiol (E2) – ng/L	69 [43-111]	40 [32-75]	42 [29-67]	Ns
SHBG – nmol/L	80.7 [53-99]	47.9 [33.4-54.3]	37.2 [27-41]	0.02
Procoagulant factors				
Factor VIII activity - %	133 [97-149]	134 [120-159]	130 [94-139]	Ns
Fibrinogen activity – mg/dL	357 [314-424]	332 [289-371]	339 [290-359]	Ns
Anticoagulant factors				
Protein C activity - %	109 [89-118]	102 [89-129]	110 [91-128]	Ns
Protein S activity - %	107 [91-114]	13[[104-146]	128 [116-134]	0.002
Protein S free antigen - %	95 [91-108]	113 [106-118]	106 [103-119]	Ns
Antithrombin - %	98 [96-109]	99 [93-108]	98 [94-102]	Ns
Thromboelastometry				
CFT-EXTEM - sec	70 [61-86]	77 [71-85]	93 [71-95]	0.01
MCF-INTEM – mm	65 [61-69]	62 [58-67]	60 [56-66]	0.02
MCF-EXTEM – mm	69 [64-72]	65 [63-69]	64 [61-68]	0.04
MCF-FIBTEM - mm	20 [14-24]	15 [14-17]	15 [11-17]	0.0007
Whole blood aggregometry				
ASPI - AUC	73 [49-92]	60 [52-69]	74 [59-80]	ns
Thrombin-generation				
Peak – nM	225 ± 37.9	245.7 ± 42.6	252.2 ± 50.1	0.054
ETP ratio (with/without TM)	0.7 ± 0.2	0.6 ± 0.2	0.6 ± 0.2	ns
Iron metabolism				
Iron – umol/L	7.9 [7.4-12]	5.2 [4.5-6.7]	20.5 [10.5-36]	0.01
Ferritin – ng/mL	23 [15-56]	12 [6-15.5]	19 [13-23.2]	0.02
Transferrin saturation - %	9 [8.9-12.1]	6 [5.2-7.6]	1.9 [1.4-5.3]	0.04

Table 1. Longitudinal trend of blood count, sex hormones, coagulation and iron metabolism parameters in transgender subjects undergoing gender-affirming hormone therapy.

Conclusions: Hereditary thrombophilia was present in 7% of transgender individuals initiating GAHT, including 2% with severe forms. Baseline differences in coagulation profiles were observed between AMAB and AFAB participants. Estrogen-based GAHT in AMAB individuals was associated with procoagulant changes, including increased platelet activity and thrombin generation. In contrast, testosterone therapy in AFAB individuals primarily led to erythropoietic and metabolic changes, with limited impact on coagulation.

COMPARISON OF FRAILTY AND COMORBIDITY INDEXES AS PREDICTORS OF CLINICAL OUTCOMES IN PATIENTS ADMITTED TO INTERNAL MEDICINE

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Background: In recent years, the profile of patients admitted for acute conditions to Internal Medicine wards has undergone a profound transformation. These individuals are vulnerable to acute stressors and often experience adverse clinical outcomes even after several weeks of intensive medical treatments. To minimize patient overtreatment and optimize the use of healthcare system resources, it is essential to identify individuals who, despite maximal therapeutic efforts, are unlikely to benefit from an escalation of care due to their limited recovery capacity. In this study we aimed at assessing the ability of frailty and comorbidity indexes in predicting a composite outcome composed of in-hospital mortality, being a bed blocker or being discharged to palliative care, in older hospitalized patients.
Materials and methods: this is a retrospective study taking advantage of the data collected in the MED-Cli study. The MED-Cli study is a single-center prospective observational trial. All adult (age ≥18 years) patients who are managed in the Internal Medicine and Nephrology Departments of IRCCS San Raffaele Hospital in Milan, Italy, and sign the informed consent are enrolled. The study is anticipated to be open for 10 years, beginning from 2022, and envisioning to enroll roughly 1000 patients per year.
For this analysis we analyzed the data extracted from 407 patients hospitalized in the year 2024 in one internal medicine department of the San Raffaele hospital.
Frailty was measured with a frailty index (FI) computed according to the criteria described by Theou et al. Comorbidity was measured with the Charlson Comorbidity Index (CCI).
The composite outcome was composed of being a bed blocker defined by a length of hospital stay greater than 17 days, in-hospital mortality or discharge to palliative care.
Descriptive statistics were used to show the baseline characteristics of the study population. Continuous variables were presented as mean and standard deviations (SD), when normally distributed, or with median and interquartile range (IQR), when data had a skewed distribution. Dichotomous variables were presented as number (N) and percentage (%). Age and sex adjusted logistic regression analysis were used to assess the association between frailty, comorbidities and the composite outcome. All statistical analyses were performed with SPSS version 25.0 (SPSS Inc., Chicago, IL, USA).
Results: The study sample had a median age of 76 years (IQR 64–84) and was composed for the 54.1% by males; the prevalence of frailty was 67.3%, with a median FI score of 0.29 (IQR 0.17 – 0.58). The median CCI was 6 (IQR 4 – 8). The study population main characteristics are illustrated in Table 1.
Frailty was associated to a greater risk of developing the composite outcome (OR 7.64, 95% CI 2.8 – 20.9, p < 0.001), compared to comorbidity index (OR 1.12, 95% CI 1.04 – 1.21, p = 0.003).
Discussion: The prevalence of frailty in our sample was very high, in line with previous studies showing frailty is really common in hospitalized patients. In a recent systematic review, Boucher et al. reported that the prevalence of frailty in older patients admitted for unplanned, acute conditions ranges from 14.3% to 79.6%. The heterogeneity in prevalence may be due to differences in frailty measures, with tools excluding cognitive dimension resulting in underestimation of frailty. They also found that frailty is a strong predictor of mortality, length of stay, and the likelihood of discharge to home with higher levels of frailty. Consistent with this and previous findings, our study identified a strong association between the degree of frailty and the risk of adverse outcomes. Although a higher CCI score was also associated with increased risk, the strength of this association was weaker compared to FI. This observation aligns with other studies demonstrating a superior predictive value of frailty measures for adverse clinical outcomes in patients admitted to intensive care units, those with traumatic brain injuries, and individuals undergoing surgery. This is likely due to the more comprehensive and multidimensional nature of frailty, which more effectively captures the patient's complexity. Moreover, it is plausible that, with advances in medical care, many comorbidities are now well managed and therefore have a reduced impact on the patient's overall vulnerability.
FI may serve as a valuable instrument to guide clinical decision-making about the more appropriate setting of care for patients admitted to hospital and to avoid unnecessary and potentially harmful interventions, optimizing patient outcomes and resource allocation.

CHARACTERISTICS AT BASELINE	median [IQR]
Age (years)	76 [64 – 84]
BMI (kg/m^2)	24.3 [21.4 – 28.1]
SBP (mmHg)	125 [110 – 140]
DBP (mmHg)	71 [64 – 80]
HR (bpm)	85 [76 – 100]
RR (apm)	18 [16 – 23]
Body temperature (°C)	36.4 [36,0 – 37,0]
Smoking (packs year)	0 [0 – 32]
Alcohol consumption (units/weeks)	7 [1 – 14]
Education years	10 [5.5 – 13.0]
CCSI	6 [4 – 8]
Braden scale	17 [13 – 21]
CIRS	5 [0 – 9]
Frailty Index	0.29 [0.17 – 0.58]
Number of therapies	11 [8 – 14]
Hospital stay (days)	17 [12 – 26]

Table 1

SAFETY AND EFFICACY OF FOSTAMATINIB IN ADULT PATIENTS WITH IMMUNE THROMBOCYTOPENIA (ITP): A SYSTEMATIC REVIEW OF THE LITERATURE ON THROMBOTIC EVENTS AND SUSTAINED RESPONSE OFF TREATMENT (SROT)

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Background: and Aims: Immune thrombocytopenia (ITP) is an acquired autoimmune disease which poses patients at risk of bleeding because of low platelet counts. Paradoxically, patients with ITP also face a higher risk of both arterial and venous thrombosis compared with the general population.3 Patients requiring treatment to raise their platelet counts who are unresponsive to first-line treatments may be managed with thrombopoietin receptor agonists (TPO-RAs) or fostamatinib. Although both TPO-RAs and fostamatinib were meant to be used continuously, recent studies have shown the possibility of a sustained response off treatment (SROT) after TPO-RA or fostamatinib discontinuation.4,5 However, the proportion of subjects treated with fostamatinib that can successfully reach SROT is currently unknown. There have been reports of arterial and venous thrombotic events in ITP patients on treatment with TPO-RAs. However, most systematic reviews found no significant difference in thrombotic events between TPO-RA users and non-users.7,8,9 Fostamatinib appears to be associated with fewer thrombotic events than TPO-RAs, but data on the rate of thrombotic events while on treatment with fostamatinib are scarce. To address these gaps, we performed a systematic review of published studies.
Methods: PubMed and Embase were searched by two researchers (S.S. and C.M.) on February 9th, 2025, with a pre-defined research string. We included peer-reviewed published studies in English describing adult ITP patients with known fostamatinib treatment status and available data on at least one of the primary outcomes. The diagnosis of ITP was based on the authors' judgment. We excluded case series describing fewer than 5 patients. The primary safety outcome was the cumulative rate of thrombotic events, whereas the primary efficacy outcome was the cumulative rate of SROT. SROT was defined as the possibility of discontinuing fostamatinib while maintaining a safe platelet count over time, as defined by the authors. Eligibility assessment was performed independently by two reviewers (C.M. and S.S.). Disagreements were solved by consensus or by a third reviewer (B.C.). Data extraction was performed independently by C.M. and S.S. Data from observational studies and randomized controlled trials (RCTs) were analyzed separately. Categorical data are presented as proportions and percentages with 95% confidence intervals calculated with the exact binomial method. Comparisons between categorical variables were performed with the Fischer's exact test. We performed a meta-analysis of the data using the random intercept logistic regression model and logit transformation, using the I2 statistic as a measure of heterogeneity (R Core Team software,

2023). We also performed a post-hoc subgroup analysis comparing the rate of SROT in patients with primary and secondary ITP. The risk of bias of eligible studies was assessed using the RoB2 and ROBINS-I version 2 tools for RCTs and observational studies, respectively.
Results: We retrieved 572 studies through our literature search. Following the exclusion of 117 duplicates and of 445 ineligible studies, we included 10 studies (8 observational studies and 2 RCTs), 9 providing information on thrombotic events and 2 on SROT, for a total of 579 adult ITP patients treated with fostamatinib (123 from RCTs and 456 from observational studies). Out of 395 adult ITP patients treated with fostamatinib in the context of observational studies, thrombotic events occurred in 5 patients (meta-analyzed frequency: 1%, 95% CI 1-3%; I2 0%, p=0.89). There were no thrombotic events recorded in the two eligible RCTs (meta-analyzed frequency for patients treated with fostamatinib: 0%, 95% CI 0-1%; I2 0%, p=1). Regarding the primary efficacy outcome, SROT was reported in 12 of the 199 patients described in observational studies (meta-analyzed frequency: 6%, 95% CI 3-13; I2 76%, p=0.04). There were no significant differences in the rates of SROT of patients with primary (n=183) and secondary (n=15) ITP (6.0% vs 6.7%, respectively; p=1.000). The observational studies eligible for the assessment of thrombotic events were found to be at severe or critical risk of bias, those eligible for the assessment of SROT at critical risk of bias, and there were some concerns of risk of bias for the 2 RCTs eligible for the evaluation of thrombotic events.
Conclusions: The findings of our systematic review, although limited by the low quality of eligible studies and by the small number of studies eligible for the evaluation of SROT (resulting in high heterogeneity), show that during fostamatinib treatment the cumulative rate of thrombotic events is low and that a clinically relevant proportion of patients can achieve a SROT after discontinuing the medication.
References: 1. doi:10.1056/NEJMcp18104792. doi:10.1182/blood.20240242503. doi: 10.3324/haematol.2009.018390.4. doi:10.1016/j.heliyon.2023.e134625. doi:10.1182/blood.20220186656. doi:10.1182/blood-2017-04-7487077. doi:10.1016/j.critrevonc.2022.1035818. doi:10.1080/09537104.2020.17451689. doi:10.3892/br.2024.1732

PREVALENCE OF STEATOTIC LIVER DISEASE AMONG PATIENTS ATTENDING A HYPERTENSION CLINIC

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Background: . Hypertension is one of the cardiometabolic risk factors used to identify patients with fatty liver who may meet criteria for metabolic dysfunction-associated steatotic liver disease (MASLD) either simple or, when alcohol intake exceeds 140 g/week for females or 210 g/week for males, with increased alcohol intake (MetALD). However, data on the prevalence of MASLD among hypertensive patients remain limited, and the utility of routine MASLD screening in this population is unclear.
Methods: . We evaluated 124 consecutive patients (74 males; median age: 62 years; median in-office systolic blood pressure: 135 mm Hg) attending the Hypertension Clinic of an academic hospital in Northern Italy. Participants completed a lifestyle questionnaire and underwent transient elastography with measurement of liver stiffness (LSM) and controlled attenuation parameter (CAP). A CAP value ≥288 dB/m was used to define MASLD, while LSM thresholds of ≥8.2 kPa and ≥9.7 kPa indicated significant and advanced fibrosis, respectively. With this sample size, the margin of error for estimating prevalence at 95% confidence was ±8%, accounting for a potential 5% loss to follow-up (BMC Med Res Methodol 2022;22:209).
Results: The median body mass index (BMI) was27kg/m² (IQR:25–31);27% of patients were obese. Median waist circumference was101cm in females and102cm in males. Teetotalers comprised49% of participants, while17% of alcohol users reported intake levels consistent with MetALD. The median CAP value was249dB/m (IQR:218–288), yielding an estimated MASLD ± MetALD prevalence of25% (95% CI:18–33%). The median LSM was4.6kPa (IQR:3.9–5.7);5.6% met criteria for significant fibrosis, and2.4% for advanced fibrosis. All patients with advanced fibrosis were older than62years. CAP and LSM were significantly correlated (Spearman rho =0.272, p =0.002). No differences in CAP or LSM values were found between patients with excessive alcohol consumption and others. Univariate analysis showed associations between MASLD and younger age (p =0.043), higher BMI (p =0.002), larger waist circumference (p =0.027), and meat consumption patterns (p =0.011). In multivariate logistic regression, however, only BMI was independently associated with MASLD. A BMI ≥27kg/m² had a sensitivity of81% and specificity of55% for identifying MASLD. Among patients aged ≤62years with a BMI ≥27kg/m², MASLD prevalence rose to43.9% (95% CI:29.2–59.7%).
Conclusions: Approximately 1 in 4 hypertensive patients met criteria for MASLD, slightly exceeding the estimated prevalence in the Italian general population (19.6%; Clinicoecon Outcomes Res. 2024;16:773–784). Significant and advanced fibrosis were infrequent. These findings suggest that routine measurement of CAP and LSM in all hypertensive patients may not be an efficient strategy for detecting MASLD or its complications.

PSORIASIFORM DERMATITIS AND ACUTE GENERALIZED EXANTHEMATOUS PUSTULOSIS (AGEP): A RARE DUAL CUTANEOUS ADVERSE REACTION DRUG INDUCED

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Background: Amiodarone is an iodine-rich class III antiarrhythmic. Due to its lipophilic nature and long half-life, it accumulates in various tissues, including the skin, causing delayed onset and persistent adverse reactions even after discontinuation.
Side effects include photosensitivity, blue-gray discoloration, and toxic epidermal necrolysis.
Rare cases of psoriasiform dermatitis typically arising one month after treatment initiation have been described, with confluent desquamating erythematous plaques on the trunk and back with mucosal sparing, which resolved after discontinuation of the drug and topical steroid therapy. The hypothesized mechanism involves activation of the enzyme dihydrofolate reductase (DHFR) by iodine, altering folate metabolism and promoting psoriatic reactivation.
Acute generalized exanthematous pustulosis (AGEP) is an acute, rare, self-limiting skin reaction with sterile pustules on erythematous-edematous skin without mucosal involvement, fever, neutrophilia, and mild eosinophilia. In most cases it is drug-induced (beta-lactams especially); there are also forms associated with infection and iodinated contrast media. The eruption appears within a few days and regresses in one to two weeks after discontinuation with scaling. Patch testing can confirm the suspected drug, although a negative result does not rule it out. Treatment consists of discontinuation of the causative agent, topical corticosteroids and, in severe cases, systemic.
A case report with dual occurrence of psoriasiform dermatitis from amiodarone and AGEP follows, highlighting the complexity of diagnosis and management of skin reactions in elderly, pluricomorbid, and polypharmacy patients.
Discussion: A 68-year-old man with chronic anemia, Chronic Kidney Disease, Chronic Obstructive Pulmonary Disease, psoriasis and paroxysmal Atrial Fibrillation for which he started amiodarone one month ago with subsequent onset of erythematous-purple, scaling and infiltrating lesions on face, trunk, limbs and palmoplantar surfaces with intense itching.
Blood tests show eosinophilia (1,52 10*9/L), increased ESR, CRP, IgE (>5000 kU/L), worsening anemia and renal function.
Therapy with amoxicillin/clavulanic acid, oxatomide, and topical betamethasone and fusidic acid is started.
Skin biopsy shows epidermal hyperplasia, hyperkeratosis, dermal leukocytic infiltrate, intraepidermal microabscesses and pustules.
Treatment response with clinical improvement and histology suggest iatrogenic psoriasiform dermatitis with plantar hyperkeratosis.
Subsequently, after ceftriaxone therapy for a bronchitic flare-up and angio-CT with iodinated contrast media for the study of an aortic aneurysm, a febrile pustular eruption appears on erythematous patches at the trunk and proximal limbs, without mucosal involvement, compatible with AGEP.
Evidence of neutrophilic leukocytosis and elevation of inflammatory indices.
When a drug reaction is suspected, amiodarone is discontinued and replaced with sotalol, systemic (intravenous) methylprednisolone and chlorphenamine are started, continuing with topical steroid therapy with resolution of pustulosis and residual desquamation, with subsequent switch to oral therapy and topical emollients.
Possible causative agents are amiodarone, ceftriaxone, and iodinated MoC.
The clinical picture and pharmacokinetics make amiodarone the most likely causative agent for psoriasiform dermatitis with subsequent AGEP.
Conclusion: Amiodarone can induce skin toxicity including psoriasiform dermatitis and pustular eruptions.
Its long tissue persistence requires prolonged surveillance even after drug discontinuation.
Early recognition, discontinuation of the suspected drug, and targeted supportive treatment are critical for effective management.
A multidisciplinary approach is critical in complex clinical settings such as elderly, pluricomorbid patients on polypharmacy.

AN UNUSUAL TRACHEAL LESION

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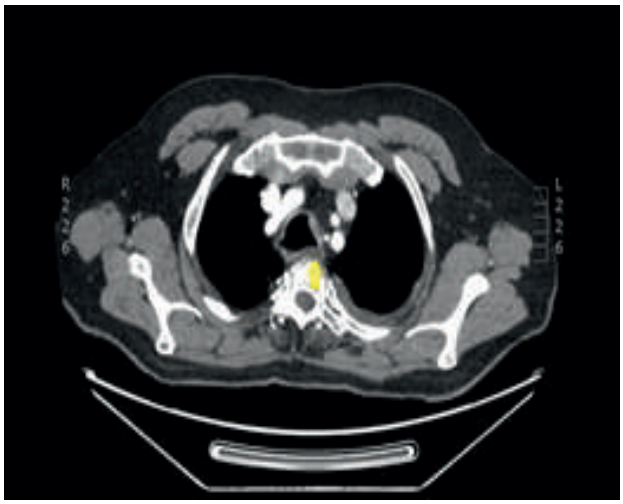
Introduction: Amyloidosis is a pathological condition characterized by extracellular deposition of insoluble fibrillar proteins (amyloid) in tissues and organs. It can occur as a systemic disorder or remain localized. Localized tracheobronchial amyloidosis is an extremely rare entity that may mimic tracheal malignancy, often resulting in diagnostic delay.
Case report: A 74-year-old male presented to the Emergency Department with chest pain and hemoptysis following thoracic trauma. Chest computed tomography (CT) revealed limited parenchymal thickening, minimal pleural effusion, and bilateral pulmonary emphysema. He was discharged with antibiotics and referred for thoracic surgical consultation, which recommended a fibrobronchoscopy (FBS). One month later, FBS showed a bleeding, hyperemic area below the glottic plane. Otolaryngological evaluation confirmed the finding and recommended a contrast-enhanced CT scan and biopsy. The CT scan revealed a dilated, malacic trachea with a pathological subglottic thickening of the left tracheal wall (7 mm thick, 3 cm craniocaudal extension), disrupting the cartilaginous wall and extending into mediastinal fat—raising suspicion of a neoplastic process (Fig.1). A segmental pulmonary embolism with early infarction was also detected. Laboratory tests showed elevated fibrinogen (484 mg/dL); other parameters were normal. Endoscopic biopsy demonstrated subepithelial eosinophilic amorphous material, Congo red positive with apple-green birefringence under polarized light—confirming tracheal amyloidosis. Transthoracic echocardiography was normal, excluding cardiac involvement and suggesting localized disease.
Discussion: Tracheobronchial amyloidosis (TBA) is a rare form of localized amyloidosis, with fewer than 150 cases reported in the literature. Unlike systemic amyloidosis, which involves multiple organs such as the kidneys, liver, heart, and nervous system, TBA is confined to the airways and does not usually progress to systemic involvement. The etiology remains largely idiopathic, although associations with chronic inflammation and smoking have been hypothesized [1].The clinical presentation is nonspecific and includes cough, dyspnea, wheezing, and, less commonly, hemoptysis. In our patient, the initial presentation with hemoptysis following trauma may have acted as a trigger for identifying an otherwise silent lesion. Radiologically, TBA can mimic neoplastic processes due to focal or diffuse tracheal wall thickening and luminal narrowing. In our case, the CT findings were suggestive of a potentially malignant infiltrative lesion, underlining the importance of histopathologic confirmation. Bronchoscopic biopsy is the gold standard for diagnosis, with Congo red staining showing characteristic apple-green birefringence under polarized light. The deposition of amyloid is typically subepithelial and may be nodular or diffuse, potentially leading to significant airway obstruction. Differential diagnosis includes squamous cell carcinoma, tracheal papillomatosis, granulomatosis with polyangiitis, and relapsing polychondritis.Treatment of TBA remains challenging due to its chronic, recurrent nature and absence of standardized guidelines. Therapeutic strategies aim at relieving symptoms and maintaining airway patency. Endoscopic debulking using mechanical resection, laser therapy, or cryotherapy has been employed with variable success [2]. In more extensive cases, tracheal stenting or surgical resection may be considered. Radiotherapy has emerged as a potential option in selected patients, offering symptomatic relief and possibly slowing disease progression [3].The prognosis of localized tracheobronchial amyloidosis is generally more favorable than systemic forms. However, recurrence is common, necessitating regular bronchoscopic surveillance. Importantly, once localized amyloidosis is confirmed, systemic involvement must be excluded through clinical, laboratory, and imaging evaluation.This case reinforces the importance of considering TBA in the differential diagnosis of persistent hemoptysis and subglottic masses, particularly in elderly patients with smoking history. Early diagnosis allows for appropriate management and can prevent complications related to airway obstruction or misdiagnosis as malignancy.
Conclusion: This case highlights the relevance of including localized tracheal amyloidosis in the differential diagnosis of persistent hemoptysis and tracheal wall thickening.Timely recognition and a multidisciplinary approach are essential to avoid misdiagnosis, optimize treatment, and improve patient outcomes.
References:
1. Racil H, et al. Hémoptysie révélatrice d'une amylose trachéobronchique. *Rev Pneumol Clin*. 2011;67(2):109–112.
2. Gorospe L, et al. Localized Tracheal Amyloidosis. *Ann Thorac Surg*. 2018;106(5):e215–e217.
3. Poovaneswaran S, et al. Tracheobronchial amyloidosis: Utilization of radiotherapy as a treatment modality. *Medscape J Med*. 2008;10(42).



AGOSTAR PROTOCOL: EVALUATION OF THE ANTI-INFLAMMATORY EFFECTS OF A STANDARDIZED ACUPUNCTURE PROTOCOL IN 27 PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASE

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Background: Chronic pain represents one of the main features of autoimmune diseases. Drug therapy cannot control pain adequately many times and brings a significant burden of side effects and adverse events. Acupuncture appears to have an important role in mediating pain and inflammation and is recommended as an adjuvant in pain treatment in many different clinical conditions.
Objectives: To evaluate the efficacy of a standardized acupuncture protocol in a cohort of patients with autoimmune diseases on inflammatory biomarkers, chronic pain, quality of sleep, social life, and quality of life in general.
Materials and methods: We conducted a single centre, prospective, interventional study, with a pre-post intervention analysis. We enrolled female patients from the Immunology Clinic of Fondazione IRCCS Ca'Granda Ospedale Maggiore Policlinico, with an established diagnosis of Systemic Lupus Erythematous (SLE), Rheumatoid Arthritis (RA) or Systemic Sclerosis (SSc), chronic pain with Visual Analogue Scale (VAS) ≥ 3, an age comprised between 18 and 65 years old, a stable clinical disease and therapy. All patients subscribed an informed consent to the study.
Patients were treated with a total of 12 acupuncture sessions, during a period of seven months, with a prespecified 6 point-12 needle procedure. The first four acupuncture sessions were on weekly basis, the second four acupuncture sessions occurred every two weeks and the last four acupuncture sessions were once a month.
We evaluated patients at baseline (T0), after one month/four acupuncture sessions (T1) and at the end of the seven months of treatment (T2). We collected blood samples for evaluation of inflammatory profile and the self-reported pain experienced in the last month through VAS. Patients were given three questionnaires on quality of life (depressive symptoms through PHQ-9 questionnaire, sleep quality through PSQI questionnaire and physical and mental functionality through SF-36 questionnaire).
Our primary endpoint was the evaluation of the intervention effects on inflammatory profile and quality of life. The secondary endpoint was the efficacy of the acupuncture protocol on chronic pain evaluated through VAS, with a clinically significance threshold of at least 2 point or 30% reduction.
We used a repeated measures ANOVA to test the effects of acupuncture on variables.
Results: A total of 27 patients were included in the analysis (15 SSc, 9 AR, 3 SLE). All patients were women.
The analysis of inflammatory profile showed a significant reduction of IL-10 after 7 months (T2) (3.1 ± 2.6 pg/mL vs 2.2± 1.9 pg/mL, p 0.018), and of the signaling receptor expressed on neutrophils and monocytes TREM-1, known to be elevated in autoimmune diseases (629±355 pg/mL vs 510±319 pg/mL, p 0.001).

Even if there was not a significant reduction of pain after the first month of treatment (VAS 6.1 ± 1.5 vs 5.4 ± 2, p 0.743), after the 7 months protocol there was a significant effect on chronic pain (VAS 6.1 ± 1.5 vs 4.1 ± 2.2, p <0.001). The effects of acupuncture on quality of life appeared to be significant just after the first month of treatment as indicated by PHQ-9 on depressive symptoms (9.7 ± 5.5 vs 6.4 ± 4.5, p 0.001), by PSQI on quality of sleep (9.1 ± 4.3 vs 7.1 ± 4.2, p 0.009) and by the SF-36 questionnaire on the mental health domain (41.4±11.4 vs 47.4±10.5, p 0.047) and on the social activities domain (50.3 ± 29.6 vs 68.8 ± 23.7, p 0.002). On the other hand, there was a non-significant effect on the physical health domain of SF-36 on (27.8 ± 9.1 vs 30.2 ± 9.8).
All these effects persisted after 7 months of treatment (even though the quality of sleep after 7 months loses significance (p 0,070).
Conclusions: This preliminary analysis indicates a significant reduction of systemic inflammation and pain after 7 months of a standardized acupuncture protocol, while it seems there is not a significant reduction after the first month of treatment. Furthermore, there appears to be a significant improvement in quality of life already after only one month, which is confirmed and maintained after 7 months. Patients felt improvement of sleep quality, reduction of depressive symptoms and a subjective significative improvement in general health perception and social activities.

HYPERCALCEMIC PRIMARY HYPERPARATHYROIDISM AND BROWN TUMOR LOCALIZED AT THE FEMORAL HEAD: WHICH TO ADDRESS FIRST? HOW CLINICAL FEATURES GUIDE THERAPEUTIC DECISION-MAKING.

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Presso il nostro ambulatorio di metabolismo minerale e malattie dell'osso abbiamo preso in carico P.R., donna di 60 anni, che ha portato in visione una MOC-DEXA femoro-lombare con T-score inferiore a 2.5 ed ha riferito una storia di pregresse fratture.
Considerando che la MOC-DEXA rappresenta un esame fondamentale ma non dirimente ai fini della diagnosi clinica di osteoporosi, perché fornisce una valutazione esclusivamente densitometrica, abbiamo eseguito quelli che sono gli esami di primo livello indicati dalle *Linee Guida per la diagnosi, prevenzione e terapia dell'osteoporosi diramate dalla SIOMMMS* (VES, emocromo completo, protidemia, calcemia, fosforemia, fosfatasi alcalina totale, creatininemia e calciuria delle 24 ore) ed anche quelli di secondo livello (calcio ionizzato, TSH, PTH sierico, 25-OH-vitamina D sierica, anticorpi anti transglutamminasi). Dall'esito di questi esami abbiamo posto la diagnosi di iperparatiroidismo primario, perché a seguito della terapia con Colecalciferolo prescrittale per l'ipovitaminosi D (essendo lei una donna in post-menopausa i valori di Vitamina D devono essere superiori ai 30 ng/ml) i suoi valori di PTH e calcio sierico non si sono normalizzati, e l'osteoporosi da cui è affetta la signora è risultata essere dunque secondaria a questo stato di iperfunzionalità delle paratiroidi.
A questo punto, in accordo con *Le linee guida sulla gestione terapeutica dell'iperparatiroidismo primario sporadico nell'adulto* (Vescini et al. , L'Endocrinologo, 2024) abbiamo fatto eseguire alla paziente una PET-colina globale che, oltre ad evidenziare l'ipercaptazione a livello delle paratiroidi, ha mostrato anche una captazione a livello della testa del femore destro, ascrivibile in questo contesto clinico all'emergenza di un tumore bruno, anche noto come osteitis fibrosa , condizioni non maligne tipiche dell'iperparatiroidismo - anche se di esso rappresentano una complicanza rara, dato che la prevalenza è stimata essere di 2/1.000 - in cui gli osteoclasti consumano l'osso normo-conformato composto dagli osteoblasti, dando luogo a formazioni cistiche con all'interno tessuto connetivo, fibroso e osseo spugnoso ma privi di matrice.
Tale diagnosi ci è stata poi confermata definitivamente dalla RMN, che in associazione alla PET-colina rappresenta la metodica più sensibile per localizzare e definire l'osteitis fibrosa.
In questo caso particolare il tumore bruno si è localizzato alla testa del femore, che è una sede meno comune, dato che normalmente emerge nel terzo distale delle diafisi delle ossa lunghe, e rappresenta un locus minoris resistentiae, vista la facilità con cui può andare incontro a frattura nel momento in cui viene indebolita, rischio fratture che è aumentato anche prendendo in considerazione l'osteoporosi da cui è affetta la paziente.
A questo punto, nell'iter diagnostico-terapeutico, ci siamo trovati di fronte al quesito su che tipo di indicazione porre per la paziente. Usualmente in condizioni del genere si procede prima con la paratiroidectomia, asportando chirurgicamente in toto le paratiroidi iperfunzionanti, in modo tale da mettere sotto controllo l'iperparatiroidismo e prevenire l'emergere di nuovi tumori bruni, evenienza questa che è abbastanza comune e che va dunque scongiurata.
In questo caso però, la localizzazione del tumore bruno in un locus minoris resistentiae e la concomitante comorbidità rappresentata dallo stato osteoporotico, espongono la paziente ad un elevato rischio di frattura della testa del femore, che avrebbe gravi ripercussioni sulla sua qualità della vita prossima e futura.
A seguito di una valutazione multidisciplinare, che ha visto coinvolti diversi specialisti, si è deciso di eseguire prima una paratiroidectomia con tecnica mini-invasiva in anestesia loco-regionale, per prevenire l'insorgenza di ulteriori tumori bruni in altre localizzazioni, ed in seguito verrà valutata anche la condizione ortopedica, per il possibile impianto di una protesi d'anca.
Nella letteratura scientifica internazionale i riferimenti alla diagnosi di tumore bruno secondario ad iperparatiroidismo primario effettuate con studio PET-Colina globale e poi confermate dalla RM sono molto scarsi, ed inoltre dalla nostra valutazione non risulterebbe esserci alcun precedente in letteratura in cui viene descritto con queste metodiche l'insorgere di un tumore bruno in questa localizzazione specifica, ovvero la testa del femore, a seguito della diagnosi di iperparatiroidismo primario.

EFFICACY OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (RTMS) AND TRANSCUTANEOUS AURICULAR VAGAL NERVE STIMULATION (TVNS) ON DEPRESSIVE SYMPTOMS: EVIDENCE FROM DEPONEST AND DIGEST STUDIES

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Depression is a major public health concern, particularly due to the high prevalence of treatment-resistant depression (TRD) in response to conventional pharmacotherapies. Additionally, depressive symptoms often co-occur with other psychiatric disorders, such as eating disorders, which can lead to significantly worse clinical outcomes. Dysregulation of the autonomic nervous system (ANS) and elevated levels of systemic inflammation play an important role in the pathogenesis and progression of depressive symptoms. Moreover, there is a bidirectional relationship between the ANS and the inflammatory response: sympathetic nervous system activation is associated with increased production of pro-inflammatory cytokines, whereas parasympathetic activity may exert anti-inflammatory effects and help regulate the inflammatory response. Thus, the frontal-vagal network has emerged as a promising target for the treatment of these disorders, and neuromodulation techniques have gained increasing attention, particularly repetitive transcranial magnetic stimulation (rTMS) and transcutaneous auricular vagus nerve stimulation (tVNS). The present study aims to compare the antidepressant effects of in-hospital rTMS treatment with at-home tVNS treatment in patients with mood or eating disorders and depressive symptoms. Participants were recruited from the Psychiatry Day Hospital at Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico (Milan, Italy), and were randomly assigned into two treatment groups. One group received rTMS targeting the left dorsolateral prefrontal cortex (20 sessions over four weeks), while the other group received tVNS applied to the left cymba concha (4 hours per day for four weeks). Both interventions were administered as adjuncts to standard pharmacotherapy. Depressive symptoms were assessed using the Hamilton Depression Rating Scale (HAM-D), a clinician-rated tool, and the Beck Depression Inventory-II (BDI-II), a self-report assessment. Subjective sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI). In addition, resting cardiac autonomic function was assessed through ECG-based heart rate variability analysis. A total of 18 patients completed the study. Of these, 78% presented with moderate to severe depressive symptoms. 8 patients were assigned to the rTMS group, and 10 to the tVNS group. Treatment with tVNS led to a significant reduction in clinician-rated depressive symptoms, with 80% of patients achieving a clinically meaningful treatment response (defined as a ≥5-point reduction in HAM-D 17 scores), compared to a 38% response rate in the rTMS group. Both neuromodulation techniques significantly reduced self-reported depressive symptoms; however, the effect was more pronounced in the tVNS group. Additionally, patients in the tVNS group showed a significant reduction in sleep disturbances (p = 0.017). A general reduction in resting heart rate was also observed across participants (p = 0.036), although no treatment-specific differences emerged in autonomic

measures. These preliminary findings suggest that tVNS may represent an effective adjunctive treatment for depressive symptoms, offering the added benefits of lower cost and greater convenience compared to rTMS.

A CASE OF ACUTE HYPONATRAEMIA IN INTRACRANIAL BLEEDING AND E.COLI BACTEREMIA: WHAT THE ROLE OF INFLAMMATION?

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Summary: We describe our experience with a case of SIADH not due to ectopic ADH secretion, in the context of a frontal subarachnoid hemorrage in septic patient. We rapidly obtained clinical resolution of symptoms by giving hypertonic salin solution (3%). Nevertheless, the pathogenesis of this case of acute hyponatremia is still unclear and further debate on the role of inflammation in non-ectopic ADH SIADH is needed.
Background: Syndrome of inappropriate anti-diuretic hormone (SIADH)(3) is the leading cause of hyponatraemia in hospitals, accounting for about a third of cases.(1,2) In "Classic" SIADH, the secretion of ADH is ectopic and autonomous by a tumor. Many of the other causes of SIADH are not due to ectopic ADH secretion and defy a unifying pathogenesis. Inflammation could be the common ground: inflammation-induced hypotonic hyponatremia syndromes may be caused by inappropriately induced ADH secretion by IL-6, or by appropriately induced ADH secretion in response to volume depletion caused by an inflammation-induced natriuretic protein (haptoglobin-related protein without signal peptide). This is a current hypothesis which deserves further investigation.(4).The symptoms of hyponatremia vary depending on the level of serum sodium and its rate of fall and range from subtle neurological abnomalies affecting gait to frequent falls, writing difficulty, headaches, confusion, seizures, coma, or death. In order to reduce the risk of osmotic demyelination syndrome, the European Clinical Practice Guidelines recommends bolus infusions of hypertonic saline in order to raise serum sodium by 5 mmol/L within a few hours. Tolvaptan raises serum sodium levels without the electrolyte loss seen in loop diuretics: the lowest dose of this drug approved by the European Medicines Agency for treating SIADH-related hyponatremia is 15mg.(2,4). Nevertheless, Lewellyn et al. demonstrated that also low-dose tolvaptan (3.75-7.5mg) effectively increases serum sodium in SIADH-associated hyponatremia. However, randomized controlled trials are needed to confirm optimal dosing strategies. (2)
Case presentation: A 61-year-old man with no past medical history, was admitted to our ward with the diagnosis of septic shock in Escherichia Coli (E.Coli) bacteremia in prostatitis: during the stay in ICU he underwent intubation and was treated with fluid therapy, vasoactive drugs and antibiotic therapy with cefotaxime. After estubation and rapid clinical improvements, the patient was moved to our unit. Nevertheless, due to persistent fever a Whole-body positron emission tomography (PET) was performed to detect possible hidden infection sites: the exam showed colic uptake. Infact, fever and diarrhea appeared and C.difficile infection was discovered. So antibiotic therapy with fidaxomicin was started. During the clinical observation, sudden neurological symptoms appeared: headache, nausea and vomiting; laboratory tests showed acute severe hyponatremia (117 mmol/L from 135 mmol/L in 48 hours). The patient was clinically euvolemic. A basal brain CT scan showed parietal and frontal subarachnoid hemorrage (with no story of trauma) and no evidence of active bleeding was detected at the following angioTC scan. Endocrinological evaluation hypothesized the diagnosis of acute severe hyponatremia in subarachnoid hemorrhage-related SIADH and suggested initial correction with hypertonic salin solution (3%): we observed rapid plasmatic sodium levels correction (Na 117 to 127 mmol/L in 6h). This case was initially considered eligible to low-dose tolvaptan therapy (7.5 mg die), but we decided not to start the therapy with a vasopressin antagonist, due to the augmented risk of dehydration in C.Difficile enteritis. On discharge, the patient was asymptomatic and natremia was over 130 mmoL/L.
Discussion: We considered this case of SIADH as a the result of both conditions of subarachnoid hemorrhage and infection and possibly with the same pathogenetic root: inappropriately induced ADH secretion by IL-6, or appropriately induced ADH secretion due to volume depletion caused by an inflammation-induced natriuretic protein? Further investigation is needed to better define specific pathological patterns leading to SIADH in all the clinical conditions that are not due to ectopic ADH secretion.

A CASE OF LONGLASTING VERTIGO AND "ASYMMETRIC" ATHEROSCLEROSIS

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A 70-year-old man was admitted for dizziness, abdominal pain, vomiting, and constipation.
His past medical history included poorly controlled type 2 diabetes mellitus (HbA1c 81 mmol/mol) with micro- and macrovascular complications, hypercholesterolemia partly controlled by ezetimibe 10mg /atorvastatin 20 mg/day, and stage IV chronic kidney disease. He denied smoking or other recreational habits.
The patient had been experiencing vertigo and postural instability for several years, recently worsening to the point of being unable to walk independently for more than 50 meters. A brain CT scan was negative for acute events, but showed chronic hypoxic damage in the periventricular white matter and early cortical atrophy. A venous ultrasound revealed partial superficial thrombosis in the lower third of the left great saphenous vein. Upon admission to the internal medicine ward the patient was alert, conscious, cooperative, and oriented.
Initial neurological exam showed no cranial nerve deficits, no focal sensory or motor deficits, correct finger-to-nose performance bilaterally, left eye blindness, no nystagmus, and a wide-based, cautious, ataxic gait for a few steps. A likely vascular origin of the symptoms was hypothesized. Blood pressure was measured bilaterally in both upright and supine positions, revealing a gradient of about 50 mmHg between the right and left arms, without significant changes during mobilization. Palpation of the radial pulses revealed significant asymmetry (L<R). The colour doppler ultrasound at the left vertebral artery detected reversed flow in V0-V1-V2 segments with normal peak systolic velocity. The right vertebral artery showed increased flow velocity (112 cm/s). A fibrolipidic plaque causing 70% stenosis of the left subclavian artery in the supraclavicular region, with a slow, monophasic intrastenotic flow (peak systolic velocity around 44 cm/s). The angio-CT of the brain and upper limbs confirmed the findings. We planned a surgery evaluation for Subclavian Steal Syndrome (SSS), with treatment including shockwave lithotripsy and stenting of the left subclavian artery (Eventus 8x37mm). The patient recovered uneventfully and vertigo ultimately disappeared.
Conclusions: SSS has a prevalence of about 1.9%, is frequently asymptomatic or is associated with atypical, often misleading clinical presentations often involving internal medicine clinics. The association of vertigo and asymmetric upper arm blood pressure is suggestive of SSS. Here, vertigo and postural instability were likely associated with ischemia of the labyrinthine apparatus or its brainstem connections and vertebrobasilar ischemia.
The diagnostic-therapeutic management of SSS is multidisciplinary and sequential in its nature and must rely on essential and initial careful and complete semeiological evaluation.

CHANGE IN PHYSICAL PERFORMANCE DURING HOSPITALIZATION IN INTERNAL MEDICINE, EFFECTS OF INPATIENTS REHABILITATION AND SHORT-TERM OUTCOMES

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Introduction: Patients admitted in hospital for acute non-surgical conditions are exposed to possible decline in physical performance despite optimal treatment of the acute disorder. This retrospective *real-world* observational study aims to determine the clinical associations of changes in physical performance during hospitalization, the effects of a rehab intervention in a subset of patients and the influence of change of physical performance on post-discharge hard clinical outcomes.
Methods: This retrospective observational study included patients admitted to a tertiary-level Internal Medicine Department between March 2023 and July 2024. For each patient, the change in the Short Physical Performance Battery (SPPB) score from hospital admission to discharge (ΔSPPB) was calculated and used for analysis. Patients with a clinical indication for rehabilitation received a daily, multimodal rehabilitation program during hospitalization. Data on all-cause mortality and hospital readmissions after discharge were retrospectively collected through clinical records and follow-up contacts. Associations between ΔSPPB and post-discharge outcomes were analyzed.
Results: Among the 262 hospitalized patients, 9 died during their hospital stay. Of the remaining cohort, 181 patients (mean age 67.4 ± 15.6 years; 57.5% male) had complete clinical data and SPPB assessments at both admission and discharge. The mean SPPB score at admission was 5.0 ± 3.9. Patients who underwent inpatient rehabilitation (n = 52, 28.7%) had significantly lower baseline

SPPB scores compared to those who did not receive rehabilitation (2.2 ± 2.6 vs. 6.3 ± 3.8; p < 0.001), were older (72.8 ± 12.7 vs. 65.4 ± 16.1 years; p < 0.001), and had a higher comorbidity burden (Cumulative Comorbidity Score: 7.4 ± 2.9 vs. 4.8 ± 3.0; p < 0.001). After matching for baseline SPPB and age, patients in the rehabilitation group showed a significantly greater improvement in physical performance compared to those who did not receive rehabilitation (ΔSPPB: 2.2 ± 2.3 vs. 1.2 ± 1.9; p = 0.02). During a mean follow-up period of 11.1 ± 7.3 months, 13 patients (7.2%) were readmitted to the hospital, and 30 patients (16.6%) died. A ΔSPPB above the median was significantly associated with a reduced risk of the composite outcome of all-cause mortality or hospital readmission (HR 0.41; log-rank p = 0.038).
Conclusions: In this real-world setting, inpatient rehabilitation was primarily offered to older patients with greater functional impairment and higher comorbidity burden at admission. These patients experienced significantly greater functional improvement during hospitalization compared to those who did not undergo rehabilitation. Moreover, a higher ΔSPPB was associated with a reduced risk of short-term mortality or hospital readmission. These findings highlight the prognostic relevance of in-hospital functional recovery and support the implementation of structured rehabilitation programs within Internal Medicine settings to improve patient outcomes.

RHEUMATIC FEVER: AN ATYPICAL CASE

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R. P., 34 years old, originally from SRI LANKA, was hospitalised at the Internal Medicine Unit of the AORN Sant'Anna and San Sebastiano in Caserta for a clinical-laboratory picture characterised by fever, arthralgias with prevalent functional limitation in the upper limbs and increased inflammation indices. The patient presented febrile. In the anamnesis, there was no history of pathology except for an episode of rheumatic fever in pediatric age. Blood chemistry tests showed normochromic normocytic anaemia, platelets, neutrophilic leukocytosis, significant increase in inflammation indices, with negative pro-calcitonin (entry values shown in Table 1)
Table 1
On culture tests, no signs of infection in progress; the Quantiferon test was negative; the results of the Vidal-Wright and other infectious disease tests practised were also negative. The total body CT scan, performed to exclude paraneoplastic genesis of fever, showed "... to the right kidney nuanced corti-comedullary areoles of reduced enhancement in the late phase (nephritic areas?)". The urine test showed no signs of pathology. The MRI of the spine as a whole, performed to exclude foci of spondylodiscitis, was normal. Autoimmunity was negative. An echocardiogram was therefore carried out which showed the presence of material deposit at the level of the mitral valve, suspicious of endo-carditic vegetation. Empirical antibiotic therapy was therefore undertaken, but without clinical-laboratory benefit. The patient continued to present with fever and diffuse arthralgias. Culture tests were repeated, which were negative: no microorganisms were isolated.
Given the positive history of rheumatic fever in pediatric age, the suspicion of exacerbation of rheumatic fever with endocardial involvement was raised. Therefore, steroid therapy was undertaken, with rapid resolution of fever and arthralgias, improvement of general clinical conditions, clear improvement of laboratory parameters (values in table 2) and resolution of the echocardiographic picture: in fact, echocardiographic examination was repeated, and it showed the absence of vegetations.
Table 2
The patient was discharged home with an indication to continue a low dose of steroid with subsequent tapering until suspension and antibiotic therapy with penicillin to be continued as prophylactic therapy for rheumatic fever.
The patient is currently in clinical well-being and continues outpatient follow-up.

REDUCED DOSE OF DIRECT ORAL ANTICOAGULANTS FOR EXTENDED PHASE OF VENOUS THROMBOEMBOLISM: A RETROSPECTIVE STUDY

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Introduction: The occurrence of a Venous thromboembolism (VTE) event is the result of a variety of risk factors and conditions, that differently affect the risk of a first and/or recurrent VTE. The recommended treatment of VTE consists of an initial phase of anticoagulant therapy for at least 3 months. In case of persistent risk factors and unprovoked thrombosis, extended anticoagulation should be considered. Similarly, continuing anticoagulant therapy in VTE provoked by a transient risk factor may be considered in patients with a history of previous VTE, VTE provoked by a minor transient risk factor. The availability of reduced doses of direct oral anticoagulants (DOACs) has simplified the management of patients candidate to long-term anticoagulation. However, there is still paucity of data on long-term outcomes in patients treated with reduced doses of DOACs.
To address this gap of knowledge, our study aimed to evaluate the effectiveness and safety of reduced doses of DOACs for the extended phase of VTE treatment beyond 12 months.
Methods: In this no-profit, observational, retrospective, monocenter cohort study, promoted by the Department of Clinical Internal, Anaesthesiologic and Cardiovascular Sciences of Sapienza University of Rome, consecutive adults patients from January 2020 through April 2024 were enrolled if affected by VTE requiring anticoagulant therapy with a reduced dose of DOACs for the extended phase of VTE treatment. At baseline, it was collected demographic variables, risk factor for VTE development, type and dosage of DOACs, duration of anticoagulation, concomitant therapies, and outcomes of interest. The primary effectiveness outcome included on-treatment recurrent VTE while the secondary effectiveness outcome on-treatment arterial events. The safety outcome included on-treatment major and clinically relevant non-major bleeding while the secondary safety outcome minor bleedings.
Continuous variables were expressed as mean (standard deviation) or median (interquartile range), according to data distribution after applying the Wilk-Shapiro test. Categorical variables were expressed as counts and percentages. Continuous variables were compared using the Student's t test or the Mann-Whitney U test, and categorical variables were with the chi-squared or Fisher's exact tests. The incidence of primary outcomes were expressed as patient/years with 95% confidence intervals (CI). RStudio was used for the analysis.
Results: 140 patients were consecutively enrolled. Mean age was 72±15 years and was lower in patients with a persistent risk factor than in patients with un-provoked VTE and with a minor transient risk factor. The proportions of female as well as mean BMI were similar. The proportion of patients with a previous VTE or with a family history of VTE was higher in patients with a persistent risk factor and with unprovoked VTE than in patients with a minor transient risk factor. 55% had lower extremity deep vein thrombosis, followed by pulmonary embolism. Overall, 73.6% of patients received apixaban and 14.3% rivaroxaban. Few patients received edoxaban and dabigatran, without relevant differences across subgroups of patients for type of DOACs. Mean treatment duration was higher in patients with a persistent risk factor and with an unprovoked thrombosis than in patients with a minor transient risk factor. There was one recurrent lower extremity deep vein thrombosis (0.7%) after 16 months of apixaban in a patient with thrombophilia. Four major bleedings (2.9%) occurred during follow-up: one in the gastro-intestinal (GI) tract after 15 months, one in the genitourinary (GU) tract after 23 months, one was cutaneous after 76 months, and one was an epistaxis after 24 months of therapy. All major bleedings occurred during apixaban administration. There were two clinically relevant non-major bleedings (1.4%) during follow-up: one in the GI tract after 36 months of apixaban, and no recurrent VTE or arterial event occurred during the 13 months of follow-up after anticoagulant withholding. The other occurred in the GU tract after 2 months of apixaban, anticoagulation was not withheld. Four acute ischemic strokes (2.9%) occurred after 7, 10, 53, and 56 months of anticoagulation, 3 during apixaban and one during dabigatran therapy.
Discussion: Our study including VTE patients up to 3 years follow-up shows a low incidence of recurrent VTE and major bleeding during reduced doses of DOACs. The incidence of arterial thrombotic events exceeded that of recurrent VTE. The lower incidence of recurrent VTE as well as the higher incidence of major bleedings than previously reported may suggest that the decision to extend treatment with reduced dose of DOACs should consider the actual bleeding risk of patients. A further finding is that the 2.9% of patients experienced an arterial event during follow-up. This rate highlights the need of attention to primary arterial events prevention. Among the limitations, it is a monocentre retrospective study and the low number of events did not allow any evaluation of potential risk factors for thrombotic and bleeding events.

4REVERSAL THERAPY OF ANTI-XA ORAL ANTICOAGULATS: MORE ON OF ANDEXANET ALFA VS. 4-FPCC

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Background: The clinical evidence on the use of Andexanet alfa (AA) in real-world settings remains sparse, particularly regarding its comparison with alternative reversal agents like 4-factor prothrombin complex concentrate (4F-PCC).
Aim: This study aims to evaluate the efficacy, safety, and clinical outcomes of AA versus 4F-PCC in the management of acute major bleeding events induced by apixaban or rivaroxaban.
Methods: A prospective, single-center cohort study was conducted, enrolling 95 patients (median age: 79 years; 58% male) with severe hemorrhages. Participants were treated with either AA (n=50) or 4F-PCC (n=45). Key outcomes assessed included hemostatic efficacy, 30-day mortality, permanent disability, length of hospital stay, thromboembolic events, and treatment costs. Hemostatic efficacy was defined as a ≤35% increase in hematoma volume for intracranial hemorrhage (ICH), and as a stable hemoglobin level without the need for further transfusions or invasive procedures at 48 hours for other major bleeding types.
Results: AA demonstrated superior hemostatic efficacy (84%) compared to 4F-PCC (66%; p=0.013). In cases of gastrointestinal bleeding, 100% of patients treated with AA achieved hemostasis, in contrast to 67% in the 4F-PCC group. For ICH, efficacy was 81% for AA and 60% for 4F-PCC, though the difference was not statistically significant. Neurosurgical cases in both groups achieved 100% hemostasis. Mortality during hospitalization was similar across both groups, as was the rate of permanent disability (Table 1). The median length of hospital stay was significantly longer for the AA group (13 days) compared to the 4F-PCC group (8 days). The incidence of thromboembolic events was comparable between groups (AA: 5%, 4F-PCC: 7%). However, the costs associated with AA were significantly higher.Post-treatment, 65% of patients resumed anticoagulation within a median of 5 days. The majority were discharged on low-molecular-weight heparin or direct oral anticoagulants (Table 1). Multivariable regression analysis revealed a positive correlation between hematoma expansion and neurosurgery (r = -0.30, p = 0.031), and between 30-day outcomes and hemorrhage type (r = 0.25, p = 0.017).

	AA	4F-PCC	p
Hemostatic efficacy – n (%)	42 (84%)	29 (66%)	0.013
Length of hospital stay – median [IQR]	13 [8-22]	8 [5-17]	ns
30-day venous/arterial events – n (%) VTE Arterial thrombosis 3	- 1 (2%) 1 (2%)	- 2 (4%) 1 (2%)	ns
Intra-hospital mortality – n (%)	10 (20%)	9 (20%)	ns
30-day mortality – n (%)	2 (4%)	-	-
Permanent disability – n (%)	16 (32%)	13 (29%)	ns
Costs – median [min-max] €	17600 [3520-31680]	563.2 [281.6-1689.6]	<0.0001
Day to anticoagulant restart - median [IQR]	5 [4-7]	5 [3-8]	ns
Anticoagulant drugs at discharge - n (%) DOAC LMWH prophylactic dose LMWH therapeutic or intermediate dose VKA	26 (65%) 5 (20%) 14 (53.8%) 6 (23%) 1 (3.2%)	32 (71%) 11 (34%) 16 (50%) 5 (16%) -	ns
Gastrointestinal bleeding	**AA**	**4FPCC**	
Patients - n	12	15	
Endoscopic intervention - n (%)	2 (16%)	5 (33%)	ns
Hemostatic efficacy – n (%)	12 (100%)	10 (67%)	ns
Hemostatic efficacy after endoscopy - n (%)	2 (100%)	3 (60%)	ns
Intra-hospital mortality - n (%)	1 (8.3%)	3 (20%)	ns
30-day venous/arterial events – n (%) VTE Arterial thrombosis	- 1 (8.3%)	- 1 (6.6%)	ns
ICH	**AA**	**4FPCC**	
Patients - n	32	20	
Surgical intervention - n (%)	8 (25%)	5 (25%)	ns
Hemostatic efficacy – n (%)	26 (81%)	12 (60%)	ns
Hemostatic efficacy after surgery - n (%)	8 (100%)	5 (100%)	ns
Intra-hospital mortality – n (%)	8 (25%)	6 (30%)	ns
ICH hematoma Expansion n- (%) < 35% ≥ 35%	- 27 (84%) 5 (16%)	- 12 (60%) 8 (40%)	
30-day venous/arterial events – n (%) VTE Arterial thrombosis	1 (3%) -	2 (10%) -	ns

Conclusion: Real-world data indicate that AA is more effective than 4F-PCC in achieving hemostasis. Both agents show comparable safety profiles. Notably, all patients with gastrointestinal bleeding treated with AA achieved optimal hemostasis. However, disability and mortality rates in patients with ICH remained high, despite the use of reversal agents. Additionally, neurosurgery was the only factor positively correlated with reduced hematoma expansion.

MULTIPARAMETRIC ULTRASOUND ASSESSMENT OF CHRONIC LIVER DISEASE: CORRELATING HISTOLOGICAL FEATURES WITH SHEAR-WAVE ELASTOGRAPHY, DISPERSION, ATTENUATION AND SPEED OF SOUND ON A NOVEL IMAGING PLATFORM

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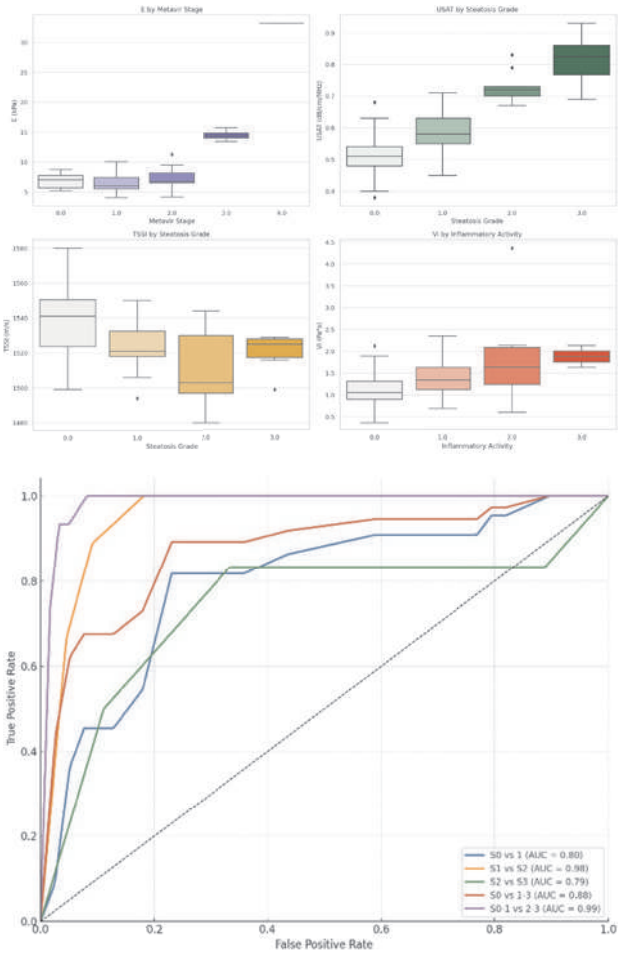
Introduction: Chronic liver disease (CLD) refers to a range of conditions from different causes leading to long-term liver damage and may progress to advanced fibrosis or cirrhosis. Multiparametric Ultrasound (MP-US) is emerging as a key tool for liver disease assessment and management, offering rapid, non-invasive insights into tissue characteristics, usually accessible only through liver histology. Steatosis and inflammation, main factors in fibrosis and cirrhosis progression, should be ideally detected and quantified early, aiding in the diagnosis and risk assessment of CLD4. MP-US combines ultrasound wave propagation techniques: Shear Wave Dispersion (SWD) evaluates frequency-dependent changes in wave velocity reflecting inflammation-related viscosity; Shear Wave Elastography (SWE) estimates liver stiffness as indirect marker of fibrosis; Attenuation Ultrasound (USAT) and speed of sound (TSSI) assess hepatic fat content measuring energy loss and sound speed.
Aims and methods: The study aimed to assess the accuracy of USAT/TSSI, SWE and SWD measured by a novel MP-US device (Resona A20, Mindray) compared to liver histology to evaluate steatosis, fibrosis and inflammation. This single-centre observational, prospective study conducted from May to November 2024 included adult patients (≥18 years) with suspected CLD, referred for MP-US evaluation and percutaneous liver biopsy. Parameters were obtained in a single session by placing a 2–3 cm diameter Region of Interest (ROI) at least 1.5 cm below the liver capsule. Five valid measurements – defined by a Motion Stability Index (M-STB) of 5 and a high reproducibility (green zone on colorimetric map) - were acquired for each technique, collecting mean, median, interquartile range (IQR), IQR/median, standard deviation (SD) and SD/mean. Histology was the reference standard for grading inflammation, fibrosis and steatosis using defined scoring systems.
Results: A total of 78 patients (46 women; mean age 51.6 years) were included: 42 with MASLD, 20 with PSVD or nonspecific cholangiopathies, 9 with AIH and 7 with PBC.USAT values increased progressively with steatosis severity, showing statistically significant differences across all stages (S0 vs S1, S1 vs S2 and S0 vs S1–3; $p < 0.001$). ROC curve analysis demonstrated high diagnostic accuracy with an AUC of 0.801 for S0 vs S1, 0.977 for S1 vs S2 and peak performance for S0–1 vs S2–3 (AUC 0.992, sensitivity 100%, specificity 95.1%). Optimal USAT cut-off values to classify mild, moderate and severe steatosis were 0.55, 0.67, and 0.75, respectively. Conversely, TSSI values decreased with increasing steatosis grade. ROC analysis revealed moderate diagnostic performance of TSSI in distinguishing S0 from S1 (AUC 0.77) and S0–1 from S2–3 (AUC 0.76). A moderate inverse correlation was observed between TSSI and USAT values ($\rho = -0.53$, $p < 0.001$). SWE values increased with fibrosis stage according to the METAVIR scoring system, demonstrating good performance in detecting advanced fibrosis ($p = 0.024$). However, most patients exhibited either no fibrosis (F0) or mild fibrosis (F1) on liver histology, limiting SWE overall diagnostic performance. Viscosity values showed a non-significant upward trend with increasing inflammation. Standard liver function tests demonstrated only a weak correlation with histological inflammation. Notably, SWD approached statistical significance in differentiating the presence of at least mild inflammation from no inflammation (A0 vs A123).
Conclusion: MP-US offers valuable non-invasive insights into liver tissue characteristics reflecting histological findings. Further studies are warranted to support the non-invasive assessment of key pathological features, potentially replacing liver biopsy.



MORE PRONOUNCED CENTRAL ADIPOSITY AND REDUCED MUSCLE MASS ASSOCIATE WITH A HIGHER DEGREE OF SYSTEMIC LOW-GRADE INFLAMMATION IN OBESITY

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Background: Systemic low-grade inflammation, commonly measured by high-sensitivity C-reactive protein (hsCRP), is a key pathophysiological component linking obesity to cardiometabolic complications. Identifying the determinants of elevated hsCRP in obese patients and evaluating its modulation through anti-obesity pharmacotherapy are essential for tailored risk stratification and management.
Methods: We analyzed data from adult patients with overweight or obesity evaluated at the Metabolic Health Outpatient Clinic of San Raffaele Hospital (Milan, Italy). Clinical, anthropometric, and body composition parameters were collected at baseline and, when available, at 3-month follow-up. HsCRP was measured centrally, and elevated values were defined as >0.3 mg/dL. Predictors of elevated hsCRP at baseline were evaluated using non-parametric tests (Mann-Whitney U for continuous variables; chi-square for categorical). In the subgroup of patients treated with semaglutide or tirzepatide and with follow-up available, baseline and 3-month hsCRP values were compared using the Wilcoxon signed-rank test.
Results: Out of 264 patients with available hsCRP at baseline, 133 (50.4%) had elevated levels. These patients had significantly higher body mass index (median 37.7, IQR 33.85–40.95 vs. 33.4, IQR 30.15–36.6; $p < 0.001$), waist circumference (110.0 cm, IQR 101.75–120.0 vs. 104.5 cm, IQR 96.0–113.0; $p < 0.001$), and fat mass percentage (42.6%, IQR 39.05–46.38 vs. 36.9%, IQR 28.95–42.08; $p < 0.001$). Conversely, fat-free mass percentage was significantly lower in the elevated hsCRP group (57.5%, IQR 53.6–61.0 vs. 61.5%, IQR 56.68–69.88; $p < 0.001$). Age also differed between groups, with individuals in the elevated hsCRP group being younger (median 51.0 years, IQR 43.0–59.0) compared to those with normal hsCRP (median 55.0 years, IQR 46.5–59.0; $p < 0.05$). No significant differences were observed in relation to sex, comorbidities (including cardiovascular disease and non-alcoholic steatohepatitis), physical activity, smoking, or sleep duration. Among the 33 patients treated with GLP-1 RAs who completed follow-up, hsCRP levels did not show a statistically significant reduction at 3 months (Wilcoxon p = 0.33). The limited sample size and short follow-up duration may have contributed to the lack of detectable change.
Conclusion: Elevated hsCRP in individuals with obesity is associated with greater adiposity and adverse body composition, particularly increased fat mass and reduced lean mass. Younger age also appears to be associated with higher systemic inflammation, warranting further investigation. In the short term, GLP-1 receptor agonist therapy does not appear to significantly reduce systemic inflammation, though further studies with larger cohorts and extended follow-up are needed. These findings support the utility of simple anthropometric and composition parameters in identifying individuals with obesity at higher inflammatory and cardiometabolic risk.

PREVALENCE, AWARENESS, AND CONTROL OF CARDIOVASCULAR RISK FACTORS AMONG SPECIALISTS IN CARDIOVASCULAR FIELD: A SURVEY

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Background: Physicians and researchers in the cardiovascular (CV) field are actively involved in promoting preventive measures based on established guidelines, but their own adherence to these recommendations has been evaluated only occasionally.
Methods: During the annual meeting of the Italian Society of Hypertension (SIIA, October 2022) and the European Society of Hypertension (ESH, June 2023), an observational study on consecutive volunteer health professionals was conducted. Participants underwent three sitting and two standing (1-3 minutes) standard blood pressure (BP) measurements and answered a questionnaire regarding demographic features, modifiable/non-modifiable CV risk factors and related treatments. Hypertension was defined as BP ≥140 and/or 90 mmHg or as a pre-existing diagnosis (with or without ongoing antihypertensive treatment). Orthostatic hypotension was defined as a decrease of systolic BP ≥20 mmHg or of diastolic BP ≥10 mmHg and orthostatic hypertension was defined as an increase of systolic BP ≥20 mmHg or of diastolic BP ≥11 mmHg during standing. The characteristics of both Italian (coming from Italy) and non-Italian (coming from 26 different countries) participants were analyzed. Based on the BP measurements obtained and the participants' self-reported information, the population was divided into normal BP, high-normal BP, newly diagnosed hypertension, controlled hypertension, and uncontrolled hypertension.
Results: In total, 191 volunteers (mean age 39.7±13.5 years; 50.3% women) were enrolled; 74.3% participants were Italian (49.3% females). Overweight/obesity (24.6%) was the most common cardiovascular risk factor, followed by sedentary lifestyle (20.4%), dyslipidemia (13.2%). Hyperuricemia and diabetes were uncommon and none of the participants with hyperuricemia were on any treatment. 74.8% of participants had normal BP values, 8.9% had high-normal BP, 8.9% had a history of hypertension and only 41.2% of them declared being on a low salt diet; 7,3% was classified as a new hypertension. Italian participants reported sedentary lifestyle more frequently than non-Italian participants (24.8% vs 8.2%, p=0.04) and only 27% of them were on a low-salt diet. Of note, Italian women were more often on a low-salt diet than non-Italian women (27% vs 10.2% p=0.016). Finally orthostatic hypertension was detected in 30% of participants, while orthostatic hypotension was found in 4.2% of participants.
Conclusions: Although these health professionals are specifically involved in CV field, an improvement in their self-awareness and management of CV risk

factors is needed, as shown by the results obtained within the examined exploratory, international sample of health professionals.

A CASE OF ANTI-HYDROXYMETHYLGLUTARYL (HMG)-COA REDUCTASE (HMGCR)-ASSOCIATED IMMUNE-MEDIATED MYOPATHY

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Le patologie infiammatorie muscolari, o miositi, sono state in passato suddivise soprattutto in relazione al loro fenotipo clinico oltre che anatomo-patologico, differenziando le forme con coinvolgimento cutaneo (dermatomiosite) e quelle che ne fossero prive (polimiosite, miosite da corpi inclusi) (Dalakas MC. *N Engl J Med*.1991;325(21):1487–98).
Da alcuni anni, invece, si è affermata una classificazione più articolata e specifica, che ha incluso l'identificazione di molti auto-anticorpi, caratteristici delle diverse forme di malattia (Lundberg I.E. et al. EULAR/ACR classification criteria. *Ann Rheum Dis*.2017;76(12):1955–64).
Tra le miopatie necrotizzanti immuno-mediate è stata identificata una forma associata ad anticorpi anti-idrossimetilglutaril (HMG)-CoA reduttasi (HMGCR), l'enzima responsabile della tappa limitante nella regolazione della sintesi del colesterolo e bersaglio dell'azione inibitoria delle statine (224th ENMC International Workshop, *Neuromuscul Disord*.2018;28:87-99). Questi farmaci possono essere associati ad una rara forma di miopatia che persiste settimane dopo la loro sospensione e che risponde a terapia immunosoppressiva (Needham M. et al. *Neuromuscul Disord*.2007;17:194-200). Alla biopsia muscolare è presente solitamente un quadro di miopatia necrotizzante, ma talora si possono trovare infiltrati cellulari infiammatori.
L'età media di presentazione è attorno ai50-60anni, la maggior parte dei casi riguarda pazienti di sesso femminile (fino ad oltre il 70%). I sintomi comprendono mialgie e/o ipostenia simmetrica dei muscoli prossimali; agli esami di laboratorio si riscontra una marcata elevazione (da10a50volte o più il valore normale) dei livelli di creatinchinasi (CK), che persiste o addirittura peggiora nonostante la sospensione del farmaco. Spesso residua nel tempo una ipostenia muscolare prossimale e talora avvengono recidive alla riduzione o sospensione dell'immunoterapia (Grable-Esposito P. et al. *Muscle Nerve*2010;41:185-90).
Sebbene si possa pensare a una associazione stretta con l'assunzione di statine, l'esposizione al farmaco si riscontra solo nel45-65% dei casi (Mammen A.L. et al. *Arthritis Rheum*2011;63:713-21; Allenbach Y. et al. *Medicine (Baltimore)*2014;93:150-7). Tra le varie statine, atorvastatina sembra essere quella più strettamente associata allo sviluppo di miopatia anti-HMGCR (Basharat P. et al. *J Am Coll Cardiol*2016;68:234-5).
I corticosteroidi rappresentano la terapia iniziale di prima linea, talora in associazione ad un secondo agente immunosoppressore (azatioprina o metotrexate). In caso di intolleranza o controindicazione alla terapia steroidea, oppure in assenza di risposta, si può ricorrere alla infusione endovenosa di immunoglobuline.
Il caso che presentiamo riguarda una paziente di 73 anni che arrivava alla nostra osservazione per difficoltà alla mobilizzazione in algie diffuse (in particolare a livello prossimale degli arti inferiori) da circa 3 settimane, accompagnate successivamente dalla comparsa di edemi declivi ingravescenti. In anamnesi la paziente presentava ipertensione arteriosa, diabete mellito e dislipidemia in terapia da tempo con ezetimibe/atorvastatina a dosaggio recentemente incrementato a 10/40 mg die.
Agli esami ematochimici di ingresso veniva riscontrata una elevazione delle transaminasi (AST 253 U/L, ALT 272 U/L) e della CK (6020 U/L). Si provvedeva a sospensione della terapia con statina, a infusione di idratazione endovenosa associata a terapia diuretica; ciononostante i valori di CK permanevano elevati e la sintomatologia stentava a migliorare. Venivano dunque eseguiti esami di approfondimento: l'elettromiografia mostrava un quadro di polineuropatia mista assonale sensitivo-motoria (facilmente associabile al diabete), mentre una risonanza magnetica di coscia confermava la presenza di miosite. Veniva inoltre eseguito uno screening autoimmune, compresa la ricerca di anticorpi anti-HMGCR (risultati positivi).
Nel sospetto di miopatia immuno-mediata HMGCR-associata, veniva avviata terapia steroidea a boli endovenosi ripetuti a dosaggio di 1 mg/Kg/die, seguiti da prednisone orale di mantenimento, assistendo a un parziale miglioramento clinico-laboratoristico con riduzione dei valori di CK (inferiori a 2000 U/L). Si provvedeva quindi alla dimissione a domicilio della paziente, proseguendo un follow-up ambulatoriale.
A distanza di un mese circa, si assisteva a nuova risalita dei livelli ematici di CK, oltre che a permanenza di ipostenia agli arti inferiori seppur ridotta rispetto alla presentazione iniziale. In seguito a condivisione del caso con il centro regionale di riferimento delle malattie muscolari, si avviava terapia con immunoglobuline in infusione endovenosa con beneficio, proseguendo terapia steroidea a scalare.
In conclusione, si è trattato di un caso di non facile inquadramento iniziale e gestione terapeutica, con necessità di esami di approfondimento per poterne definire la genesi come immuno-mediata, oltre che di prolungato monitoraggio, ricorso a confronto con centro di riferimento e avvio di terapie di secondo livello.

PROGNOSTIC IMPACT OF PERIPHERAL ARTERY DISEASE IN HEART FAILURE WITH PRESERVED EJECTION FRACTION

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Background: Heart failure with preserved ejection fraction (HFpEF) is a growing public health burden, particularly in Western countries and in the elderly population. Recent epidemiological data suggest that HFpEF accounts for more than 50% of all HF cases, with a high hospital readmission rate. It is a complex clinical syndrome characterized by preserved left ventricular systolic function and impaired diastolic relaxation, often occurring in older patients and those with multiple comorbidities.
Despite advances in diagnosis and treatment, the prognosis for HFpEF remains poor and heterogeneous. Recent studies have shown that the mode of death in patients with HFpEF is significantly affected by the presence and severity of comorbidities such as chronic kidney disease, diabetes, and peripheral artery disease (PAD).
Peripheral artery disease (PAD), a manifestation of systemic atherosclerosis, is frequently underdiagnosed in HFpEF patients, which may contribute to adverse outcomes through mechanisms such as impaired microvascular function, endothelial dysfunction, and systemic inflammation. Latest studies have highlighted that PAD is associated with increased risk of cardiovascular events and all-cause mortality in different HF populations. However, its prognostic role in patients with HFpEF, particularly those hospitalized for acute decompensation, remains poorly defined.
This study aimed to investigate the prognostic impact of PAD in a cohort of patients with HFpEF hospitalized for acute heart failure (AHF).
Materials and methods: A single-centre, retrospective study included patients hospitalized over a 4-year period for AHF, defined as the rapid onset and worsening of signs and symptoms of HF. PAD was defined by a documented history of intermittent claudication, previous revascularization, or imaging diagnosis. Demographic, clinical, and laboratory data were collected.
Primary outcome was all-cause, in-hospital mortality.
Results: Overall, 398 patients were included (median age 83 years, 56.0% female). Patients were divided into two categories, those affected by PAD and those free. At univariate analysis PAD prevalence was higher in the deceased patients than surviving ones (32.4% vs 12.4%, p=0.004). Moreover, at multivariate analysis PAD emerged as a strongly independent risk factor for adverse outcomes (HR 4.95 [1.59 – 15.39], p=0.006).
Conclusion: Among patients with HFpEF hospitalized for AHF, PAD was independently associated with an almost 5-fold increased death risk. These findings highlight the importance of recognizing PAD as a high-risk comorbidity in the HFpEF population.
Therefore, early identification and integrated management of PAD in this setting may improve long-term outcomes.

HAEMOLYTIC REACTION TO UPADACITINIB IN A PATIENT WITH GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY

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Introduction: Inflammatory bowel diseases (IBD) are chronic, debilitating conditions that considerably impair quality of life of these patients.
The recent introduction of novel therapies, such as Janus kinase (JAK) inhibitors, has substantially broadened the avaible therapeutic landscape for the management of these diseases. However, small molecules may lead to drug-drug interactions and post-marketing adverse events reporting remains essential to identify rare events and thus to optimize the use of this drug category.
Case presentation: A 65-year-old male patient with Crohn's disease (CD) of the terminal ileum, diagnosed 5 years prior, was admitted to our clinical unit due to jaundice and anaemia three days after initiating Upadacitinib (UPA) 45 mg/day.

His past medical history included hypertension. His family history was negative for cardiovascolar events and malignancies, but positive for glucose-6-phosphate-dehydrogenase (G6PD) deficiency.
After diagnosis, therapies with azathioprine and, then, with Adalimumab were administered, but, in 2021, a CT-scan showed a stenosis of the terminal ileum, necessitating ileocecal resective surgery.
After surgery, treatments with Infliximab, Ustekinumab, Vedolizumab and Risankizumab failed or were stopped due to adverse events.
In June 2024, Upadacitinib 45 mg/die was commenced. After only three days, onset of jaundice occurred and he was admitted to our department.
At admission, blood tests showed: total bilirubin 21.5 mg/dl, indirect bilirubin 20.53 mg/dl, haemoglobin (Hb) 7.7 g/dl, negative direct and indirect Coombs test, G6PD level 1.3 U/g Hb (reference range: 10.10-14.19 IU/g Hb).
Considering these results, this acute hemolytic episode was attributed to G6PD deficiency. No dietary/other pharmacologic triggers were identified. Suspecting an adverse drug reaction, Upadacitinib therapy was immediately discontinued.
During hospitalization, an improvement of bilirubin levels was observed (total bilirubin at discharge: 2.67 mg/dl; indirect bilirubin 1.65 mg/dl). The patient refused a re-challenge with Upadacitinib.
In October 2024, off-label therapy with Golimumab was started, resulting in progressive clinical improvement. No further adverse drug reactions were observed.
Discussion: According to the Naranjo algorithm this event was classified as probably related to Upadacitinib.
Although genotype analysis was not performed, the patient's origin suggests the possibility of a Mediterranean variant of G6PD deficiency. According to the new World Health Organization (WHO) classification, this event was categorized as class B. To date, no data of hemolytic crisis in G6PD-deficient patients treated with Janus kinase (JAK) inhibitors have been reported in literature.
Up to now, five reports on hemolysis are reported in the Eudravigilance register but without mention on G6PD deficiency.
Despite upadacitinib is a more selective inhibitor of JAK1, due to the cooperative nature of JAKs, it may exert off-target inhibitions on other JAK isoforms' pathways.
Recently it has been demonstrated that G6PD is a novel phosphorylation substrate of JAK2. IL-6 stimulation has been reported to induce G6PD expression through the JAK2/STAT3 signaling pathway. Conversely, inhibition of JAK2 resulted in a significant decrease in G6PD activity.
In conclusion, it is conceivable that upadacitinib triggered a haemolytic crisis in G6PD deficiency, warranting careful investigation and clinical observation in these patients.

PLATELET ACTIVATION AND NOX2-MEDIATED OXIDATIVE STRESS IN PATIENTS WITH MECHANICAL PROSTHETIC HEART VALVES (MPHVS)

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Aims: Mechanical prosthetic heart valves (MPHVs) carry a thrombotic risk, higher for mitral than for aortic ones. The pathophysiological mechanism for this difference is unkwnown. Our hypothesis was that platelet activation and oxidative stress may be involved.
Materials and methods: 60 MPHV patients (30 mitral and 30 aortic), referring to the Atherothrombosis Centre of Policlinico Umberto I, Rome, were included. All the subjects signed an informed written consent for the study. During the visit medical history was collected, and blood samples were taken to evaluate platelet activation (through CD40L and thromboxane - TXB2), and NADPH oxidase type 2 (NOX2) activation, an enzyme involved in oxidative stress and promoter of platelet activation.
Results: Table 1 reports population's characteristics. Groups were comparable for age, sex, and main cardiovascular risk factors. Patients with mitral MPHVs showed higher levels of platelet activation, according to TXB2 (251.00 vs 146 pg/mL, p<0.001) and CD40L (6.00 vs 4.00 ng/mL, p=0.012) (Fig. 1). Moreover, NOX2 activity was increased in patients with mitral MPHVs, as shown by serum levels of sNOX2-dp (29 vs 24 pg/mL, p=0.001) and H2O2 (23 vs 17 µM, p=0.011) (Fig.2).
Discussion: and conclusion: patients with mitral MPHVs show higher levels of platelet activation and oxidative stress than patients with aortic MPHVs. More data are needed for further therapeutic implications.
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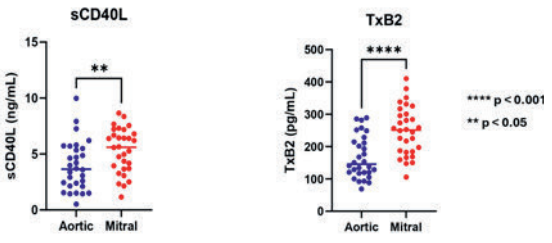
	Aortic (N=30)	Mitral (N=30)	P
Age [IQR]	54.5 [47.0-61.1]	58.4 [51.5-67.0]	0.197
Female sex (%)	14 (46.7)	18 (60.0)	0.301
Caucasian (%)	28 (93.3)	26 (86.7)	0.389
Hypertension (%)	18 (60.0)	16 (53.3)	0.602
Diabetes (%)	7 (23.3)	3 (10.0)	0.166
Previous stroke/TIA (%)	2 (6.7)	3 (10.0)	0.640
PAD (%)	1 (3.3)	4 (13.3)	0.161
Previous MI (%)	2 (6.7)	2 (6.7)	1
Smoke (%)	3 (14.3)	4 (16.7)	0.826
Alcool (%)	7 (31.8)	7 (31.8)	0.827
Dyslipidaemia (%)	11 (36.7)	11 (36.7)	1
Heart failure (%)	6 (20)	4 (13.3)	0.488
LLA (%)	8 (33.3)	10 (41.7)	0.551
ACE-I/ARBs (%)	8 (33.3)	16 (64)	0.032
Beta-blockers (%)	16 (66.7)	13 (52.0)	0.296
CCB (%)	3 (12.5)	3 (12.5)	0.957
Antiarrhytmics (%)	2 (8.3)	10 (40.0)	0.010
Diuretics (%)	9 (37.5)	14 (56.0)	0.195

Table 1: population characteristics.
Abbreviations: ACE-I, Angiotensin-Converting Enzyme Inhibitors (ACEI); ARBs, angiotensin receptor blockers; CCB, calcium channel blockers; IQR, interquartile range; LLA, lowering lipids agents; MI, myocardial infarction; PAD, peripheral artery disease; TIA, transient ischemic attack.

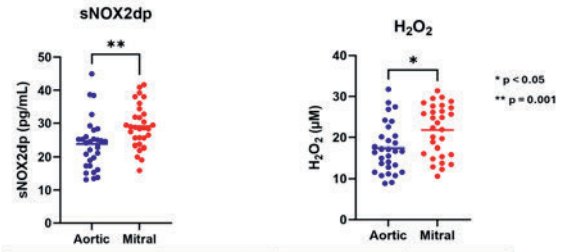
Figure 1: platelet activation in aortic and mitral MPHVs



	Aortic (N=30)	Mitral (N=30)	p
TXB2 (pg/mL) [IQR]	146.00 [119.25-218.25]	251.00 [184.25-305.00]	0.000
sCD40L (ng/mL) [IQR]	4.00 [2.00-5.25]	6.00 [4.00-7.00]	0.012

Abbreviations: IQR, interquartile range.

Figure 2: NOX2-mediated oxidative stress



	Aortic (N=30)	Mitral (N=30)	p
sNOX2dp (pg/mL) [IQR]	24.00 [17.00-26.50]	29.00 [25.50-33.25]	0.001
H_2O_2 (µM) [IQR]	17.00 [12.75-20.75]	23.00 [15.75-27.25]	0.011

Abbreviations: IQR, interquartile range.

TWO PECULIAR CLINICAL CASES OF PARANEOPLASTIC THROMBOPHILIA AND NBTE

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Background: Cancer is frequently associated with a hypercoagulable state, due to malignancy-related procoagulant factors and the host's inflammatory response. Up to 20% of oncologic patients develop clinically evident thrombosis. Paraneoplastic thrombophilia may manifest as venous thromboembolism, superficial thrombophlebitis, arterial thrombosis, disseminated intravascular coagulation (DIC), thrombotic microangiopathy, and non-bacterial thrombotic endocarditis (NBTE). The latter is rare and underrecognized, characterized by sterile valvular vegetations, typically affecting previously healthy valves. NBTE is often misdiagnosed or undiagnosed, with a post-mortem incidence of 0.9–1.6% in adults. We report two cases managed in our Internal Medicine department (San Raffaele Hospital, February 2025).
Case1 A 63-year-old man, presented with fever, three weeks of lower back pain, and limb hypesthesia. His medical history was notable for alcohol use disorder. Physical examination was unremarkable. Labs showed severe acute kidney injury and high inflammatory markers. Total-body CT revealed bilateral hydronephrosis, a wedge-shaped left kidney lesion, multiple lymphadenopathies, and bone lesions. Ureteral stenting improved renal function. Fever persisted despite broad-spectrum antibiotics and negative cultures. TEE revealed aortic valve vegetation. Brain MRI showed cortical-subcortical and cerebellar lesions (embolic or metastatic). PET-CT showed pathological uptake in lymph-nodes, thyroid, adrenals, and bones. Fine-needle aspiration of a cervical node revealed adenocarcinoma of unknown origin. The sterile vegetation, embolic events, and lack of response to antibiotics indicated NBTE. Awaiting cytology, the patient developed multiple brain infarcts with worsening neurological status despite anticoagulation. He became unfit for cancer treatment and was transitioned to comfort care. He died shortly after.
Case2 A67-year-old woman with a history of breast cancer (three years before), buccal squamous cell carcinoma (twenty years before), and pharyngeal carcinoma (treated one year before presenting to our hospital), underwent follow-up PET-CT. No active malignancy was detected, but a right ventricular thrombus, jugular vein thrombosis, and peripheral ground-glass lung opacities were found. Cardiac CT confirmed an apical intraventricular thrombus and a small filament on the aortic valve. Anticoagulation was initiated. She then had an ischemic stroke with right hemiplegia and dysarthria. Fever and respiratory failure followed, unresponsive to antibiotics. Bronchoalveolar lavage fluid cultures grew MDR P. *aeruginosa* and S. *maltophilia*. Blood cultures remained negative. Repeated chest CT was again negative for malignancy, but showed worsening lung lesions, biopsy was not feasible due to their location, but they wer emostly infrctual in aspect. Despite multidisciplinary discussion, invasive procedures for thrombus and valvular vegetation removal was excluded due to intraoperatory risk. She developed recurrent strokes and embolisms despite anticoagulation. Palliative care was started. Post-mortem examination showed widespread metastases, including a large cardiac mass and probable meningeal micrometastases. Final histology is pending.
Discussion: We presented two cases of paraneoplastic thrombotic syndromes (NBTE and intracardiac/jugular thromboses) with severe embolic complications involving CNS and lungs. In both, thrombotic events were the first cancer sign—preceding even imaging in the second case. Rapid decline prevented targeted treatment despite early suspicion and work-up. Awareness of cancer-associated thrombophilia, especially rare forms, is essential. Management requires early recognition, anticoagulation, and cancer screening. NBTE should be suspected in case of embolic events, negative cultures, and oncologic risk. If missed, it may progress to DIC and death. NBTE led to cancer diagnosis in 66.4% of reported cases, mostly in advanced stages. Stroke is the most frequent presentation. Table 1 compares the incidence of paraneoplastic thrombophilia manifestations. The above cases represent some of the rarest and most difficult-to-diagnose forms of paraneoplastic thrombophilia, often confirmed only post-mortem. Echocardiographic screening may be useful in high-risk cancer patients, especially with lung or pancreatic adenocarcinoma. Internists play a pivotal role in the management of patients with cancer and NBTE coordinating care, supporting the patient, and guiding end-of-life decisions.

ATYPICAL HAEMOLYTIC URAEMIC SYNDROME: A CASE ASSOCIATED WITH ACUTE POLYNEUROPATHY TREATED WITH PLASMA-EXCHANGE

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La Sindrome Emolitico Uremica (SEU) è caratterizzata dalla presenza in contemporanea di trombocitopenia, anemia emolitica microangiopatica e insufficienza renale acuta. Si parla genericamente di SEU atipica (SEUa) in assenza di correlazione con un batterio produttore di tossina Shiga (Thompson G.L., Kavanagh D., *Int J Lab Hematol.*2022;44, Suppl.1:101-113). Si tratta di una forma rara che può insorgere a qualsiasi età, solitamente in seguito a un evento scatenante (ad esempio un'infezione delle vie respiratorie o gastrointestinale). Il coinvolgimento del sistema nervoso centrale avviene in circa il20-50% dei casi di SEU, interessando tipicamente pazienti pediatrici e manifestandosi con crisi comiziali, alterato stato di coscienza e sintomi da danno a livello del tronco encefalico (Moustafa A.M. et al., *Radiol Case Reports*2023;18,2268-73). L'interessamento del sistema nervoso periferico, invece, avviene molto raramente e in letteratura ne sono stati descritti solo alcuni casi (Santangelo L. et al., *Ital J Pediatr.*2021;47:181). Il trattamento della SEUa in generale, così come in caso di coinvolgimento neurologico, consiste nel ricorso alla plasmaferesi e, più recentemente, nell'utilizzo di anticorpi monoclonali inibenti l'attivazione del complemento (eculizumab). Presentiamo un caso di un paziente di 28 anni, originario della Costa d'Avorio, precedentemente in buona salute, che accedeva in pronto soccorso per inappetenza, vomito e dolore addominale da alcuni giorni, seguiti da macroematuria e successivamente anuria. Agli esami ematochimici di ingresso risultava una grave insufficienza renale acuta (creatinina 9.9 mg/dl) con acidosi metabolica, severa piastrinopenia (16000/mcL), elevazione degli indici di citolisi (lattato-deidrogenasi – LDH – 865 mU/mL, creatinkinasi – CK – 1337 U/L), marcata leucocitosi neutrofila con netto rialzo degli indici di flogosi (proteina C reattiva 169 mg/L, procalcitonina 114 ng/mL). Gli accertamenti radiologici (radiografia del torace, TC addome) non evidenziavano lesioni acute in atto ad eccezione di diffuse raccolte fluide endoaddominali.
Per rapido peggioramento emodinamico, il paziente veniva ricoverato in Terapia Intensiva, sottoposto a intubazione orotracheale e avvio di ventilazione invasiva. Veniva inoltre praticato supporto volemico e vasopressorio, antibioticoterapia empirica con piperacillina/tazobactam e trasfusione di piastrine.
Gli esami colturali (emocolture, urocoltura, coprocoltura) e la ricerca di ceppo produttore di tossina Shiga risultavano negativi, così come la sierologia per i virus dell'epatite B e C e dell'immunodeficienza umana. Il dosaggio del complemento (C3 e C4) era nella norma e lo screening per autoimmunità non era dirimente. Veniva confermata la positività degli indici di emolisi (iperbilirubinemia indiretta, aptoglobina consumata) con comparsa di anemizzazione, in assenza di sanguinamenti. Il dosaggio della attività di ADAMTS13 risultava di norma, escludendo una forma di porpora trombotica trombocitopenica; nel sospetto, comunque, di microangiopatia trombotica veniva avviata terapia steroidea (metilprednisolone 1 mg/kg/die).
Si assisteva ad un progressivo miglioramento clinico-laboratoristico con mantenimento di diuresi valida senza necessità dialitiche, iniziale risalita dei valori piastrinici, stabilizzazione emodinamica e respiratoria con possibilità di trasferimento in reparto di Medicina Interna. Permaneva, tuttavia, un'alterazione del quadro neurologico: inizialmente il paziente presentava clonie e agitazione psicomotoria con alterato stato di coscienza, successivamente predominavano marcata ipostenia agli arti, disartria e un quadro di disfagia totale. Venivano quindi eseguiti approfondimenti neurologici che concludevano per un iniziale mioclono a genesi non comiziale (all'elettroencefalogramma segni di sofferenza cerebrale diffusa; alla risonanza magnetica dell'encefalo dubbie lesioni a livello centro-pontino e al passaggio bulbo-midollare di significato incerto), seguito da una forma di polineuropatia acuta (deficit sensitivo-motorio misto all'elet-

tromiografia, dissociazione proteico-citologica all'esame del liquor). Si procedeva pertanto ad avvio di plasmaferesi (5 sedute in totale), con progressivo miglioramento stenico e funzionale globale, oltre che a livello foniatrico-logopedico. Parallelamente si assisteva a completa normalizzazione dei valori di funzionalità renale (creatinina 0.85 mg/dl) e dell'emocromo (piastrine 173000/mcL).
In conclusione, si tratta di un caso complesso, a gestione multidisciplinare (con colleghi rianimatori, nefrologi, ematologi, neurologi), con evoluzione favorevole, a partire però da una grave presentazione di esordio con multiplo danno d'organo (insufficienza renale acuta, anemia emolitica, piastrinopenia, severa insufficienza respiratoria, danno neurologico), probabilmente scatenata da un fatto infettivo gastrointestinale, in assenza però del tipico riscontro di ceppo batterico produttore di tossina Shiga.

EFFECT OF ANTITHROMBOTIC PROPHILAXIS, ANTICOAGULATION, ANTIPLATLET THERAPY AND CENTRAL TIP ON CATHETER-RELATED THROMBOSIS

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Background: Catheter-related thrombosis (CRT) is the most common non-infectious complication associated with midline and peripherally inserted central catheters (PICC). The development of CRT is influenced by factors related to the catheter's design and the insertion process, as well as patient-specific factors. Line-related factors, such as the choice of venous approach, catheter material, and diameter, are crucial for minimizing thrombotic risk. Patient-related factors include hypercoagulable conditions (e.g., malignancy, sepsis, critical illness, renal failure, prior venous thromboembolism) and the administration of drugs requiring a central line. The literature presents conflicting evidence regarding the protective effect of anticoagulation therapy and prophylaxis in reducing CRT. While some studies report a significant benefit, others have found no statistically significant reduction in CRT risk.
Objectives: This retrospective study compared the incidence of thrombotic complications between patients receiving antithrombotic prophylaxis or anticoagulant therapy and those not undergoing such treatment. The secondary objective was to evaluate the influence of antiplatelet therapy, catheter tip position, number of lumens, additional CRT risk factors, and the infusion of drugs requiring a central catheter on the development of CRT.
Materials and methods: We retrospectively enrolled patients aged over 18 years who received a PICC or midline catheter during their clinical care at Luigi Sacco Hospital in Milan between May 1, 2021, and March 31, 2023. Patients were stratified into three groups: no antithrombotic therapy (group 0), prophylaxis (group 1), or anticoagulation (group 2). We applied inverse probability propensity score weighting to address potential confounders inherent in this retrospective design. Six confounders were considered: type of anticoagulation (none, prophylaxis, or full anticoagulant therapy), antiplatelet use, catheter tip position (central vs. peripheral), number of lumens (one vs. two), presence of CRT risk factors, and the use of drugs requiring central catheter administration. A logistic regression model was employed to evaluate the predictive value of these confounders on CRT occurrence. The average treatment effect (ATE) was calculated, and odds ratios (ORs) with 95% confidence intervals (CIs) were reported. Statistical analyses were conducted using R version 4.0.0 (2020-04-24).
Results: 1,431 patients were analyzed: 309 in Group 0, 777 in Group 1, and 345 in Group 2. The incidence of CRT was 3.9% in Group 0, 1.7% in Group 1, and 0% in Group 2. After applying propensity score weighting, thromboprophylaxis was associated with a significant reduction in CRT risk ($p < 0.001$; OR 0.217, 95% CI 0.142–0.315), while full anticoagulation offered an even more substantial risk reduction (OR 0.108, 95% CI 0.070–0.157). Similarly, antiplatelet therapy ($p < 0.001$; OR 0.342, 95% CI 0.182–0.595) and proper central catheter tip positioning ($p < 0.001$; OR 0.068, 95% CI 0.013–0.200) were found to be strongly protective. In contrast, the number of lumens, traditional CRT risk factors, and the infusion of drugs requiring central access did not significantly correlate with CRT development.
Conclusions: Our study results indicate that antithrombotic prophylaxis, anticoagulation therapy, antiplatelet therapy, and central catheter tip positioning significantly reduce the incidence of catheter-related thrombosis (CRT). In particular, patients receiving full anticoagulation demonstrate a risk reduction comparable to that achieved through proper central tip positioning. This supports the hypothesis that, in the presence of anticoagulation, midline catheters may serve as a viable alternative to PICCs, with potential benefits in terms of cost savings and a reduced need for placement verification.

432. EFFECTIVENESS AND SAFETY OF SECUKINUMAB IN GIANT CELL ARTERITIS PATIENTS AFTER TOCILIZUMAB FAILURE.

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Background: Treating giant cell arteritis (GCA) can be quite a challenge. The interleukin (IL)-6 receptor inhibitor tocilizumab (TCZ) is a highly effective drug for this disease but a subgroup of GCA patients experiences suboptimal response to this treatment. The IL-17A antagonist secukinumab (SEC), in a recent phase II trial, has shown promising effect in effectively induce and maintain sustained remission in GCA [2], and a corresponding phase III trial is currently underway. Notably in both trials GCA patients who did not respond to TCZ were excluded leaving a significant gap in understanding the positioning of SEC in this population.
Objectives: The aim of our retrospective multicentre study was to assess, in a real-world setting, the effectiveness and safety of SEC in GCA patients with an inadequate response to TCZ.
Methods: We included consecutive patients who met the 2022 ACR/EULAR classification criteria for GCA and were treated with SEC for ≥ 6 months following an inadequate response to TCZ. Failure to TCZ was defined as recurrence of GCA-related clinical signs, symptoms or imaging findings. Demographic, clinical, biological, pathological, and radiological aspects were anonimously collected. SEC effectiveness was assessed at 6 months. Clinical symptoms were categorised into four groups: cranial (including headache, scalp tenderness, jaw claudication), cranial ischaemic (permanent vision loss, stroke), constitutional (fever, weight loss), polymyalgic (girdles stiffness, peripheral arthritis).
Results: Six patients with GCA were included, all patients were female, with a median age of 72 years (interquartile range [IQR], 67-73) at diagnosis. At disease onset, all patients had cranial symptoms, 4 had constitutional symptoms, and two had polymyalgic symptoms; no patient experienced ischaemic complications. Diagnosis was confirmed by vascular ultrasound (US) in three patients and by 18-fluorodeoxyglucose positron emission tomography (FDG-PET) in the remaining three patients; in one patient, a temporal artery biopsy revealed signs of active vasculitis.
In four patients (75%) TCZ was started within 2 months from the diagnosis, due to glucocorticoid (GC)-related side effects, while the remaining two patients (25%) began TCZ after 13 and 18 months due to disease flares. TCZ-related complications included mild neutropenia (2 cases), hypercholesterolemia (1 case), and intestinal infarction (1 case).
TCZ failure occurred after a median of 14 months (IQR, 11–22), in five patients we observed the recurrence of constitutional symptoms (with one also presenting cranial symptoms) while the remained patient experienced polymyalgic symptoms. Disease activity was confirmed by vascular imaging in four cases (temporal and axillary US in 1 case; FDG-PET in 3 cases).
In all cases, SEC replaced TCZ without a washout phase and was accompanied by an increased dose of glucocorticoids. All six patients underwent an induction phase of weekly subcutaneous SEC 300 mg up to week 4, followed by maintenance dosing of 300 mg every four weeks. After 6 months, all patients achieved clinical and laboratory (i.e., no increase of acute phase reactants) remission. Three patients discontinued GC within 4 months from SEC initiation and 3 patients continued low-dose prednisone. None of the patients experienced adverse reactions during the treatment.
Conclusions: This is the first study to evaluate the potential role of SEC for GCA patients who failed TCZ therapy. Further studies in larger cohorts are required to confirm these data.

CLINICAL, ANTHROPOMETRIC PROFILE, AND CARDIOVASCULAR RISK STRATIFICATION IN OVERWEIGHT OR OBESE ADULTS ATTENDING THE CENTRE OF EXCELLENCE FOR METABOLIC HEALTH: PRELIMINARY DATA

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Background / Aims: With a projected prevalence of 13% by 2030, obesity is expected to account for 8% of the total healthcare burden in Italy. This study aims to investigate the healthcare burden and distribution of metabolic risk factors within a patient population addressing to a Multidisciplinary Outpatient Clinic for Overweight and Obesity at our hospital.
Materials And Methods: Medical history, anthropometric and laboratory data were collected. Risk assessment was performed using the ESC SCORE2 algorithm. Data are expressed as median inter-quartile range (IQR).A regression tree analysis (CART) was performed to identify risk predictors of a composite outcome, defined by the presence of at least two of the following: glucometabolic alterations (IFG, Impaired fasting glucose and/or HBA1C in prediabetic range), hypo-HDL, hypertriglyceridemia, uncontrolled blood pressure, non-alcoholic fatty liver disease (NAFLD) or obstructive sleep apneas (OSAS).
Results: Of the160 patients studied, the median age was 54 (46.3,61.2) years, 79.4% were women and median Body Mass Index (BMI) was 34.0 (31.4,39.2) kg/m2. Principal comorbidities included hypertension (44.6%), dyslipidemia (43.7%), NAFLD (35.4%) and OSAS (17.2%). IFG was present in 28.8% of patients, prediabetes in 47%, LDL cholesterol over target in 71.6%, hypo-HDL in 77% and hypertriglyceridemia in 30.5%, with no significant differences in distribution across obesity classes.The CART model identified a waist- to-height ratio of over 0.62 and macrosomia as the main predictors of the composite outcome. According to SCORE2, 31 (21.4%) patients had a low 10-years cardiovascular (CVD) risk. Notably, 25.8% of these patients met the criteria for our composite outcome.
Discussion and Conclusion: Our preliminary data suggest a high prevalence of cardiometabolic risk factors even in lower BMI categories, highlighting a need for early screening and intervention. SCORE2 may underestimate risk in overweight and obese populations.
Keywords: Obesity; Metabolism; Risk

VISCERAL LEISHMANIASIS COMPLICATED BY SEVERE PANCYTOPENIA AND DISSEMINATED INTRAVASCULAR COAGULATION: A DIAGNOSTIC CHALLENGE

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Background: Visceral leishmaniasis (VL), caused by protozoa of the genus *Leishmania*, is the most severe systemic form of leishmaniasis. It is characterized by irregular fever, pancytopenia, hepatosplenomegaly, and polyclonal hypergammaglobulinemia. Diagnosis is often delayed in non-endemic countries due to low specificity of clinical manifestations and low incidence.
Case presentation: We report the case of a 68-year-old man with a history of statin-induced necrotizing myositis, undergoing immunomodulatory treatment with methotrexate, admitted for intermittent fever up to 40 °C and worsening asthenia. Initial examinations revealed hepatosplenomegaly, diffuse lymphadenopathy, polyclonal hypergammaglobulinemia, and severe pancytopenia. Despite broad-spectrum empirical antibiotic therapy, clinical deterioration ensued, necessitating transfusions and showing progressive signs of disseminated intravascular coagulation (DIC), notably elevated D-dimer and fibrinogen consumption. The onset of thrombo-hemorrhagic events was prevented through prophylactic treatment with plasminogen.
The clinical picture necessitated early differential diagnosis between a lymphoproliferative disorder and a systemic infectious disease. Among these, suspicion of visceral leishmaniasis, raised early based on the suggestive clinical-laboratory findings and subsequently reinforced by serological positivity, was definitively confirmed through direct identification of amastigotes in bone marrow smear and axillary lymph node fine-needle aspiration biopsy, thus resolving the diagnostic uncertainty.
The patient promptly commenced specific treatment with liposomal amphotericin B, leading to rapid resolution of fever, improvement in asthenia, and progressive recovery of bone marrow function. The therapy initially caused a deterioration in renal function, which spontaneously resolved after discontinuation of the drug.
During hospitalization, reactivation of Epstein-Barr Virus (EBV) was also detected, interpreted as an epiphenomenon of the marked immunosuppression secondary to VL.
Conclusions: This case highlights the diagnostic complexity of visceral leishmaniasis in non-endemic areas.
In the presence of a typical clinical-laboratory profile, early suspicion is crucial to avoid potentially fatal complications such as DIC. The effectiveness of treatment with liposomal amphotericin B confirms the importance of including VL in the differential diagnosis of prolonged fevers with pancytopenia and organomegaly, especially in immunocompromised individuals, even in low-incidence settings.

DEVELOPMENT AND VALIDATION OF AN INTERPRETABLE MACHINE LEARNING-BASED CALCULATOR FOR PREDICTING 5-YEAR WEIGHT TRAJECTORIES AFTER BARIATRIC SURGERY: A MULTINATIONAL RETROSPECTIVE COHORT SOPHIA STUDY

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Predicting weight loss before bariatric surgery is difficult because of the individual variability in the change of weight. We try to develop a machine for predicting 5 year weight loss trajectory after bariatric surgery. In the study we enrolled adults (aged ≥18 years) from ten prospective cohorts (including ABOS [NCT01129297], BAREVAL [NCT02310178], the Swedish Obese Subjects study, and a large cohort from the Dutch Obesity Clinic [Nederlandse Obesitas Kliniek]) and two randomised trials (SleevePass [NCT00793143] and SM-BOSS [NCT00356213]) in Europe, the Americas, and Asia, with a 5 year follow-up after Roux-en-Y gastric bypass, sleeve gastrectomy, or gastric band. We excluded patients with a previous history of bariatric surgery or large delays between scheduled and actual visits. The training cohort comprised patients from two centres in France (ABOS and BAREVAL). In the study 10 231 patients from 12 centres in ten countries were included, 75·3% were female, 24·7% were male. The primary outcome was BMI at 5 years. It was used a model that reduced the opportunity to select variables and the classification and regression trees algorithm to build interpretable regression trees. The performances of the model were assessed through the median absolute deviation (MAD) and root mean squared error (RMSE) of BMI. Seven variables were selected: height, weight, intervention type, age, diabetes status, diabetes duration, and smoking status. At 5 years, across external testing cohorts the overall mean MAD BMI was 2·8 kg/m2 (95% CI 2·6-3·0) and mean RMSE BMI was 4·7 kg/m2 (4·4-5·0), and the mean difference between predicted and observed BMI was -0·3 kg/m2 (SD 4·7). This model is incorporated in a web-based

prediction tool to help inform clinical decision before surgery. This machine learning-based model is internationally validated.

FAMILIAL DILATED CARDIOMYOPATHY IN A PATIENT WITH RETINITIS PIGMENTOSA - CASE REPORT

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Dilated cardiomyopathy (DCM) is characterized by dilation of the left ventricle due to a lower resistance of the myocardium: some muscle cells are replaced by fibrous tissue with an increase in the cardiac cavity but with reduced systolic function. The prevalence of DCM is approximately 1/2,500 individuals but, probably, it is underdiagnosed. Patients present with heart failure, arrhythmias and increased risk of sudden death. A large part of the cases, estimated even over 30%, is to be considered of genetic etiology: familial dilated cardiomyopathy (FDC). FDC is mainly caused by mutations in genes such as lamin (LMNA gene), dystrophin, titin (TTN gene) and ZASP/Cypher (LDB3 gene), which encode for the proteins of the cytoskeleton and sarcomere of cardiac muscle cells. Generally, transmission is autosomal dominant, but forms with X-Linked transmission and autosomal recessive transmission have also been reported. Genetic dilated cardiomyopathy may also be associated with myopathies that affect skeletal muscle, such as Duchenne muscular dystrophy. There is also a variant of CMD associated with cardiac electrical conduction disorders. Treatment of FCD is aimed at controlling the progression of heart failure and arrhythmias. Pharmacological treatment generally involves the use of ACE inhibitors and beta-blockers. In the presence of arrhythmias, the possible use of cardiac resynchronization, defibrillators or pacemaker implantation is also envisaged. Patients with severe heart failure, severe reduction in functional capacity and reduced left ventricular ejection fraction have low chances of survival and may require heart transplantation.
Case report: 58-year-old man, BMI 22. In anamnesis urinary calculosis, rotator cuff syndrome, lumbar-sacral disc herniation, visual impairment due to retinitis pigmentosa. Familiarity for familial dilated cardiomyopathy (LMNA mutation) with a nephew who died of sudden death. Found mutation of LMNA c. 949 G>A in heterozygous and of the MYBPC3 gene in heterozygous, classified as a variant of uncertain significance. For about six months he has had arterial hypertension treated with ramipril 2.5 mg/day. For this reason he began to undergo cardiological checks with ECG, cardiac echocolordoppler (December 2024). In consideration of the family history and the arrhythmic risk associated with the LMNA mutation, a dynamic Holter ECG is indicated (January 2025) which shows phases of first-degree AV block, rare monoform isolated ventricular extrasystole, frequent atrial extrasystole, some atrial couples and triplets and episodes of non-sustained atrial tachycardia. MRI with contrast medium is recommended, which the patient refuses due to claustrophobia. In consideration of the family history and the LMNA score in relation to the first-degree AV block (14.7% at 5 years), a transvenous dual-chamber, single-chamber ICD is indicated, which is implanted without complications (February 2025). The patient continues with monthly cardiological checks and is currently asymptomatic for angina, dyspnea and palpitations and is being treated with ramipril and bisoprolol.
Conclusions: The illustrated clinical case shows how family history is important to identify families with FDC. Screening families with dilated cardiomyopathy through pedigree study and the use of appropriate genetic tests allows the identification of patients in the early or presymptomatic phase. In this case, a heterozygous LMNA mutation and a heterozygous MYBPC3 mutation were found. Mutations in LMNA are associated with a variety of clinical phenotypes. In rare cases, mutations in the LMNA gene can manifest as a more complex syndrome involving both the cardiac muscle system and the visual system. These cases fall within the syndromic laminopathies. Some point mutations in LMNA have been associated with syndromic phenotypes that combine cardiomyopathy and visual changes, including retinitis pigmentosa and other retinal dystrophies. Although retinitis pigmentosa is generally associated with mutations in specific retinal genes, there are case reports reporting the coexistence of DCM and RP in patients with LMNA mutations. A case report published in the European Heart Journal Supplements describes a patient with hereditary dilated cardiomyopathy and retinitis pigmentosa, suggesting a possible hereditary syndromic form. The simultaneous presence of DCM and RP in a patient should prompt the clinician to consider a possible multisystem genetic syndrome. In such cases, it is advisable to perform a thorough genetic analysis to identify any mutations in LMNA or other associated genes. The coexistence of dilated cardiomyopathy and retinitis pigmentosa, although rare, has been documented in the literature and may be associated with mutations in the LMNA gene. A comprehensive genetic evaluation is essential for an accurate diagnosis and for the clinical management of the patient.

LONG-TERM MANAGEMENT OF UPPER EXTREMITY CATHETER-RELATED THROMBOSIS IN FEMALE PATIENTS WITH CANCER: A RETROSPECTIVE COHORT STUDY

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Background: Catheter-related thrombosis (CRT) of the upper extremities is a common complication in patients with cancer carrying central venous catheters (CVCs). Despite its clinical prevalence, optimal management strategies remain uncertain due to limited high-quality evidence, particularly regarding the duration and intensity of anticoagulation.
Objectives: To evaluate the efficacy and safety of long-term anticoagulation therapy in women with cancer and confirmed upper extremity CRT.
Methods: We conducted a retrospective analysis of female patients with active cancer and ultrasound-confirmed upper extremity CRT, treated at the Thrombosis Clinic of Fondazione Policlinico Universitario A. Gemelli IRCCS between November 2022 and January 2025. The analysis was limited to patients who had completed at least 3 months of anticoagulant treatment. Acceptable treatments included low-molecular-weight heparins (LMWHs), fondaparinux, vitamin K antagonists (VKAs), and direct oral anticoagulants (DOACs). Effectiveness was assessed in terms of venous thromboembolism (VTE) recurrence and recanalization rates; safety was evaluated based on bleeding events, classified as major bleeding (MB) or clinically relevant non-major bleeding (CRNMB) according to International Society on Thrombosis and Haemostasis (ISTH) criteria.
Results: A final number of 113 women was included in the analysis. Mean age was 56.79 ± 13.32 years. Patients were affected by ovarian (37.2%), endometrial (16.8%), cervical (4.4%), breast (32.7%), colo-rectal (4.4%), or other (3.6%) cancer. CVCs were peripherally inserted central catheters (PICC) in 19.5%, chest ports in 46.0%, and arm ports in 34.5% of patients. The median follow-up was 568.5 days with an Interquartile Range (IQR) of 300-910 days. In the first 3 months patients were treated predominantly with parenteral therapeutic anticoagulation (69.5%). A smaller proportion of patients (14.8%) was treated with full dose DOACs during the first 3 months. No patients were treated with VKAs. Between 3 and 6 months, the number of patients receiving full anticoagulation decreased, for both oral and parenteral molecules. Beyond 6 months, reduced dose DOACs were the preferred choice in 80.9% of patients. Details about anticoagulation regimens over time are shown in Figure 1. In the first 3 months, no VTE recurrences were observed. Between 3 and 6 months, 2 patients experienced VTE recurrence, with an incidence in this period of 1.9%. Beyond 6 months, 2 VTE recurrences were documented, with an incidence in this period of 2.1%. The total VTE recurrence rate was of 0.5 events/100 person-years. Recanalization was complete in 32.8% of patients in the first 3 months, in 58.3% between 3 and 6 months, and in 61.8% after 6 months. Distribution of recanalization rate over time are shown in Figure 2. Bleeding complications were not negligible, with 4 CRNMB in the first 3 months (2.7%), 1 MB (1.9%) and 3 CRNMB (2.8%) between 3 and 6 months, 1 MB (1.0%) and 5 CRNMB (5.2%) after 6 months. The total bleeding (MB+CRNMB) rate was of 1.9 events/100 person-years.
Conclusion: Long-term anticoagulation in cancer-associated upper extremity CRT appears effective in preventing VTE recurrence but carries a progressively increasing bleeding risk beyond the initial treatment phase. Therefore, tailoring the duration and intensity of anticoagulation to each patient's clinical condition is essential to balance thromboembolism prevention with bleeding complications.

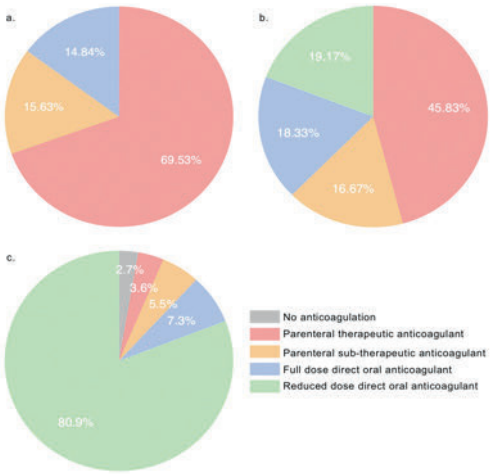

Figure 1. Anticoagulation regimen in the study population at different follow-up intervals.

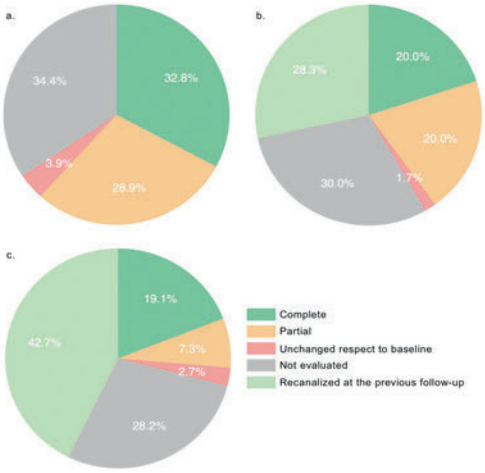

Figure 2. Thrombosis recanalization in the study population at different follow-up intervals.

BEDSIDE CEUS: THE BOLOGNA CENTER EXPERIENCE

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Background: Contrast-enhanced ultrasound (CEUS) is widely used for assessing the perfusion of specific organs or lesions. While CEUS has been extensively studied in outpatient settings, its use as a bedside method is still limited, apart from preliminary data in trauma and during the COVID-19 pandemic. Our ultrasound service routinely performs CEUS evaluations at the bedside for urgent cases involving patients who are often non-transportable and/or critically ill, making traditional radiological exams unfeasible.
Methods: We conducted a retrospective analysis of bedside CEUS exams performed at the Sant'Orsola-Malpighi University Hospital in Bologna (Italy) in 2024.
Results: 62 exams were performed, with 23 women (37%) and a mean age of 59.7 years. In no case was the procedure deemed unfeasible. The contrast medium used was a 2.4 cc bolus of SonoVue (Bracco SpA, Milan, Italy), a suspension of phospholipid-stabilized sulphur-Hexafluoride (SF6) micro-bubbles, followed by a 10 mL injection of saline solution. The contrast medium was prepared by the physician performing CEUS or by the ward nurse. Contrast medium infusion was performed by ward nurses without complications or procedural failures. In 60 cases, the contrast agent was administered intravenously, while in 2 cases (3.2%), it was delivered intracavitary to evaluate the placement of two abdominal drains. In 29 cases (46.7%), the referring department was the intensive care unit, 7 cases (11.2%) the coronary intensive care unit, 9 cases (14.5%) surgical wards, 1 case (1.6%) general medicine ward, 2 cases (3.2%) cardiology, 6 cases (9.6%) infectious diseases ward, 2 cases (3.2%) neonatology, 1 case (1.6%) emergency medicine, 1 case (1.6%) otolaryngology, 2 cases (3.2%) liver transplant unit, and 2 cases (3.2%) nephrology and dialysis.
CEUS was most frequently requested for post-operative collection evaluation (8 cases, 12.9%), liver or splenic focal lesion evaluation (7 cases, 11.2%), trauma outcome assessment (3 cases, 4.8%), urosepsis evaluation (15 cases, 24.2%), and infectious foci search (5 cases, 8%). Other indications included post-kidney transplant follow-up (3 cases, 4.8%), non-traumatic hematoma/collection evaluation (4 cases, 6.4%), liver transplant outcome assessment (3 cases, 4.8%), and post-embolization procedure assessment (5 cases, 8.0%).
In 23 cases (37%), additional tests were required, including 9 computed tomography (CT), 8 ultrasound exams, 4 magnetic resonance (MR) and 1 PET scan. CEUS led to interventional procedures in 15 cases (24.2%), specifically 1 thoracentesis, 7 drainages/aspirations of collections, 3 embolization procedures, 1 biopsy, 2 ERCPs, and 1 paracentesis.
Conclusion: CEUS has proven to be a feasible method at the patient's bedside. In 37% of cases, further diagnostic tests were requested, many of which were routine and not urgent. CEUS can accurately answer specific clinical questions, such as a point-of-care test. Finally, CEUS can point out significant interventional procedures in approximately a quarter of patients, and these procedures were often performed under ultrasound guidance.

ULTRASOUND AND COLOR DOPPLER IMAGING IN DUNBAR SYNDROME: EXPERIENCE FROM THE BOLOGNA CENTER

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Background: Dunbar syndrome, also known as Median Arcuate Ligament Syndrome (MALS), is a condition in which the median arcuate ligament (a fibrous band of the diaphragm) compresses the celiac artery, leading to restricted blood flow. It is estimated to affect between 0.1% and 2% of people based on autopsy studies and diagnostic imaging.
Materials and methods: A retrospective analysis was conducted on ultrasound and color-Doppler examinations performed at the ultrasound center (Serra) of the Policlinico Sant'Orsola-Malpighi in Bologna (Italy) during the period of 2014-2024.
Results: A total of 111 patients with a confirmed diagnosis of MALS were examined, 76 (68.4%) of whom were female. The mean age was 41 years. The color-Doppler analysis showed a mean peak systolic velocity (PSV) value with neutral breathing of 228.2 (± 56.6) cm/s, a PSV during inspiration of 170.9 (± 46.5) cm/s, and a PSV during expiration of 289.7 (± 67.5) cm/s. By performing a sub-analysis according to the degree of stenosis calculated at the celiac trunk level, the mean expiratory PSV was 245.8 (± 46.5) cm/s for 50% stenosis, 258.0 (± 42.6) cm/s for 60% stenosis, 338.5 (± 54.3) cm/s for 70% stenosis, and 390 (± 42.4) cm/s for stenosis greater than 80%.
Discussion and Conclusion: ultrasound and color-Doppler examination is an optimal tool for the screening, diagnosis and monitoring of patients with suspected MALS. A PSV value > 200 cm/s with neutral breathing is confirmed to be an optimal cut-off for identifying patients with this morphological alteration of the celiac trunk.

MICROBIOLOGICAL PROFILE OF INFECTIONS IN KIDNEY TRANSPLANT PATIENTS DIAGNOSED WITH ACUTE PYELONEPHRITIS: A SINGLE-CENTER PROSPECTIVE STUDY

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Background: Kidney transplant recipients are particularly susceptible to opportunistic and nosocomial infections, often complicated by acute pyelonephritis, which represents a significant cause of morbidity and hospitalization. Identifying the main pathogens involved is essential to optimize empirical management and prevent antibiotic resistance.
Methods: A prospective analysis was conducted on 154 patients admitted to various hospital wards at the Sant'Orsola-Malpighi University Hospital in Bologna with a diagnosis of acute pyelonephritis, confirmed by contrast-enhanced ultrasound (CEUS) and/or contrast-enhanced abdominal CT scan. Patients with clinical and radiological evidence of acute pyelonephritis involving

the renal graft were selected. Microorganisms isolated from microbiological samples were analyzed, with particular attention to Gram-negative bacteria and fungi.
Results: A total of 50 patients with clinical and radiological signs of acute pyelonephritis involving the renal graft were enrolled. The mean age of the population was 56 years, ranging from 21 to 80 years. The sex distribution showed a male predominance, with 61.5% men and 38.5% women. Most patients were admitted to the Nephrology department (80% of the sample). The median time between symptom onset and hospital admission was 6 days, with a range from 0 to 26 days. The interquartile range (IQR) was between 3 and 9 days, indicating variability in clinical presentation timing. The most frequently isolated pathogen was Klebsiella pneumoniae (48%), followed by Escherichia coli (30%) and Pseudomonas aeruginosa (10%). Additionally, 4 cases of Enterococcus faecalis (8%) were identified, along with isolated cases of Candida spp. and Staphylococcus aureus. The distribution reflects a typical profile of nosocomial infections with a predominance of Gram-negative organisms.
Conclusions: In patients with acute pyelonephritis involving the renal graft, K. pneumoniae and E. coli are the predominant pathogens, underscoring the need for targeted prevention strategies and antibiotic stewardship. Future studies should investigate the correlation between time since transplantation, antibiotic prophylaxis, and the emergence of multidrug-resistant infections.

DYSAUTONOMIA IN EHLERS-DANLOS SYNDROME AND ITS IMPACT ON QUALITY OF LIFE AND ANXIETY AMONG DIFFERENT SUBSETS OF DISEASE

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Ehlers-Danlos syndrome (EDS) is a group of heritable connective tissue disorders originating from impaired collagen formation. It is defined by one or more of several common features such as skin hyperextensibility, joint hypermobility, and tissue fragility as well as chronic pain and autonomic dysfunction, which can be major symptoms. Furthermore, these patients experience higher rates of anxiety and sleep disturbances and report lower work capacity than healthy controls. Variability in clinical features allows to distinguish 13 different types of EDS, which the most common are hypermobile, classical and vascular forms. Genetic testing is used to confirm the diagnosis for all cases except hypermobile EDS, as the genetic basis for this form is currently undefined. However, a characterization of autonomic profiles of specific disease subsets is still lacking. Additionally, the relationship between dysautonomia and impairment of quality of life in EDS subjects still needs to be investigated.
To analyze the presence of dysautonomic disturbances among the most common EDS variants and determine their repercussions on anxiety and depression, sleep patterns and professional performance.
The study sample comprises 50 patients, 21 with hypermobile EDS (34 ± 10 years old; 100% female), 9 with classical form (42 ± 13 years old, 77,8% female), 5 with vascular form (41 ± 13 years old; 40% female), and 15 with hypermobility spectrum disorder (HSD; 33 ± 10 years old, 66,7% female) were consequently enrolled from the EDS center of Policlinico Hospital, Milan, in a cross-sectional analysis. They completed questionnaires about dysautonomia (Composite Autonomic Symptom Score 31 Questionnaire, COMPASS-31), sleep quality (Pittsburgh Sleep Quality Index, PSQI), work ability (Work Ability Index, WAI), and anxiety and depression (Patient Health Questionnaire 4, PHQ-4). Moreover, the COMPASS-31 questionnaire was also analyzed according to its subdomains, which provided information about the degree of specific autonomic dysfunctions, particularly orthostatic intolerance, vasomotor, secretomotor, gastrointestinal, bladder, and pupillomotor dysfunction. We performed one-way ANOVA to compare scores among EDS subtypes, Student's T-test for independent samples to compare the group of patients with EDS and HDS and finally Spearman correlation test to investigate relationships between dysautonomia and its subdomains, sleep quality, anxiety, and work capacity.
Patients with hypermobile EDS showed significantly worse overall dysautonomia scores compared to patients with vascular form (p=0.014), along with gastrointestinal dysfunction sub-scores, which were significantly higher in patients with hypermobile EDS compared to the other group (p=0.022). We also found a borderline result that shows that the hypermobile EDS group has worse overall dysautonomia scores compared to patients with HSD (p=0.054), and especially regarding bladder dysautonomia (p=0.078), although the results are not statistically significant. A significantly negative correlation was found between overall dysautonomia and work capacity score (r=0.73, p<0.001); there was a positive correlation between overall dysautonomia score and sleep disturbances score (r=0.66, p<0.001), anxiety (r=0.32, p=0.029) and depression scores (r=0.36, p=0.011). We found a positive correlation between secretomotor dysautonomia subscore and both anxiety (r=0.30, p=0.042) and depression scores (r=0.35, p=0.016). Similarly, gastrointestinal dysautonomia subscore correlated with anxiety (r=0.33, p=0.024) and depression scores (r=0.43, p=0.002). Finally, all the dysautonomia subscores were found correlated with work disability score and sleep disturbances score: for example, the gastrointestinal dysautonomia subscore was negatively correlated with the work ability score with r=0.64 (p<0.001) and with the sleep disturbances score with r=0.65 (p<0.001).
Hypermobile EDS patients present higher grades of dysautonomia compared to vascular EDS subjects. Moreover, more severe dysautonomic impairment positively correlates greater anxiety and depression symptoms, with worse sleep and worse work capacity, therefore overall worse quality of life. From these results we observed that dysautonomia appears to be an important variable to consider while approaching patients with EDS. Eventually, further research is required to deeply assess differences in autonomic profiles of different EDS subtypes, possibly contributing to better disease management and reducing its impact on quality of life.

EFFICACY AND SAFETY OF BELIMUMAB IN PREGNANCY

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Introduzione: Il lupus eritematoso sistemico (LES), con o senza associazione alla sindrome da anticorpi antifosfolipidi (APS), rappresenta una sfida significativa per le giovani donne con desiderio di gravidanza. Sebbene la letteratura scientifica e le principali linee guida cliniche (raccomandazioni SIR-SRMR 2023), offrano indicazioni per la gestione delle gravidanze spontanee in questa popolazione, le evidenze sono meno definite nel contesto delle tecniche di procreazione medicalmente assistita, in particolare per la fecondazione in vitro (FIVET). L'assenza di raccomandazioni specifiche genera incertezze cliniche rendendo il percorso verso la gravidanza più complesso.
Caso clinico: Presentiamo il caso di A.B., donna di 25 anni, affetta da lupus eritematoso sistemico (LES) diagnosticato all'età di 20 anni, con interessamento muco-cutaneo e articolare, positività per anticorpi antifosfolipidi e in trattamento con idrossiclorochina (200 mg/die), cardioaspirina e basse dosi di prednisone (5 mg/die). La paziente ci veniva attenzionata in seguito a ripetuti tentativi infruttuosi di fecondazione in vitro (FIVET). Alla prima visita la paziente presentava un elevata attività di malattia (SLEDAI 11) veniva avviata terapia con belimumab (200 mg/week) e si programmava follow-up congiunto con il team ginecologico al fine di ottenere una remissione della malattia in previsione di un nuovo tentativo di transfer embrionario. Dopo cinque mesi di trattamento con belimumab, la paziente aveva raggiunto un buon controllo della malattia (SLEDAI 5) e si è proceduto con un nuovo ciclo di FIVET, con esito positivo. Durante la gravidanza è stata mantenuta eparina a basso peso molecolare e idrossiclorochina fino alla 38° settimana, belimumab fino alla 20° settimana, cardioaspirina fino alla 25° settimana. Il prednisone è stato somministrato solo al bisogno, a basse dosi. L'intero decorso gestazionale è stato regolare, con un buon controllo della malattia. Il parto è stato concordato e programmato con successo, al termine dell'epoca gestazionale, senza complicanze per la madre e per il bambino.
Conclusioni: Questo caso clinico supporta le evidenze in letteratura riguardo al rapido raggiungimento della remissione della malattia con belimumab in pazienti affette da LES. Inoltre, conferma il profilo favorevole di sicurezza ed efficacia del farmaco quando somministrato fino alla 20° settimana di gestazione, rafforzandone il potenziale ruolo nella gestione multidisciplinare della gravidanza in pazienti con LES.

METABOLIC ENCEPHALOPATHY CAUSED BY VITAMIN D INTOXICATION IN AN OLD WOMAN WITH PRIOR COGNITIVE IMPAIRMENT

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Vitamin D plays a critical role in calcium homeostasis. While hypovitaminosis

D is quite common in older patients, the hypervitaminosis due to excessive vitamin D administration is a very rare occurrence particularly with the native form cholecalciferol. We report a case of severe hypercalcaemia and metabolic encephalopathy secondary to vitamin D overload in an older woman with mild cognitive impairment.An 84-year-old woman was admitted to the hospital because of lethargy, acute confusion, nausea, constipation and polyuria, developing over one week. She had a history of dyslipidemia (on ezetimibe-rosuvastatin), long-term tobacco use (~15 cigarettes/day for 40 years), and depressive disorder previously treated with venlafaxine. Up to a week before, she was independent in activities of daily living (ADL 6/6).On physical examination, the patient was drowsy but awake, slightly dehydrated, and abstemious. Cardiopulmonary and abdominal examinations were within normal limits and no malignancies were identified. Neurological evaluation revealed no focal deficits. Brain CT showed chronic small vessel ischemia; EEG revealed generalized cortical slowing with diffuse paroxysmal discharges. MMSE score dropped from 25.85/30 to 23.8/30; verbal memory resulted impaired as shown by Ray Auditory Verbal Learning test result that was 1.4, below the cut-off value of 4.69.At admission labs showed: corrected serum calcium 16.6 mmol/L (ionized Ca^{2} 2.07 mmol/L), creatinine 1.6 mg/dL, hypokalemia (2.8 mmol/L), and metabolic alkalosis (pH 7.48, HCO_3 38.3 mmol/L). Phosphorus and glucose levels were normal. PTH levels were suppressed (5.81 pg/mL), ruling out the hypothesis of primary hyperparathyroidism. Serum 25(OH)D was markedly elevated (479 µg/L), suggesting vitamin D intoxication. After further history taking, her caregiver revealed chronic use of over-the-counter supplements—leading to a daily intake of calcium carbonate (1000 mg), cholecalciferol (14,000 IU), and vitamin K2 (50 µg)—started in the previous six months, without medical supervision and online bought by a relative.The medical treatment of such condition included intravenous fluids, oral potassium repletion, low-dose furosemide (25 mg/day), and three alternating daily 300 mg dose of intravenous clodronate. The therapeutic aim was to suppress osteoclastic bone resorption and restore calcium balance. Electrolyte disturbances normalized within the succeeding 72 hours. By day 4, calcium levels restored within the normal range, and neurocognitive features dramatically improved. The patient was discharged on day 7. Post-discharge labs confirmed stable calcium (9.2 mg/dL) and 25(OH)D levels decline (212 µg/L).Hypercalcemia is an uncommon reversible cause of encephalopathy in the elderly. The differential diagnosis should also consider exogenous vitamin D intoxication resulting from prolonged high-dose cholecalciferol, emphasizing the risk of unsupervised dietary supplements. Severe hypercalcemia requires early identification and tailored treatment strategies.This report highlights the importance of cautious use of vitamin D and other supplements, particularly in cognitively impaired older patients.

PRIMARY HYPERPARATHYROIDISM AS A TRIGGER FOR FRACTURE IN A CASE OF POLYOSTOTIC PAGET'S DISEASE

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Paget's disease (PD) of bone is a skeletal disorder characterized by focal abnormalities in bone remodeling that can increase the risk of fractures.
The case described is of a 44-year-old woman with onset of PD at age 20 and involvement of the skull, right femur, and tibia. Study of family members showed eight members with the same disease with frameshift mutation D107Rfs*3 of the PFN1 gene, which codes for profilin 1. This is a particular form of PD that does not respond to treatment with bisphosphonates, as evidenced, in this case, by the need for repeated courses of therapy with zoledronate 5 mg i. v. The patient presented, months later, with heart failure and a fracture. v. The patient presented, three months after VIII administration of zoledronate, with persistence of elevated ionized calcium (1.33 mmol/L) and slightly increased PTH (84.9 pg/mL) with hypercalciuria (11.9mg/Kg/24h) in the presence of normal dietary calcium intake and sufficient vitamin D status (43 ng/mL). Suppressed TSH was reported with normal fT3, fT4 and autoantibody values. Imaging with scintigraphy, ultrasound, PET with 18F-Choline confirmed a thyroid nodule with a tendency to autonomy in the left thyroid lobe and hyperfunctioning parathyroid tissue in the posterior apical sectors of the same lobe. While awaiting surgical evaluation, the patient underwent new administration of zoledronate (IX). BMD values evaluated with DXA were within the normal range. 3 months after the last dose of zoledronate, the patient suffered a diaphyseal fracture of the right tibia during the march, which was surgically treated with an intramedullary nail. The biohumoral evaluation, one month after the fracture, showed high bone turnover, associated with primary hyperparathyroidism and normal thyroid function.
Although Paget's disease may promote bone fracture per se, the association with other endocrine disorders, and in particular primary hyperparathyroidism, may increase the likelihood of bone fracture.

STATINS DO NOT AFFECT BONE MINERAL DENSITY CHANGE UNDER TERIPARATIDE

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Teriparatide [rhPTH(1–34)] is an anabolic treatment for patients with severe osteoporosis. Statins, HMG-CoA reductase inhibitors, have been proven to prevent osteoclastic bone resorption effects. The combined action of rhPTH and statins has never been investigated.
The aim of this research was to investigate the bone mineral density (BMD) changes in rhPTH treated postmenopausal women with severe osteoporosis in accordance with their use of statins.
Women were eligible patients if they had received a complete 24-month rhPTH treatment course for the secondary prevention of fragility fractures. All participants were administered a subcutaneous dose of 20 mcg rhPTH every 24-h and were supplemented with 25,000 IU oral cholecalciferol every 14 days. The use of statins was ascertained from medical records. Bone turn-over markers, including alkaline phosphatase (ALP), osteocalcin (BGP) and C-terminal collagen type 1 telopeptide (CTX) were measured at baseline and then every 6-months, and BMD were assessed at baseline and at the end of observation period.
All the participants (n=104, mean age 68 yr) receiving rhPTH significantly improved their BMD at lumbar spine [+7% and +11% in not statins (n=74) vs statins (n=30) users, without any differences between groups], while reported not significant BMD change at femoral neck irrespective of statins use [-7% and +2% in not statins (n=74) vs statins (n=30) users, without any differences between groups]. Markers of bone turn-over increased significantly at 6 months and maintained higher in comparison with baseline in both groups without intergroups significant difference.
Statins do not impair rhPTH efficacy in term of BMD modification at lumbar spine and femoral neck in postmenopausal women with sever osteoporosis. Further perspective studies are urgently needed to explore possible benefits of combination treatment with rhPTH and statins.

HOW CLINICAL FEATURES CAN GUIDE THE DIAGNOSTIC AND THERAPEUTIC MANAGEMENT OF ARRHYTHMIC PHENOMENA IN YOUNG ADULTS: A CASE REPORT

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V.A., un giovane adulto di 21 anni, è stato inviato dal medico curante presso l'ambulatorio di Medicina Interna del Dipartimento di Medicina Clinica e Chirurgica dell' AOU Federico II di Napoli per episodi di cardiopalmo.
Il paziente conduce una vita attiva, lavora e pratica tre volte a settimana una moderata attività fisica presso una palestra, attività per la quale nel corso degli anni ha sempre ricevuto l'idoneità all'attività sportiva da parte del suo medico curante, presenta una anamnesi patologica remota muta, nessuna familiarità per eventi cardiovascolari maggiori o morte cardiaca improvvisa, non ha abitudine tabagica e non consuma alcolici né sostanze d'abuso.
Il paziente ha fatto accesso presso il nostro ambulatorio per una tachicardia che si presenta circa una volta alla settimana, con emergenza improvvisa durante la notte - nel corso del sonno, da cui lo desta – accompagnata da un corteo di sintomi che il paziente descrive tanto forti da essere invalidanti, fra questi oltre alla tachicardia vi sono la dispnea, una parziale afasia e paralisi, che gli rendono anche estremamente difficile comunicare o prendere alcun tipo di iniziativa nel corso di questi eventi, che si risolvono poi spontaneamente nel corso di qualche decina di minuti. A tal proposito ci riferisce che in determinate circostanze, vista la natura improvvisa, violenta ed invalidante della sintomatologia, ha cominciato a dormire nella stessa stanza dei genitori, per permettergli di

rendersi conto della situazione ed eventualmente intervenire per soccorrerlo. In accordo con quelle che sono state le indicazioni di Giada e Raviele (*Il cardiopalmo, iter diagnostico, Giornale Italiano di Cardiologia*) sull'inquadramento diagnostico del cardiopalmo eseguiamo dunque esami di primo livello quali prelievi ematochimici, da cui si evince un profilo di eutiroidismo con assenza di alterazioni di rilievo all'emocromo ed alla biochimica, un tracciato elettrocardiografico a 12 derivazioni a riposo, da cui risultava una bradicardia alla frequenza di 50bpm all'interno di un quadro di alterata ripolarizzazione ventricolare, con un punto J sopraslivellato nelle derivazioni precordiali di destra ed una caratteristica forma 'coved shape' dell'onda T nelle stesse derivazioni, potenzialmente compatibile con un pattern di Brugada.
Abbiamo dunque eseguito un secondo tracciato, questa volta con le derivazioni modificate, che ha evidenziato sempre delle alterazioni della ripolarizzazione, ma non ascrivibili a quelle tipiche dei pattern di Brugada. Vista la sintomatologia riferita dal paziente e le anomalie elettrocardiografiche riscontrare alla valutazione ambulatoriale, gli abbiamo prescritto l'esecuzione di esami di secondo livello quali un Holter ECG delle 24 ore ed un ecocolor-doppler cardiaco a riposo.Questo esame ha evidenziato diverse fasi, diurne e notturne, di blocco atrio-ventricolare di II grado tipo Mobitz 1, con assenza di pause significative e la presenza di sporadiche extrasistoli sopraventricolari isolate. Nel corso delle 24 ore prese in esame dall'Holter però il paziente non ha manifestato alcuna sintomatologia, per cui non è stato possibile analizzare il ritmo nel corso degli episodi tachicardici. L'ecocolor doppler cardiaco a riposo ha evidenziato l'assenza di cardiopatie strutturali, una normale cinesi globale e segmentaria e delle dimensioni cavitarie nei limiti della norma, con gli apparati valvolari normofunzionanti.
Una tachicardia notturna in un giovane adulto sano, che si sottopone a controlli medici periodici che non hanno mai evidenziato alterazioni a livello del distretto cardiovascolare, che si è sottoposto ad un ecocolordoppler cardiaco a riposo che non ha evidenziato alterazioni strutturali o cinetiche delle camere cardiache o dei grandi vasi, che non ha in anamnesi familiarità per eventi o patologie cardiovascolari, normalmente non dovrebbe spingerci nel proseguire l'iter diagnostico cardiologico, data la prevalenza di cause "benigne" o comunque non cardiache che possono generare questa condizione in un giovane sportivo (reflusso gastroesofageo, ernia iatale, ansia, eccessiva attività fisica, disturbi del sonno).
In questo caso però il corteo di sintomi descritti dal paziente ed in particolar modo la loro intensità e l'impatto che avevano sulla sua vita, tali da risultare invalidanti, ci ha spinto a ritenere opportuno un ulteriore approfondimento diagnostico ponendo l'indicazione all'impianto di un dispositivo loop recorder, per monitorizzare il ritmo cardiaco del paziente nel corso dei prossimi mesi.
La clinica è dunque stata dirimente nell'indirizzare il nostro iter diagnostico-terapeutico e le indicazioni da dare al paziente.

EFFICACY AND SAFETY OF DIFFERENT ANTICOAGULANT TREATMENT REGIMENS FOR ISOLATED INTERNAL JUGULAR VEIN THROMBOSIS: A CASE SERIES

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Typical venous thrombosis affects the system of the lower limbs, while the atypical ones affect different districts. Isolated internal jugular veins thrombosis (IIJVT), as atypical one, are classified as upper extremity deep vein thrombosis (UEDVT). The prevalence of this atypical form is between 0,5% and 3,47% of patients presenting with deep vein thrombosis (DVT). The most common clinical presentation is arm edema and pain, but it can also be asymptomatic. Mechanical transient factors are usually the most common causes, like central venous catheter (CVC) or lateral cervical abscess, also known as Lemierre's syndrome. Among permanent factors that can induce IIJVT, active cancer and thrombophilia are the most frequent.
The risk of pulmonary embolism (PE) from UEDVT differs in various studies, but given the known benefits of anticoagulation in preventing PE in patients with LEDVT and the estimated risk of PE in patients with UEDVT most clinicians empirically treat UEDVT in the same way as LEDVT. Nevertheless, atypical site are treated with VKA and there are few data about treatment with DOAC. Furthermore, although patients with UEDVT less frequently have signs of clinically overt PE at time of presentation, their 3-month clinical outcomes are similar, and the rate of recurrence in patients with catheter-related UEDVT is higher, suggesting that appropriate therapy should not differ from typical thrombosis. Considering that patients treated with VKA should check the INR to optimize the posology, patients often have low compliance with therapy and reduced outcomes in terms of recanalization or embolism.
No randomized controlled trials have been performed on the optimal treatment for patients with IIJVT. Therefore, there is still debate about what the best therapy is and how side-effects can be minimized.
For these reasons, we collected a case series of 29 patients from 2014 to 2024 who referred consecutively at the Centre of Anticoagulant therapies of Policlinico Umberto I, in Rome for IIJVT. The aim of this study was to compare the type of anticoagulant regimen (VKA, DOACs and parenteral ones) to observe differences in terms of bleedings and thromboembolic events. We collected information like age, sex, presence of symptoms, cause of VTE events, comorbidities, resolution of thrombosis, thrombophilia screening and other concomitant drugs. We enclose 17 patients treated with VKA, 6 with DOACs and 6 with parenteral anticoagulants. The IIJVT diagnosis was made with a color-doppler ultrasound. Patients were examined after 3, 6 and 12 months and after the first year of treatment, annually.
Main outcome were events including death from any cause, recurrence of thrombosis and bleedings.
For clinical characteristics of patients see Table 1. There was no difference among three groups regarding sex, age, presence of symptoms at diagnosis, history of cancer, genetic thrombophilia and of the main cardiovascular risk factors. The only significant difference was regarding the cause of IIJVT: Lemierre's syndrome was more frequent in patients treated with VKA while CVC in patients with DOACs. The mean lenght of treatment was 37 months. Among DOACs, apixaban was the most used Warfarin for VKAs and low molecular weight heparin for parenteral anticoagulant therapy.
Regarding the main outcomes, see Table 2. Bleeding were more frequent in the VKAs group, with no major bleeding and 3 CRNMB. Death occurred more frequently in the parenteral group and it was due to cause other than cardiovascular or thromboembolic ones. Recurrences of thromboembolic event occurred only in VKAs group, and 60% were after suspension of anticoagulant treatment.
Based on this case series, VKA, DOACs and parenteral anticoagulant do not seem to have the same safey and effectiveness in patients with isolated internal jugular vein thrombosis, since there have been more VTE recurrence and more bleeding events in the VKAs group.
The present study have limitation since it is a small case series of a monocentric collection with retrospective data. A lot of remaining questions remain open on this topic: if we should collect color-doppler ultrasound to check after 3-6 months form the event the recanalization to guide the anticoagulant treatment lenght. Furthermore, it would be useful for the comparison among DOACs to understand the most effective.

Table 1. Clinical characteristics of patients with jugular vein thrombosis

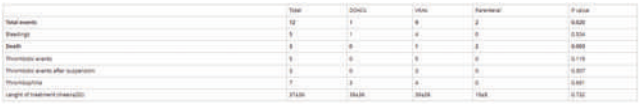

Table 2. Follow-up and outcomes of patients with jugular vein thrombosis

NOT THAT UNCOMMON: ACQUIRED HEMOPHILIA, A CASE REPORT

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Introduction: Acquired hemophilia A (AHA) is a rare hematological disorder caused by autoantibodies against coagulation factors, most commonly factor VIII (FVIII). These antibodies can cause severe hemostatic defects through two main mechanisms: increasing FVIII clearance or interfering with its activity. The estimated incidence is 1–2 cases per million people per year, with a significant increase in individuals over 85 years old (14.5 cases/million/year). The pathogenesis of AHA remains incompletely understood. Potential predisposing factors include polymorphisms in immune-regulatory genes and autoreactive T cells. Between 30–50% of cases are associated with underlying conditions such as malignancies (adenocarcinomas and hematologic tumors), autoimmune

diseases, pregnancy/postpartum, some medications, and advanced age. The main clinical manifestation is bleeding, which is often spontaneous and severe, affecting subcutaneous tissue in 80% of cases. However, visceral, retroperitoneal, or muscular hemorrhages may also occur, though less frequently. Unlike congenital hemophilia, hemarthroses are rare. Herein, we present a paradigmatic case of AHA, characterized by significant bleeding and anemia, whose purpose is to emphasize the importance of early recognition and timely treatment of this disease to avoid severe and potentially fatal hemorrhagic complications.

Case description and discussion: A76-year-old man with a past medical history of monoclonal gammopathy consistent with Waldenström's disease initially presented with spontaneous hematomas. Laboratory tests showed isolated prolongation of activated partial thromboplastin time (aPTT) with normal prothrombin time (PT), which, however, was not deemed clinically significant. The patient was therefore discharged with a prescription for amoxicillin/clavulanate, without further hematologic evaluation. The patient was eventually re-admitted to the emergency room (ER) due to a wide hematoma on his left arm following SARS-CoV-2vaccination. Laboratory tests performed in the ER showed prolongation of aPTT (2.42sec), PT was normal. The patient underwent further investigations, including an aPTT mixing test. This test involves mixing patient and normal plasma (1:1) to evaluate a prolonged aPTT. Correction of aPTT suggests a clotting factor deficiency, while persistent prolongation indicates the presence of an inhibitor. In our patient aPTT was normalized after mixing at first. Nonetheless, a second mixing test performed after two hours of incubation at37°C showed persistence of prolonged aPTT, suggesting the presence of a time- and temperature-dependent inhibitor, which is particularly suggestive of the presence of a FVIII inhibitor. Given the patient's hematological history and laboratory tests, we suspected AHA: reduced FVIII activity (2%,) and FVIII inhibitor at a titer of8Bethesda units (BU) allowed us to confirm the diagnosis. Over the course of hospitalization, the patient developed a large dorsal swelling that Xrays revealed to be a right posterior paraspinal hematoma, and subsequently new widespread ecchymoses with an extensive, actively bleeding hematoma in the right thigh. The latest guidelines on the management of bleeding in patients with acquired hemophilia recommend the use of a bypassing factor for hemostatic purposes. The patient was therefore treated with recombinant activated factor VII (rFVIIa, Novoseven®) and blood transfusions, with adequate hemostatic control. In order to eradicate the inhibitor, immunosuppressive therapy is recommended, including monotherapy with corticosteroids (CTS), CTS combined with cyclophosphamide or rituximab, triple therapy with cyclophosphamide, rituximab, and dexamethasone (CyDRi), and plasmapheresis in refractory cases. Immunosuppressive therapy with methylprednisolone (1mg/kg/day) and rituximab was initiated. During follow-up, FVIII levels increased from2% to103%, while inhibitor titers decreased from8BU to0BU, allowing for the gradual discontinuation of corticosteroid therapy.

Recent therapeutic advances for this disease have been particularly encouraging. Over the past decade, emicizumab—a bispecific monoclonal antibody that functionally replaces FVIII—has emerged as a cornerstone treatment. Experimental approaches such as the anti TFPI antibody concizumab and the siRNA agent fitusiran are now being explored to rebalance hemostasis by modulating natural anticoagulant pathways.

Conclusion: AHA is a rare condition that can be fatal if not promptly diagnosed and treated. This case underscores the importance of not underestimating an unexplained alteration in coagulation tests, but also of performing serial mixing tests to diagnose acquired hemophilia, avoiding false negatives caused by the time- and temperature-dependent nature of the inhibitor. Management requires a multidisciplinary approach, combining hemostatic therapy with tailored immunosuppressive strategies based on disease severity and underlying conditions. Emerging therapeutic strategies may improve disease management in the future.

ACUTE HEPATIC PORPHYRIA AS A CHRONIC CONDITION: LONG-TERM OUTCOMES FROM A PATIENT SUPPORT PROGRAM INTEGRATING GIVOSIRAN THERAPY

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Acute Hepatic Porphyria (AHP) is a rare, severely disabling disorder that is not only characterized by acute, potentially life-threatening attacks but also by its chronic, progressive nature with multisystem involvement. Increasingly, AHP is recognized for its persistent impact between attacks, with patients frequently experiencing chronic pain, fatigue, nausea, mood disturbances and impaired daily functioning. These symptoms often extend beyond acute episodes, contributing to a substantial and lasting disease burden that requires ongoing clinical and psychological support. This chronicity necessitates a shift from crisis management to long-term, person-centered care. A key therapeutic advancement is Givosiran, an RNA interference therapy administered monthly via subcutaneous injection, which reduces the accumulation of toxic heme precursors. Clinical trials have demonstrated that Givosiran not only reduces the frequency of acute attacks but also alleviates chronic symptoms, significantly improving patients' long-term quality of life. A 48-month open-label extension study confirmed a sustained 97% reduction in annualized attack rates and a 96% reduction in hemin use, alongside a clinically meaningful improvement in patient-reported outcomes, such as a +15.8-point increase in EQ-VAS scores, exceeding the minimal clinically important difference. In this study, we focus on 24-month follow-up data from a longitudinal Patient Support Program (PSP) by PHDlifescience, aimed at monitoring and supporting individuals with AHP over time. Eighteen patients were enrolled, of whom nine completed the full follow-up. Patients were assessed at five time points (T0–T4) using validated tools: the SF-12v1 (for physical [PCS] and mental [MCS] health), the Brief Fatigue Inventory (BFI), and the Brief Pain Inventory, including Pain Severity (PSS) and Pain Interference (PSI) scores. Higher BFI, PSS, and PSI scores indicate greater symptom burden; higher PCS and MCS reflect better health. All statistical analyses were performed using R (v4.3). Clinical parameters (blood pressure, heart rate, respiratory rate, oxygen saturation, temperature, dosage, and adverse events) remained stable throughout the study. Fatigue (BFI) showed a worsening trend, increasing from a median of 52 at baseline to 62 at T4, with consistently wide interquartile ranges (e.g., IQR=64 at T2), reflecting the variability typical of chronic conditions. PCS scores remained stable (median ~37), suggesting persistent functional limitations. MCS improved initially (from 31.2 at baseline to 42.7 at T2) but declined at T4 (34.3), indicating a temporary psychological benefit. Pain-related outcomes (PSS, PSI) peaked mid-study and declined thereafter, highlighting a fluctuating but ongoing pain burden. These results reinforce the understanding of AHP as not only an acutely severe disorder but a chronically disabling one, marked by clinical heterogeneity and psychological vulnerability. While structured support programs may offer short-term relief, their long-term efficacy varies and is highly individual. Sustained treatment with Givosiran has consistently demonstrated stable biochemical control and clinically meaningful improvements. Effective AHP management requires flexible, multidimensional strategies tailored to evolving physical, psychological, and social needs. Crucially, empowering patients and promoting self-management may reduce unplanned healthcare utilization, optimize resource use, optimize resource use, and help contain care costs. In the present study, while patients report an initial improvement in mental well-being (MCS) by T2, both stress and perceived problem severity (PSS, PSI) worsen in the same period before improving again at T4 (Figure 1). Physical functioning (PCS) shows modest changes, whereas fatigue (BFI) increases consistently over time, underscoring the chronic nature of the condition and the importance of sustained, multidisciplinary interventions.

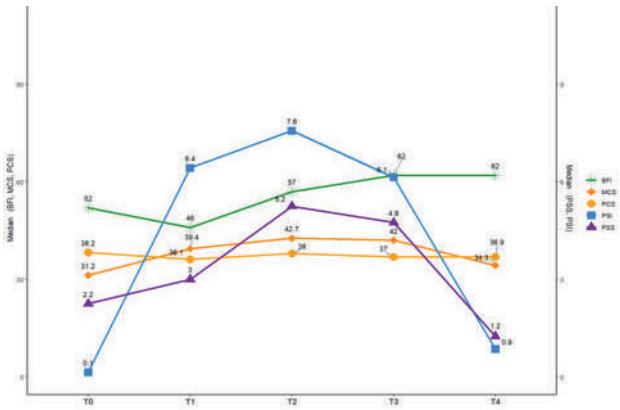

Figure 1. Temporal trends in patient-reported outcomes from baseline (T0) to follow-up (T4).

ANTICOAGULATION IN OBESE PATIENTS: A REVIEW OF THE LITERATURE AND CURRENT GUIDELINES

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Introduction: Obesity is a chronic and multifactorial disease, which affects 13% of the global population. Diagnosis is based on BMI, with obesity defined as ≥30 kg/m^2. Fat distribution varies by sex and hormonal status, in particular visceral fat predominates in men and postmenopausal women, leading to a higher risk of cardiovascular diseases. In fact, abdominal obesity promotes hypertension, insulin resistance, causing type 2 diabetes mellitus, and cardiovascular diseases such as atrial fibrillation (AF). High BMI is also associated with elevated risk of venous thromboembolism (VTE).
Pharmacokinetics and pharmacodynamics of anticoagulants are notably altered in obese patient. For this reason managing anticoagulation therapy in morbidly obese patients may be very challenging.
Oral Anticoagulation The choice of an oral anticoagulant therapy for obese patients should take into account the different intestinal absorption, metabolization and elimination of these individuals, and these issues impact even more in obese patients undergoing bariatric surgery. Bariatric procedures, distinguished into restrictive, malabsorptive, or mixed procedures, can significantly affect the bioavailability of oral drugs, including anticoagulants. Identifying the specific type of surgery is essential to assess its impact on drug absorption and guide treatment choices.
Vitamin K Anticoagulants (VKAs) Patients with high BMI are largely underrepresented in the major clinical trials. For this reason a real benefit in using DOACs versus VKAs in these patients has not been documented yet. VKAs seem to show a decreased risk of stroke and cardioembolic events compared to DOACs in some of these studies; this could be partially explained by a better time within the therapeutic range of obese patients. In contrast, it is also documented that DOACs, in particular apixaban, is associated with a decreased risk of stroke and bleeding events compared to warfarin (Table 1). VKAs may also represent a reasonable choice over DOACs in patients who underwent bariatric surgery, where INR monitoring allows easy dose adjustments.
Direct Oral Anticoagulants (DOACs) DOACs represent the best option over VKAs for VTE treatment and prevention of stroke; evidence supports their safety and efficacy in patients with BMI up to 40 kg/m^2 or weight ≤120 kg. In morbidly obese patients, apixaban and rivaroxaban seem to be effective and safe for both VTE treatment and AF, while dabigatran and edoxaban use is not suggested in VTE treatment, due to lack of clinical and pharmacokinetics data or unconvincing data (Table 2).
In patients who underwent bariatric surgery, DOACs should be used with caution. Among all DOACs, apixaban absorption seem to be the least affected by bariatric procedures and it represents a reasonable choice in these patients, especially when it is not used in the immediate postoperative period (Table 3, Figure 1).
Parenteral Anticoagulation Unfractionated heparin (UFH) is the drug of choice in patients with severe kidney impairment or high risk of bleeding, although it requires frequent laboratory monitoring to achieve and maintain therapeutic levels. It is also a reasonable choice in patients whose poor subcutaneous absorption is suspected.
Low-molecular-weight heparins (LMWHs) like enoxaparin are widely used in clinical practice, but present dosing challenges due to fat distribution, affecting absorption (Table 4). Weight-based dosing and anti-Xa monitoring can optimize therapy, especially in high BMI patients. Clinical data remain limited for tinzaparin and fondaparinux in morbid obesity, suggesting caution in their use in these patients (Figure 2).
Conclusion: In conclusion, management of anticoagulation in obese patients is challenging and necessitate a patient-tailored approach. The pharmacokinetics and pharmacodynamics of anticoagulants can be significantly affected in this population, leading to an increased risk of both thromboembolic events and bleeding complications. Further research is needed to guide our clinical practice, in order to achieve proper anticoagulation in obese patients.

	Weight	Patients (n)		Efficacy (event rate per 100 patient/years) OR number of events (n OR %)	Major bleeding rate
BALLA et al.[1]	BMI 18.5-24.9 Kg/m^2	3289	Rivaroxaban: 1618	2.93 (n: 166)	3.69 (n: 179)
			VKA: 1671		
	BMI 25-29.9 Kg/m^2	5535	Rivaroxaban: 2738	2.28 (n: 266)	3.61 (n: 314)
			VKA: 2797		
	BMI ≥ 30 Kg/m^2	5206	Rivaroxaban: 2657	1.88 (n: 179)	3.33 (n: 279)
			VKA: 2549		
HOHNLOSER et al.[2]	60-120 Kg	15.172	Apixaban: *	1.23 (n: 173)	2.15 (n: 277)
			VKA: *	1.44 (n: 201)	3.02 (n: 379)
	>120 Kg	982	Apixaban: *	0.44 (n: 4)	1.55 (n: 13)
			VKA: *	1.13 (n: 11)	2.08 (n: 19)
BORIANI et al.[3]	BMI 18.5 ≤ 25 Kg/m^2	4491	Edoxaban: 2933	n: 193	n: 157
			VKA: 1558	n: 80	n: 126
	BMI 25 ≤ 30 Kg/m^2	7903	Edoxaban: 5974	n: 262	n: 264
			VKA: 2629	n: 145	n: 208
	BMI 30 ≤ 35 Kg/m^2	5209	Edoxaban: 3506	n: 137	n: 188
			VKA: 1703	n: 83	n: 130
	BMI 35 - 40 Kg/m^2	2099	Edoxaban: 1413	n: 52	n: 76
			VKA: 686	n: 18	n: 54
	BMI ≥ 40 Kg/m^2	1149	Edoxaban: 785	n: 21	n: 43
			VKA: 364	n: 5	n: 30
MALIK et al.[4]	BMI > 30 Kg/m^2	*	DOACs: *	5.8%	5.5%
			VKA: *	5.5%	5.8%
BARAKAT et al.[5]	BMI 18.5 ≤ 30 Kg/m^2	18.339	DOACs: 8969	2.66	4.20
			VKA: 9370	6.02	9.10
	BMI 30 ≤ 40 Kg/m^2	13.376	DOACs: 7059	2.35	3.81
			VKA: 6317	4.90	8.88
	BMI ≥ 40 Kg/m^2	3924	DOACs: 2170	1.70	3.22
			VKA: 1754	3.64	8.10

Table 1. DOACs vs VKAs efficacy and safety in patients with high BMI.

DOAC	BMI ≤ 40 Kg/m^2 or weight≤ 120 Kg	BMI >40 Kg/m^2 or weight >120 Kg		
		AF	VTE treatment	VTE prevention
Rivaroxaban	Suggested	Suggested (standard doses)	Suggested (standard doses)	Suggested (standard doses)[1]
Apixaban	Suggested	Suggested (standard doses)	Suggested (standard doses)	Suggested (standard doses)[1]
Edoxaban	Suggested	Suggested (standard doses)	Not suggested[2]	Not suggested[2]
Dabigatran	Suggested	Suggested (standard doses)	Not suggested[3]	Not suggested[3]

Table 2. Guidance Statements for DOACs use in Patients with Obesity

DOAC	Sites of absorption	Restrictive procedures (e.g. sleeve gastrectomy)	Malabsorptive procedures (e.g. jejunoileal bypass)	Combined restrictive and malabsorptive procedures (e.g. RYGB)
Apixaban	- Upper GI tract - Colon - Distal small bowel	Unlikely affected	Unlikely affected	Possibly affected
Rivaroxaban	- Stomach - Small bowel	Possibly affected	Possibly affected	Possibly affected
Edoxaban	- Proximal small bowel	Possibly affected	Possibly affected	Possibly affected
Dabigatran	- Stomach - Proximal small bowel	Possibly affected	Possibly affected	Possibly affected

Table 3. Absorption of DOACs in patients who underwent bariatric surgery

	BMI 30 to 39 Kg/m^2	BMI 40 ≥ Kg/m^2	High VTE-risk bariatric surgery with BMI ≤ 50 Kg/m^2	High VTE-risk bariatric surgery with BMI >50 Kg/m^2
VTE treatment	Standard treatment dosing (i.e., 1 mg/Kg every 12 h based on TBW)			
VTE prophylaxis	30 mg every 12 h OR 40 mg every 24 h	Empirically increase by 30% the following: 30 mg every 12 h OR 40 mg every 24 h	40 mg every 12 h	60 mg every 12 h

Table 4. Suggested doses of subcutaneous enoxaparin in adult patients with high BMI and normal kidney function

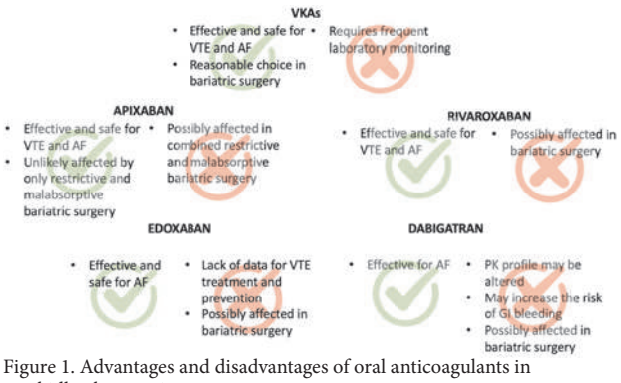

Figure 1. Advantages and disadvantages of oral anticoagulants in morbidly obese patients.

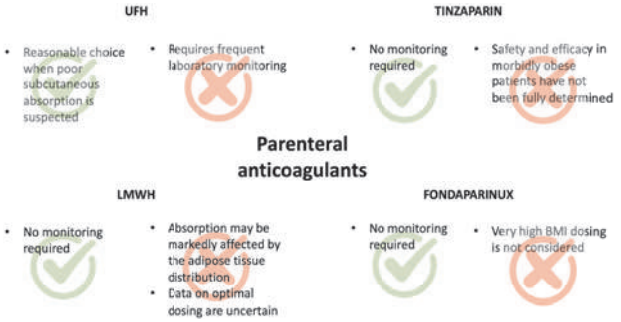

Figure 2. Advantages and disadvantages of parenteral anticoagulants in morbidly obese patients.

A CASE OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGITIIS (EGPA)IN A PATIENT WITH A HISTORY OF ASTHMA AND NASAL POLYPOSIS

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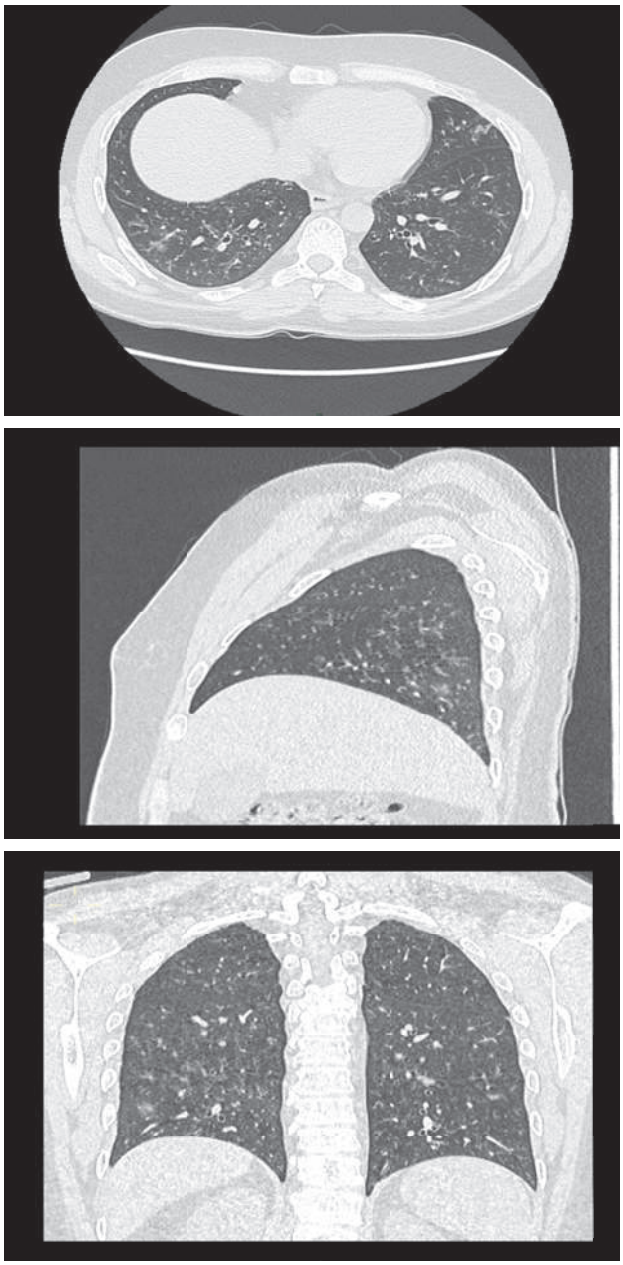
Background: We present a case of a young patient with history of asthma, nasal polyposis, mycotic eosinophilic rhinosinusitis.
Presentation Clinical Case: A 39-year-old man was admitted to the the emergency room(ER) of our hospital for fever ,asthenia, dyspnea and cough. The remote pathological history indicated asthma, multiple surgery treatments for nasal polyposis with histologic report of the presence of eosinophils, allergy to aeroallergens, mycotic eosinophilic rhinosinusitis. During hospitalization was necessary a chest CT scan found in the basal segments of the lower lobes bilaterally with ground-glass attenuation micronodules with a tree-in-bud sign of probable phlogistic significance and moderate pleuricopericardial effusion. Laboratory tests showed elevated phlogosis markers ,hypereosinophilia, positive IgM and IgG antibodies for Mycoplasma pneumoniae and respiratory biofire on positive Mycoplasma pneumoniae swab; negative Chlamydia antibodies. On the patient's medical history and on the suspicion of eosinophilic granulomatosis with polyangiitis, c-ANCA,p-ANCA, Echocardiogram and Cardiac MRI were requested. The laboratory tests indicated high levels of c-ANCA. Echocardiogram showed left ventricular hypertrophy, arrhythmia and mild pericardial effusion. Cardiac MRI confirmed a pattern of pericarditis. The patient was treated with high doses of corticosteroids, immunosuppressive drugs and a monoclonal antibody. periodical follow ups were programmed to evaluate the therapeutic benefits. Clinical and laboratory results were observed at the patient's hospital exit.
Conclusions: Eosinophilic granulomatosis with polyangiitis is a rare case of systemic vasculitis that may be observed almost exclusively in patients with asthma an tissue eosinophilia .Differential diagnosis with other types of pneumonia infections, eosinophilic pneumonias, cryptogenic lung infections has been very important for early diagnosis. Target therapy fundamental to the prevention of damage progression.



EVALUATION OF SELECTED BIOMARKERS OF OXIDATIVE STRESS IN ANDERSON-FABRY DISEASE AND ANALYSIS OF THE FREQUENCY OF MITOCHONDRIAL HAPLOGROUPS IN THE STUDIED SAMPLE

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Background: Fabry disease (FD) is a rare X-linked lysosomal storage disorder. It is characterized by the accumulation of globotriaosylceramide (Gb3) and related glycosphingolipids due to deficient alpha-galactosidase A activity. New evidence suggests that oxidative stress signaling may be crucial in both pathophysiology and disease progression. Mitochondrial DNA (mtDNA) haplogroups could influence the oxidative stress in FD. Patients with FD exhibit elevated lipid and protein oxidative damage, reduced antioxidant defenses, and increased inflammatory biomarkers.
Aims: We evaluated (I) whether there are signs of oxidative stress in blood; (II) if there is an association between oxidative stress biomarkers and clinical manifestations of the disease and/or a difference between the classical form and late-onset variants; and (III) if oxidative stress parameters over time correlate with Lyso-Gb3 and the onset and progression of the disease in a subgroup of 8 treatment-naive patients with normal Lyso-Gb3 levels, to evaluate whether oxidative stress biomarkers might serve as early markers of the disease. This project also aimed to assess the frequency of mitochondrial haplogroups, their potential role in genetic susceptibility in Fabry disease, and whether they could influence the plasma oxidative stress status in these patients.
Methods: Participants admitted to the study were adult individuals of both sexes followed at the Units of the participating centres were caucasian patients aged between 18 and 75 years affected by Fabry Disease (with either clinical or genetic diagnosis). A 2 ml aliquot of blood was collected during the first routine blood draw and frozen at -80 °C until mitochondrial DNA analysis. All Caucasian mitochondrial haplogroups (H, I, J, K, T, U, V, W, and X) of the enrolled patients were evaluated through standard PCR-RFLP techniques along with the following oxidative stress markers: AOPP (advanced oxidation protein products), FRAP (ferric reducing ability of plasma), and total thiol groups. In selected cases, during the course of the disease affecting the patients, the previously evaluated oxidative stress markers (FRAP, AOPP, thiols) were reassessed; a 3 ml blood sample was collected during the first routine blood draw to monitor the patient's clinical status. The results were compared with those obtained from a population of 77 healthy controls (32 men, mean age 61.5 ± 18.2 years) with no familial relationship to the patients, according to the guidelines of the coordinating centre.
Results: The mean values for all oxidative stress parameters in healthy controls were within the normal range, while AOPP levels were significantly higher ($p < 0.00001$), and FRAP and thiols were significantly lower in FD compared to healthy controls ($p < 0.00001$). These parameters did not differ significantly between patients on enzyme replacement therapy (ERT) and non-ERT patients (AOPP: $p = 0.129$, FRAP: $p = 0.441$, thiols: $p = 0.315$), nor by gender ($p = 0.799$ for AOPP, $p = 0.901$ for FRAP, $p = 0.367$ for thiols, respectively), or by age of disease onset. In this study, we observed a significant imbalance in the oxidative stress status in patients with FD at various stages of the disease, including cases where Lyso-Gb3 was normal and organ damage had not yet manifested.
Discussion: Our results confirm the activation of oxidative stress in FD. We observed elevated levels of AOPP and reduced levels of antioxidants (FRAP and thiols) in patients compared to healthy controls. These parameters were altered despite ERT. Considering the studies on oxidative stress published so far, we might hypothesize a vicious cycle between Lyso-Gb3 deposition and oxidative stress: Lyso-Gb3 accumulation induces organ damage, endothelial dysfunction, increased superoxide and free radicals, oxidative DNA damage, and altered oxidative response, which in turn exacerbates organ damage and remodelling. Based on these observations, specific oxidative stress markers could be even more sensitive than Lyso-Gb3 in the early stage of the disease, potentially serving as new early biomarkers with a role in diagnosis and treatment timing. The hypothetical role of mtDNA haplogroups in the pathogenesis of FD remains unclear. It has been proposed that mtDNA haplogroups might be involved in the modulation of oxidative stress in FD. Patients with FD exhibit elevated lipid and protein oxidative damage, reduced antioxidant defences, and increased inflammatory biomarkers. Indeed, the production of reactive oxygen species (ROS) is also physiologically related to different variants of mtDNA, as various mitochondrial haplogroups exhibit functional differences linked to reduced ATP production, increased ROS generation, and diminished calcium buffering. Specific mtDNA haplogroups could lead to varying mitochondrial and mtDNA vulnerability to oxidative stress, potentially affecting different tissues to varying extents, thus modulating the phenotype and natural progression of the disease. The possible role of haplogroups H and I and the HV cluster in FD should be confirmed in larger cohorts, and the assessment of oxidative stress requires further investigation.

RESPIRATORY PHENOTYPE ANALYSIS IN PATIENTS WITH ANDERSON-FABRY DISEASE

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Background and Aims: Fabry disease (FD) is a rare X-linked lysosomal disorder caused by mutations in the *GLA* gene, which encodes the enzyme α-galactosidase. Due to its X-linked inheritance, male patients typically present with more severe forms of the disease, while females show milder to moderate manifestations. The accumulation of globotriaosylceramide (Gb3) in various tissues and organs underlies the clinical manifestations of the disease, which range from muscular involvement to renal, peripheral nervous system, and cardiac complications. FD patients often exhibit poor exercise tolerance and commonly report fatigue, the pathophysiology of which is not yet fully understood. In fact, little is known about the involvement of the respiratory system in patients with FD. In this study, we aimed to analyze the respiratory phenotype in FD patients to better understand the potential role of pulmonary involvement in the onset of fatigue and reduced exercise capacity.
Methods: We enrolled patients diagnosed with FD and performed basic spirometric testing. Spirometry tests that did not meet current guideline standards were excluded from the analysis. Tests suggesting obstructive pulmonary disease were also excluded.
Results: From March 2022 to December 2024, 60 patients with FD and 58 controls matched for age, sex, and comorbidities were enrolled. Table 1 summarizes the main characteristics of the study population and the results of the standard lung functional test.

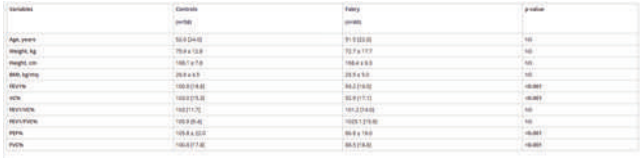

Table 1.

FD patients showed lower percentage values of FEV1, Tidal Volume (VC), PEF, and FVC compared to the control population, while the Tiffenau Index (FEV1/FVC) was similar between the two groups. We then aimed to assess the effect of disease severity on pulmonary involvement by stratifying the population by sex, considering that, as previously mentioned, male patients tend to have more severe forms of the disease than females. As shown in Table 2, when comparing only female FD patients to female controls, FD is still associated with lower percentage values of FEV1 and PEF relative to predicted values.

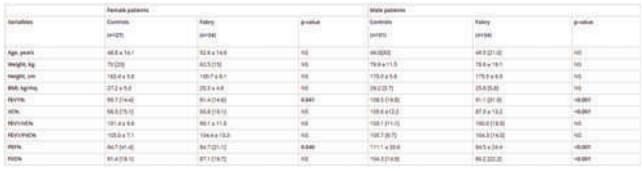

Table 2. Lung functional test results according to sex

These findings were also confirmed in male patients when compared to male controls, where the difference in terms of percentage of predicted FEV1 was even greater (Table 2). This analysis also showed that male patients exhibited reductions in FVC and VC.

Finally, we explored the impact of age on respiratory function in patients with FD by dividing the population into two subgroups using 45 years as the cut-off (< 45 years and ≥ 45 years). Older patients showed greater impairment of the respiratory system, even when compared to age- and sex-matched controls, with a significant reduction in FEV1, VC, PEF, and FVC (Table 3). Surprisingly, younger patients also exhibited comparable results, with a significant reduction in the aforementioned parameters

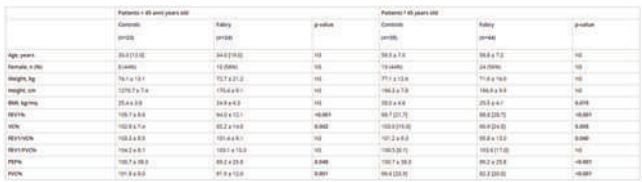

Table 3. Lung functional test results according to age

Conclusions: Patients with Fabry disease, in the absence of underlying obstructive lung disease, exhibit impaired respiratory function as detected by

basic spirometry. Regardless of age, this impairment is significant when compared to a sex- and age-matched control population, although it is more pronounced in patients aged ≥ 45 years. Male patients also show greater respiratory involvement compared to females, consistent with the typically more severe disease phenotype in men. Nevertheless, the mere presence of Fabry disease is associated with detectable alterations in respiratory function, as assessed by basic spirometry.

INFLAMMATORY BOWEL DISEASE IS ASSOCIATED WITH INCREASED INTESTINAL EXTRACHROMOSOMAL CIRCULAR DNA: AN EMERGING BIOMARKER FOR IBD TYPE AND ACTIVITY

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Introduction: Inflammatory Bowel Diseases (IBD) are chronic inflammatory disorders of the gastrointestinal tract, characterized by a relapsing-remitting course, primarily comprising Ulcerative Colitis (UC) and Crohn's Disease (CD). These conditions, which lack a clearly defined cause, pose significant interest to the medical community for identifying reliable predictors of disease progression and treatment response. The specific profile of extrachromosomal circular DNA fragments (eccDNA) has emerged as a promising diagnostic and prognostic biomarker for various types of cancer. However, their role in IBD patients, including the specific gene fragments they carry, has not been thoroughly investigated so far.
Materials and methods: This monocentric, observational, case-controlled study enrolled consecutive patients diagnosed with IBD and non-IBD healthy controls undergoing colonoscopy for colorectal cancer screening. Disease activity in IBD patients was assessed using different scoring systems: the Partial Mayo Score (PMS) and Mayo Endoscopic Subscore (MES) for UC, and the Harvey-Bradshaw Index (HBI) and Simple Endoscopic Score for CD (SES-CD) for CD. Colonic biopsies were obtained from both inflamed and healthy mucosa of IBD patients and from non-IBD controls. Purification of human eccDNA was optimized according to the Circle-Seq method, including eccDNA enrichment, removal of linear and mitochondrial DNA, rolling-circle amplification and sequencing; subsequently, eccDNAs were identified using Circle Finder pipeline. The study compared the relative abundances of genes within eccDNAs between IBD patients and non-IBD controls, focusing on those that were differentially abundant, defined as Differentially Produced per Gene eccDNAs (DPpGCs).
Results: Seventy-one patients with IBD (35 with CD, 36 with UC) and 16 healthy controls (HC) were included in the study. Colonic mucosal samples from IBD patients revealed a higher average abundance of eccDNAs compared to samples from HC. This increase was consistent across all chromosomes, suggesting a global upregulation of eccDNA production throughout the human genome. Furthermore, there was a slight yet statistically significant trend towards larger eccDNAs sizes in IBD patients compared to HC.
Even when considering only eccDNA derived from genic elements ("genic eccDNAs"), IBD patients exhibited a significantly higher abundance of eccDNA in the gut compared to non-IBD controls. Further analysis focused on DPpGCs with a fold change >1 log2 between IBD patients and HC, with a significance threshold of <0.01. Forty-nine genes were found to be enriched in IBD patients, including GRID2 and NRG1. Similarly, in CD patients, 176 genes, such as FGF14, SOX5, and ZBTB20, were significantly enriched compared to HC. In UC patients, 31 genes, including NRG1, SPOCK3, and ATP13A4, showed enrichment compared to HC. Moreover, IBD patients in endoscopic remission (SES-CD < 3, EMS of 0-1) tended to have fewer eccDNAs in their intestines compared to those with active disease, although this difference did not reach statistical significance. Five DPpGCs, including FARS2, HERC3, and PNK2, were identified when applying the aforementioned criteria. When analyzing UC and CD seperately, we found a statistically significant increase of eccDNA production in active UC patients, but not in CD. Furthermore, we saw that NRG1 was significantly overrepresented in patients with active UC, suggesting its role as a UC-specific biomarker.
Conclusions: In conclusion, this study demonstrates a unique pattern of eccDNA production in IBD. We showed that circles harboring specific genes can distinguish UC and CD from healthy controls with statistical significance ($p < 0.01$), indicating that eccDNA profiling might represent a novel diagnostic tool for IBD patients.

THE EFFICACY OF TIPS (TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT) IN ESOPHAGEAL VARICES RESISTANT TO PROPHYLACTIC THERAPY WITH LIGATION AND TO THERAPY WITH BETA BLOCKER

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Introduzione: Le varici esofagee rappresentano ancora oggi una severa complicanza dell'ipertensione portale con un tasso di mortalità ancora elevato. Presentiamo un caso di un giovane uomo di origine Africana che giungeva alla prima osservazione clinica con un quadro di epatopatia cronica evoluta in cirrosi ad eziologia sconosciuta.
Caso Clinico: Un uomo di 45 anni originario dell'Etiopia in Italia stabilmente da molti anni accedeva presso l'Ospedale di Gorizia nel Gennaio 2023 per malessere, astenia e discomfort addominale. All'anamnesi patologica remota e prossima per quanto indagabile (in considerazione della barriera linguistica e della condizione socio-assistenziale non ottimale del paziente) non risultava assunzione di farmaci, esposizione a fattori e comportamenti a rischio nè episodi febbrili ricorrenti. Esame obiettivo nella norma eccetto murmure vescicolare ridotto al campo basale sinistro e dolorabilità alla palpazione profonda in ipocondrio sx, fianco e fossa iliaca sx con milza palpabile 4 cm sotto il margine costale. All'esame emocromocitometrico si evidenziava piastrinopenia severa (PLT 37000x10^3/µL), Hb 13.3 g/dL, formula leucocitaria nella norma. Al profilo coagulativo tempo di protrombina lievemente aumentato (INR 1.43), funzionalità renale nella norma. Indici di citolisi e colestasi lievemente alterati (AST 98 UI/L, ALT 111 UI/L, GGT 145 UI/L, Fosfatasi alcalina 195 UI/L, Bilirubina totale 1.81 mg/dL, Bilirubina diretta 0.95 mg/dL), sintesi epatica nella norma, non carenza marziale nè vitaminica. Esame chimico-fisico delle urine e elettroforesi siero-proteica nella norma. Markers neoplastici (alfa-feto proteina e Ca19.9) negativi. Alla TC addome si riscontrava fegato cirrotico (dimensioni ridotte, profilo parenchimale irregolare, ipertrofia del lobo caudato), splenomegalia severa (21.5 cm) a parenchima omogeneo, senza riscontro di mielofibrosi, non lesioni focali epatiche, minima falda di versamento ascitico in addome. All'esofagogastroduodenoscopia (EGDS) ad aprile 2023 presenza di varici esofagee (F3 sec.Japanese Research Society). Emergeva dunque un quadro di cirrosi epatica nelle classi di Child-Pugh-Turcotte A5 e MELD-Na 13 a causa da determinare. Trasferito a maggio 2023 presso la nostra struttura, Clinica Medica di Udine, si procedeva a esaminare le cause di ipertensione portale escludendo cause infettive di splenomegalia (test per Toxoplasma gondii, Treponema pallidum, Schistosoma negativi), neoplastico-ematologiche (mielofibrosi), cardiologiche, patologie delle vie biliari (autoimmunità negativa per anticorpi ANA, ENA, AMA, ASMA, MPO, LKM-1, PR3, tTG, non colangite sclerosante primitiva alla ColangioRM), non trombosi portale, neoplasie, patologie granulomatose o Sindrome di Budd-Chiari. Escluse cause su base esotossica, dismetabolica, infettiva (sierologie negative per HBV, HCV, CMV, EBV e Idatidosi), cause rare (Wilson, Emocromatosi). Eseguite 2 biopsie epatiche transgiugulari con Hepatic Venous Pressure Gradient (HVPG) marcatamente aumentato (19 mmHg). All'esame istologico metaplasia colangiocitica, lieve infiammazione portale senza steatosi. Pertanto si concludeva per diagnosi di cirrosi epatica criptogenetica (CPT A5, MELD-Na 13). Per le varici esofagee (F3 sec.JRS) eseguite plurime legature con emostasi meccanica (04-07-08-09/2023) con persistenza di varici F2 segni rossi positivi per cui veniva mantenuta profilassi primaria con beta-bloccante. Dopo discussione

collegiale con gli Epatologi del Centro Trapianti di Fegato e i Radiologi Interventisti si procedeva previo consenso informato del paziente a posizionamento di TIPS con netta riduzione del valore di HVPG (4 mmHg). Successivamente il paziente ha presentato Encefalopatia Porto-Sistemica (EPS) di grado 1-2 sec. West-Haven tipo B Overt (Animal test < 10), iperammonemia (229.1 µMol/L), iperbilirubinemia indiretta (circa 4 mg/dL), incremento di lattato deidrogenasi (393 U/L) e aptoglobina consumata (<10 mg/dL). Con avvio di terapia catartica (Lattulosio e Rifaximina orale) passaggio a EPS Covert (Animal test > 15). Escluse altre cause di emolisi tramite studio del profilo trombofilico con tipizzazione linfocitaria per Emoglobinuria Parossistica Notturna (EPN), mutazione per JAK2 negativa, per cui l'iperbilirubinemia indiretta è stata attribuita a emolisi post-TIPS. All'EGDS post-posizionamento TIPS (Luglio 2024) riscontro di varici esofagee di grado F1.
Conclusioni: Le varici esofagee sono una severa complicanza della cirrosi epatica. In questo specifico caso clinico di cirrosi epatica criptogenetica nonostante le ripetute sedute di legatura endoscopica profilattica delle varici non siamo riusciti ad ottenere una completa eradicazione delle stesse. Per la costante presenza di varici F2 con segni rossi positivi abbiamo effettuato la procedura di TIPS che ha permesso di portare il gradiente HVPG nei limiti di norma riducendone il calibro e consentendo (data la ridotta compliance del paziente) la sospensione della terapia con beta bloccante.

EPIDEMIOLOGICAL, GENETIC, AND CLINICAL FEATURES IN ITALIAN AND LEBANESE SUBJECTS WITH FAMILIAL MEDITERRANEAN FEVER (FMF)

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Background: Familial Mediterranean Fever (FMF) is an autoinflammatory hereditary monogenic disease characterized by recurrent febrile painful attacks due to serositis. It is particularly prevalent among ethnic groups in the Mediterranean basin. FMF manifestations can vary significantly among patients living in different Mediterranean regions.
Aims: To compare the demographic and clinical manifestations, along with genetic data, in two well-characterized FMF cohorts residing in Italy (Apulia) and Lebanon.
Methods: We analyzed a cohort of 443 FMF patients, 165 individuals residing in Italy (females: males = 90:75) and 278 (females: males = 173:105) living in Lebanon. We collected demographic data, clinical data, genetic testing (*MEFV* gene), and type of therapy through clinical notes/interviews. Further detailed data were analyzed in two subgroups of Italian (n=54) and Lebanese (n=42) patients using a 55-item questionnaire. Patients were investigated about knowledge, management of the disease, misdiagnoses, attack frequency per year, duration of one attack (days), mean body temperature, prevalence and frequency of symptoms, and severity scores before and after treatment.
Results: In the whole group, Italian patients were significantly (p<0.00001) older (38.5±1.6 vs. 27.0±0.9), older at disease onset (20.8±1.4 vs. 12.5±0.6), at diagnosis (29.4±1.6 vs. 15.4±0.6), and had a longer diagnostic delay (8.4±0.9 vs. 2.9±0.3) than Lebanese patients, respectively. *MEFV* genetic testing showed E148Q, R202Q, and R761H variants were the most prevalent in Italian patients, and M694V and E148Q in Lebanese patients. Italian patients showed a lower prevalence of homozygotes and pathogenic variants than Lebanese patients. The prevalence of major FMF symptoms was significantly lower (p<0.00001) in Italians (10-92%) than in Lebanese patients (30-99%). Italian patients had a lower frequency of attacks per year compared to the Lebanese cohort, while the duration of attacks was comparable. All Italian patients were treated compared to 88.5% of Lebanese patients, where colchicine remained the primary treatment for both groups. However, the use of biological drugs was significantly higher among patients in the Italian cohort. In two subgroups of 54 Italian and 42 Lebanese patients, we showed that smoking habits were comparable, while alcohol consumption was significantly higher in the Italian subgroup. Italian patients reported lower knowledge and a family history of the disease than Lebanese patients. All Italians were on regular medical follow-up, compared to 83.3% of Lebanese patients. Italian patients were mostly diagnosed by internists, and Lebanese by gastroenterologists or pediatricians. Italian patients were more frequently misdiagnosed, often with appendicitis, while Lebanese patients were misdiagnosed with gastrointestinal diseases. Moreover, Italian patients mainly reported a lower frequency of FMF symptoms during attacks associated with lower severity scores before and after treatment compared to Lebanese patients, with a better response to treatment.
Conclusion: In this novel study, we show that FMF epidemiological, genetic, and clinical profiles were different according to the country of residence. In particular, we show that the FMF presentation in the Italian cohort was associated with milder manifestations and better response to treatments in a cohort that was older, older at diagnosis, and onset of disease. Lebanese patients exhibited more symptoms, likely due to a higher prevalence of pathogenic *MEFV* variants. The role of gene-environment interactions across different geographical areas requires further studies.

SAFETY OF ANTICOAGULANT TREATMENT IN PATIENTS WITH SPLANCHNIC VEIN THROMBOSIS AND HISTORY OF PORTAL HYPERTENSION-RELATED BLEEDING

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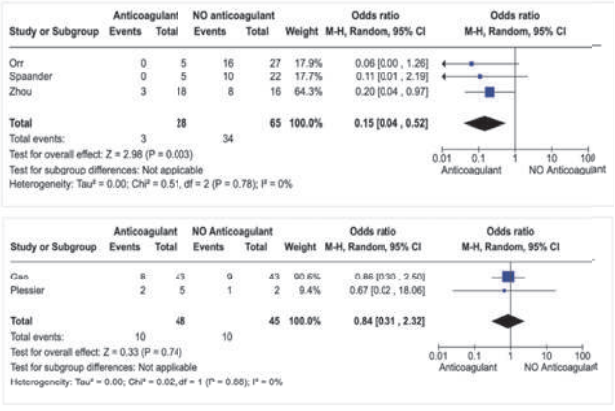
Background & Aims: Splanchnic vein thrombosis (SVT) can be associated to liver cirrhosis, or prothrombotic conditions, including myeloproliferative disorders, intra-abdominal inflammation, solid cancers, or surgery. While anticoagulation therapy improves outcomes in non-cirrhotic patients and reduces all-cause mortality in cirrhotic populations, its safety in patients with a history of portal hypertension (PH)-related bleeding is less clear. This systematic review examines the impact of anticoagulant therapy on re-bleeding risk in SVT patients with a history of PH-related bleeding.Methods: A systematic review and meta-analysis were conducted according to PRISMA guidelines. A comprehensive search of PubMed, Web of Science, and Scopus was performed for studies published up to September 2024. Studies were included if they compared SVT patients with a history of PH-related bleeding receiving anticoagulant therapy versus those not receiving anticoagulants. The primary outcome was the cumulative incidence of PH-related re-bleedings.
Results: Of 2,853 identified studies, five (186 participants) met the inclusion criteria: two randomized controlled trials (RCTs) and three observational studies. The cumulative incidence of PH-related re-bleeding was significantly lower in the anticoagulant group at 17.10% [95% CI 17.02, 17.19] compared to the control group at 40.00% [95% CI 39.90, 40.09]. The overall odds ratio (OR) from observational studies was 0.15 [95% CI 0.04, 0.52], indicating a reduced bleeding risk, while the OR from RCTs was 0.84 [95% CI 0.31, 2.32], showing a non-significant trend.Conclusion: Anticoagulant therapy may reduce re-bleeding risk in SVT patients with a history of PH-related bleeding, but further high-quality studies are needed.



Abbreviations: AC (anticoagulant group), C (control group), CI (confidence interval), NRSs (Non-Randomized Studies), PH (portal hypertension), RCTs (Randomized Controlled Trials), SVT (splanchnic vein thrombosis).

PLASMA AMMONIA LEVELS OVER THE COURSE OF A HOSPITALISATION FOR OVERT HEPATIC ENCEPHALOPATHY

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Background: and aim: The diagnostic and prognostic role of ammonia in the assessment of Overt Hepatic Encephalopathy (OHE) remains debated. The aim of the present study was to assess the time-course of ammonia levels during a OHE-related hospitalisation in relation to OHE duration/severity and the length of hospitalisation.
Methods: All the 104 patients (males=77%; mean yrs of age =72±11) admitted into the Liver Unit, Internal Medicine Ward 5, Padova University Hospital (Italy) between January 2021 and July 2024 with a verified discharge diagnosis of OHE were included. Clinical and laboratory indices, including ammonia levels prior to (within 6 months before admission), during (average of 3 measurements, up to 10) and after (within 6 months after discharge) the hospitalisation were recorded, along with the duration of the hospitalisation, precipitants, ammonia-lowering treatment and psychoactive treatment, where applicable.
Results: Over the studied time frame, 58 (56%) patients had single OHE hospitalisations while 20 (19%) had 2-7 OHE hospitalisations. Of the 104 hospitalisations, 31 (30%) were for grade II, 66 (63%) grade III and 7 (7%) grade IV OHE. Of the 58 single hospitalisations, 23 (40%) were for grade II, 33 (57%) for grade III and 2 (3%) for grade IV OHE. Ammonia levels increased progressively and significantly with increasing OHE grade (II: 118±47 umol/L; III: 155±62; IV: 219±65; p<0.001, post hoc significant for grade II vs grade III and IV, p<0.05 and p<0.01 respectively). Ammonia levels prior to admission/after discharge (87±35 umol/L and 79±42 umol/L, respectively) were significantly lower than those on admission (148±63 umol/L; p<0.0001). Hospitalisations for grade IV OHE were longer (12.3±6.5 days) than those for grades III (5.8±4.8 days; p<0.01). Patients qualified as not fully recovered on discharge had lower levels of ammonia on admission (124±60 umol/L) compared to their counterparts who recovered completely (155±63 umol/L; p<0.05). Similarly, ammonia levels on admission were significantly lower in patients on chronic treatment with psychoactive drugs (117±57 umol/L vs. 158±62; p<0.01). All the above held true when analyses were restricted to the 58 single hospitalisations.
Conclusions: Ammonia levels correlated with OHE presence and severity, and with the duration of hospitalisation. Incomplete recovery and chronic treatment with psychoactive drugs were associated with lower ammonia levels, suggesting confounding in the expression of the OHE phenotype.

GUT MICROBIOTA SIGNATURE IN PATIENTS WITH ARTHERIAL HYPERTENSION: A ROLE FOR MICROBIALLY CONJUGATED BILE ACIDS?

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Artheryal hypertension (AI) is a major global health concern and a leading risk factor for cardiovascular morbidity and mortality, especially when associated with metabolic syndrome (MS). An impaired BA metabolism is a significant contributor factor in metabolic syndrome (MetS) and an inverse relation between conjugated BA levels and systolic blood pressure has emerged1. Moreover, emerging evidence revealed that a dysbalanced composition of gut microbiota (GM), a condition called dysbiosis, is associated not only to an impaired BA metabolism, but also with AI2. In this study, we aimed to characterize the GM composition in 94 patients with MS patients by 16S rRNA sequencing. Participants underwent clinical anamnesis, and a complete clinical and biochemical assessment. All criteria for MS, namely waste circumference, HDL-cholesterol, fasting glycemia, AI, and triglyceride scores, were used separately to stratify patients. GM composition was analyzed over these subgroups. Differently from other MS criteria, patients' stratification according to AI was the only criteria showing a significant difference in terms of GM α- and β-diversity. We identified 35 differentially abundant taxa and, among them, 25 differentially abundant genera in patients with AI when compared to patients without AI. We observed a higher abundance of Actinobacteriota in patients without AI from Phylum to genus levels. In particular, this differential abundance was represented by the Clavibacter genus. Also, the order Bacillales_A and its genus Rummeliibacillus was over-represented in patients without AI. The genera most represented in patients with AI were CAG-485, Ruminococcus_F, Aphodomorpha, Brochothrix, Psychrobacter, Lentilactobacillus, and Negativibacillus. Within the Firmicutes, an interesting hit was represented by the genera Enterocloster, significantly lower in patients with AI. Enterocloster, and in particular Enterocloster Boltae, can conjugate bile acid (BAs) generating the so-called Microbially Conjugated Bile Acids (MCBAs)3, a relatively recent discovery in the GM field, representing a unique class of BAs conjugated in the gut and not in the liver. In particular, Entercloster has been shown to conjugate Cholic acid with the aminoacids glycine, tyrosine and phenylalanine. MCBAs have been suggested to play a role in regulating blood pressure with different mechanisms, such as regulating renal water and electrolytes homeostasis, reducing vascular resistance and modulating inflammatory pathways in the gut-liver axis, indirectly influencing blood pressure. Therefore, Given the inverse relationship between conjugated bile acids and systolic blood pressure, lack of Enterocloster in AI patients likely suggests a potential mechanistic link. These findings place Enterocloster and MCBA pathways as promising biomarkers and therapeutic targets in AI. Further studies are ongoing in an independent cohort of patients with AI to validate these associations.

AUTOMATED GENERATION OF ARTIFICIAL INTELLIGENCE BASED FLASHCARDS FOR EMERGENCY MEDICINE: A TOOL FOR RESIDENT TRAINING AND CLINICAL DECISION SUPPORT

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Introduction: Emergency Medicine (EM) training requires fast, effective educational tools to support learning in high-pressure clinical environments. Flashcards are widely used to reinforce knowledge and promote active recall. Recently, Large Language Models (LLMs), such as those developed by OpenAI, have shown promise in automatically generating high-quality medical education content.
Aim: To evaluate the quality and reliability of flashcards automatically generated by LLMs for Emergency Medicine training, compared with manually curated content developed by clinical experts, through a dedicated app containing both versions for randomized review and evaluation.
Materials and methods: In the first development phase, a team of physicians manually created a set of flashcards based on current clinical guidelines. A multidisciplinary group of clinicians and computer scientists designed an automated content generation process using OpenAI's platform, refining the prompts through iterative feedback and review. An internal validation was conducted by comparing AI-generated flashcards to the manually curated ones using semantic similarity metrics (cosine similarity, Word Mover's Distance WMD) and expert clinical evaluations (Likert scales) measuring clarity, accuracy, relevance, and informativeness.
Results: LLM-generated flashcards demonstrated high semantic alignment with manual content (cosine similarity = 0.86; CI 0.84–0.87; WMD = 0.13; CI 0.12–0.14). Clinical reviewers gave high ratings for clarity (4.86/5), correctness (4.84/5), and relevance (4.82/5), though informativeness was slightly lower (4.42/5), due to occasional omissions in differential diagnosis, diagnostic workup, or guideline updates.
Conclusions: The internal validation phase confirmed that LLMs can rapidly generate reliable and educationally sound flashcards for Emergency Medicine residents. However, human oversight remains essential to ensure content completeness and accuracy. A multicenter external validation phase is now underway through a dedicated app, involving over 200 Italian EM residents. Additionally, a cohort of residents from Yale University is contributing to the qualitative evaluation, offering international insights to refine and enhance the automated content generation process.

EVALUATION OF THE COLONIZATION AND MODIFICATION OF THE GUT MICROBIOTA BY A STRAIN OF L REUTERI LMG-P 27481 IN HEALTHY SUBJECTS: A PILOT INTERVENTIONAL STUDY

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Background: Many literature studies reported the beneficial effects of probiotics on human health, but few articles have evaluated the "real effects" on the modulation of microbiota after their use. *Lactobacillus reuteri* is one of the most studied probiotic with the best effects on gut microbiota.
Aims: The primary aim of our study was the evaluation of the intestinal col-

onization by a probiotic strain *L reuteri-LMG P 27481* administered orally for 28 days and the effects on the modification of the gut bacterial flora through the analysis of the gut microbiota. The secondary aim was the evaluation of side effects through a validated scale known as Gastrointestinal Symptom Rating Scale (GSRS).
Patients and Methods: This is an interventional, open-label, single-center study conducted on 20 healthy adults (10 men and 10 women M/F; mean age 34 +15) selected from the staff of San Carlo di Nancy Hospital from September to December 2024 who received for 28 consecutive days a probiotic Reuterin® LMG (L. reuteri LMG P 27481) in drops at a concentration of 1x10^9 (5 drops per day). Microbiota analysis was performed (Genomix4Life S.r.l. Salerno, at enrollment (T0), at the end of probiotic supplementation (T1) and after a 14-day follow-up period (T2).
Results: Our study not highlighted a significative gut colonization by the administered probiotic, but we observed interesting quantitative and functional variations. Regarding the *Firmicutes/Bacterioidetes* ratio, the change from T0: 1.08% → T2: 1.21% was recorded; with an increase in *Firmicutes* from T0: 40% to T1: 41.3% and decrease of *Bacterioidetes* from T0 48.9% to T1 45.5%. The biodiversity index (Shannon) remained almost stable throughout the observation period (T0: 0.27 → T2: 0.26). Intestinal permeability, on the other hand, showed a reduction (T0: 27.9 → T1: 22), with an increase in the "barrier effect" (from T0: 30.1 to T1 34.9). The dysbiosis index showed minimal changes in the eubiotic sense (from T0: 42.7 to T1: 40.9). Short-chain fatty acids (SCFA), key products of microbial fermentative activity and indicators of epithelial and immune health, showed an increase (T0: 24 → T2: 26). The absence of unexpected systemic effects highlighted a high safety profile. 80% of patients reported a reduction in abdominal pain, an increase in the number of evacuations /week for patients suffering from constipation.
Conclusions: The intake of *Lactobacillus reuteri LMG-P 27481* in healthy subjects showed transitory variations in some functional and metabolic gut functions, especially an improvement in the barrier effect and intestinal permeability. These results support the safety of the product, but further investigations are needed in specific clinical contexts (subjects with dysbiosis, IBS or in post-antibiotic follow-up). The absence of colonization raises questions about the actual usefulness of the strain in conditions of eubiosis, suggesting that future studies should include target populations with greater range for modulation of the microbiota.

UNUSUAL ASSOCIATION OF CERVICAL LYMPHADENOPATHY AND DILATED CARDIOMYOPATHY: A DIAGNOSTIC CHALLENGE

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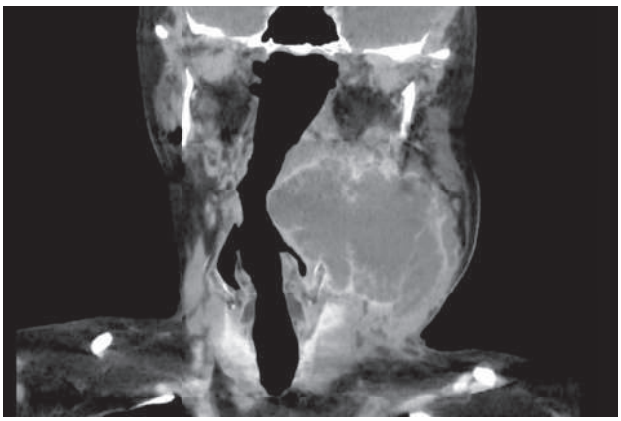
Clinical Case: A 59-year-old man with no relevant medical history presented to the Emergency Department with a two-week history of left laterocervical swelling and local inflammatory signs. Neck ultrasound showed multiple lymphadenopathies. On admission, he was hemodynamically stable and afebrile. Contrast-enhanced CT of the face and neck confirmed a large, heterogeneous, multicystic left laterocervical mass with necrotic areas and compression of adjacent structures (Figure 1).



An ENT evaluation raised suspicion of a lymphoproliferative disorder. The patient was admitted and underwent fine-needle aspiration and core needle biopsy. Empiric corticosteroids and prophylactic antibiotics were started.
Whole-body CT, performed due to suspected malignancy, revealed thrombosis of a distal branch of the left renal artery with associated renal infarction.
Considering a possible cardioembolic source, transthoracic echocardiography showed severe global systolic dysfunction, mild left ventricular dilation, and mid-to-basal akinesia of the lateral and inferior walls. Cardiac MRI confirmed these findings. The patient reported no symptoms of myocarditis or coronary syndrome which was ruled out by coronary angiography. The findings were also consistent with primary dilated hypokinetic cardiomyopathy, so genetic testing was performed.
During hospitalization, the swelling and local inflammation gradually improved. Blood tests showed mild neutrophilic leukocytosis with normal inflammatory markers. Serologies for HIV, EBV, CMV, Leishmania, and Toxoplasma were negative, as was Quantiferon-TB. Biopsy cultures were negative. Both fine-needle aspiration and core biopsy showed necrotic-inflammatory material with no neoplastic cells. Corticosteroids were tapered and discontinued in order to repeat histological assessment.
At discharge, the diagnosis remained unclear, with a lymphoproliferative disorder as the leading hypothesis. While awaiting definitive histology, if a malignancy is confirmed, paraneoplastic ventricular dysfunction should be considered, given the exclusion of ischemic, myocarditic, and known genetic causes.

INCIDENCE AND PREDICTORS OF PROXIMAL EXTENSION RATE OF DISTAL DEEP VEIN THROMBOSIS IN INTERNAL MEDICINE WARD: A PROSEPCTIVE MULTICENTER EVALUATION FROM THE AURELIO STUDY

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Introduction: Venous thromboembolism (VTE) represents a significant cause of morbidity and mortality in hospitalized medical patients, with distal deep vein thrombosis (DDVT) being a common and undervalued subtype. DDVTs are often perceived as self-limiting and less dangerous. However, DDVT can lead to potentially serious complications, such as pulmonary embolism (PE), underscoring the need for careful evaluation and management. Although DDVTs are generally considered less severe than proximal DVT, the clinical course remains a subject of considerable interest. A subset of DDVT may extend proximally, posing a significant risk for PE. However, the incidence of DDVT in the medical inpatient population, the specific characteristics of patients particularly predisposed to these types of thromboses, and the proportion of these thrombi that progress proximally remain poorly characterized in the literature.
The aim of this study is to evaluate the incidence of asymptomatic DDVT at admission and DDVT during hospitalization, as well as to assess the clinical factors associated with these thrombotic events.
Materials and methods: This multicenter, prospective observational study was conducted in 8 internal medicine wards throughout Italy. Centers were affiliated with the Ultrasound Study Group of the Italian Society of Internal Medicine enrolling from 2015 to 2024, 1,458 consecutive adult patients with acute medical conditions requiring hospitalization. Exclusion criteria included hospitalization for less than 5 days, anticoagulant therapy at admission, acute symptomatic VTE, major bleeding, recent surgery. CUS and color Doppler ultrasonography were performed within 2 days from admission and at discharge. Study outcomes included the rate of asymptomatic DDVT at admission, DDVT during hospitalization, and the analysis of the factors associated with thrombotic events.

Results: A total of 1,458 patients (737 females, mean age 71 16 years) were recruited. The mean length of hospital stay was 13 days. Asymptomatic thrombosis involving the distal venous system was detected in 59 patients (4%) upon admission; of these, 28 were IDDVT, representing nearly half of the diagnosed thromboses (47%). Compared to patients without vein thrombosis, those with asymptomatic thrombosis were older and had higher D-dimer levels, IMPROVE and PADUA scores. All patients with asymptomatic DDVT at admission were promptly treated with a therapeutic dosage of anticoagulants. 266 out of 1,399 patients (19%) without asymptomatic DDVT received prophylaxis with parenteral anticoagulants; they were older and exhibited higher rates of hypertension, acute infection, pneumonia, active cancer, previous VTE and reduced mobility. They also had elevated D-dimer levels and higher PADUA and IMPROVE scores. At discharge, 9 additional cases of DDVT were identified (3 IDDVT [33%] and 6 DDVT).
68 DDVT were observed during hospitalization, of which 46% IDDVTs and 54% involved the distal system and extended to the proximal system. No significant differences were observed in the main clinical characteristics between the two groups. At univariate analysis, patients with DDVT were older, had a higher BMI, a higher frequency of active cancer, reduced mobility, higher D-dimer levels, lower albumin levels. A multivariate analysis identified variables associated with DDVT revealing significant associations with reduced mobility and active cancer. To analyze the variables associated with IDDVT, which was observed in 2.6% of patients, a univariate analysis and a logistic regression analysis identified pneumonia and active cancer as significant determinants of DDVT.
Discussion: The AURELIO study demonstrated that DDVT are relatively common among hospitalized medical patients. In approximately 50% of cases, the distal thromboses extended into the proximal venous system. This finding is highly significant as it indicates that IDDVT might have complications, including progression to the proximal venous system. In the AURELIO study, 50% of included DDVT patients had thromboses involving the proximal venous system. Unlike previous studies, which did not examine these outcomes in acutely hospitalized medical patients, the AURELIO study stands out due to its prospective design. Multivariate analysis of the determinants of IDDVT underscores the significance of active malignancies as a primary risk factor in hospitalized medical patients. In this regard, a study by Dentali et al highlighted that symptomatic IDDVT in patients with active cancer are associated with a high risk of thromboembolic recurrence (13.2% per year).
Limitations of the study include the relatively small number of thrombotic events and the lack of detailed anatomical and thrombus type information on the specific distal sites affected. An additional limitation is the lack of follow-up after hospital discharge.
In conclusion, this study highlights the high prevalence of DDVT in hospitalized medical patients and underscores the need to consider their potential complications, including a high risk of proximal extension and subsequent thromboembolic events.

PARAINFECTIOUS NECROTIZING MYOSITIS WITH SEVERE DYSPHAGIA, LARYNGOPHARYNGEAL CANDIDIASIS AND MULTIFOCAL PNEUMONIA: A COMPLEX CLINICAL CASE

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Case presentation: A 50-year-old male patient, with a history of bilateral orchiectomy for seminoma receiving testosterone replacement therapy, was admitted to the emergency department with a one-month history of progressively worsening pharyngodynia, high fever, erythematous/crusted skin petechiae and dysphagia, followed by diffuse myalgias and worsening proximal muscle weakness. Laboratory tests showed high levels of creatine kinase (up to22,500/mm^3), systemic inflammation, neutrophilic leukocytosis (increase up to22.500/mmc), and anemia with hemoglobin from16g/dL to9g/dL. Upper gastrointestinal endoscopy and nasal fibroscopy were performed and showed pharyngo-laryngeal candidiasis.
PET/CT and contrast-enhanced CT scan revealed extensive bilateral muscle involvement and also pulmonary infiltrates, leading to acute respiratory failure. Muscle biopsy showed specific characteristics of necrosis and inflammatory infiltrate, whereas autoimmunity testing was non-specific and inconclusive. With EMG excluding neurological causes of muscular necrosis, a diagnosis of necrotizing inflammatory miopathy was made, with a systemic involvement, complicated by severe dysphagia due to a combination of pharyngolaryngeal muscular involvement and candidiasis, following a flu-like sindrome. Treatment with corticosteroids, intravenous immunoglobulins and antifungal agents, led to clinical, laboratory, and radiological improvement, with a reduction of serum creatinkinase levels, resolution of candidiasis, and improvement in pulmonary function. Dysphagia represented the most slowly resolving symptom, necessitating targeted swallowing rehabilitation, but ultimately resulting in complete functional recovery.
Discussion: Necrotizing inflammatory myopathies (IMNM) are a very rare and severe subgroup of inflammatory myopathies, frequently characterized by massive muscle necrosis with mild inflammatory infiltrate. The parainfectious form is even more rare and less documented, especially when associated with mucosal candidiasis and multifocal pneumonia.
This case documents a IMNM following a flu-like syndrome, with a multisystemic presentation, potentially leading to critical illness for acute respiratory failure, and showing ubiquitous muscular involvement, including those responsible for swallowing. The slow but progressive improvement following immunomodulatory therapy is consistent with the clinical course of this condition, which is known to have a variable prognosis.

CASE REPORT: DE NOVO MUTATION OF A-GALACTOSIDASE A IN A FEMALE PATIENT WITH END-STAGE RENAL DISEASE: REPORT OF A CASE OF LATE DIAGNOSIS OF ANDERSON-FABRY DISEASE

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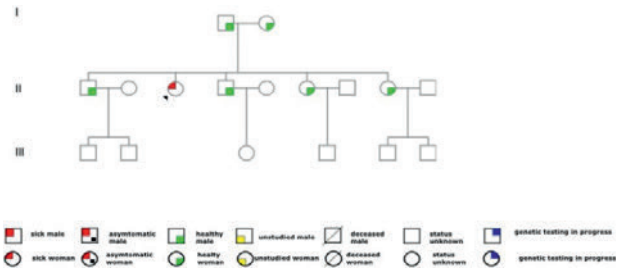
Background: Anderson–Fabry disease (AFD) is an X-linked disease that results from reduced activity of the enzyme galactosidase alpha (GLA). When the GLA gene sequence is altered by mutations that alter the normal DNA sequence, variants of the alpha-galactosidase A enzyme are produced, which may or may not function. These mutations are responsible for Fabry disease, and to date, over 800 different mutations of the gene have been described in patients with Anderson–Fabry disease. In this case, we report the case of a woman who is the sole family member with this type of mutation.
Case presentation: We report a case of a 52-year-old woman with end-stage chronic kidney disease in dialysis treatment. The patient's alpha-galactosidase activity was 6.6 nmol/ml/h in whole blood, and lyso-GB3levels were 11.45 nmol/L (normal range < 2.3nmol/L). Alpha-galactosidase A gene sequence analysis revealed a pathogenic variant of c.947dupT in exon 6, leading to the p. I317NfsTer16 amino acid substitution. The genetic analysis did not detect the same mutation in any of the other screened family members. The patient exhibited 24h pathological proteinuria in blood chemistry analysis; the electrocardiogram documented sinus rhythm at a heart rate of 72bpm, left ventricular hypertrophy with overload, and abnormalities of the atriogram. Echocardiography documented a normal-sized left ventricle with concentric hypertrophy. Once this pathology was documented, the patient underwent drug therapy with agalsidase beta. It was considered appropriate to deepen the patient's diagnostic process by performing a skin biopsy, and histological examination showed the presence of neuropathy of the small fibres with predominantly somatic involvement, with positivity forGb3.
The patient was administered therapy with agalsidase beta at a dose of 1mg/kg once every 2weeks intravenously. Comorbid therapy was optimised by inserting ACE-I and drugs for neuropathic pain, considering the presence of acroparesthesia. In particular, regarding her known small fibre neuropathy, she complained of burning pain, allodynia, needle sensation of the extremities, and hyperaesthesia.
Conclusion: The international Fabry disease genotype-phenotype database (dbFGP) reports a pathogenic variant c.947dupT in exon 6 that is probably associated with a classical phenotype of Fabry disease. In this case report, we report the case of a woman who is the sole family member with this type of pathogenic variant. Similar situations have not been described in the literature for this pathogenic variant, and it represents an important case of inter- and intrafamilial variability in patients with Fabry disease. The literature shows that de novo pathogenic variants are frequently found in the context of Fabry disease.
The detection of a de novo mutation in just one family member is a rare occurrence that highlights the importance of genetic counselling, early diagnosis, and, finally, extended genetic screening for Fabry disease in patients affected by renal disease of unknown aetiology.



DIFFUSE MYALGIAS AND ASTHENIA IN A PATIENT WITH AN ATYPICAL PRESENTATION OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

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Case presentation: A 61-year-old patient was admitted to the hospital after a mild flu-like syndrome, followed by the onset of muscular symptoms (disabling myalgias particularly in upper limbs and muscle fatigability with preserved strengt) worsening over the course of a few weeks, associated with subtle respiratory signs (mild anterior rhinorrhea).He had a history of childhood asthma, persistent nasal congestion for approximately one year and a hyperCKemia (with usual CK around 500 IU/L) that developed five years before.
Physical examination at admission was normal. Laboratory tests showed marked eosinophilia (7230/μL), elevated creatin kinase levels (930 IU/L) associated with moderately elevated CRP and ESR levels. Hepatic, cholestasis and renal indices were normal. Electromyography was performed and found to be normal. In the suspicion of a vasculitic process, further laboratory tests were obtained, that showed the presence of a high pANCA IgG (anti-MPO) titer (>134 U/mL) and elevated IgG4 levels.A CT scan was also performed, which showed patchy ground-glass peribronchial opacities and inflammatory involvement of the frontal and ethmoidal maxillary sinuses. No lesion suggestive for malignancy was observed.To exclude an infectious etiology, microbiological tests were requested on blood, urine and feces and resulted negative, as did serological testing.Respiratory signs associated with history of asthma and pANCA positivity with hypereosinophilia and typical radiological picture, were suggestive for the diagnosis of Eosinophilic Granulomatosis with Polyangiitis.To support this diagnosis, a nasal biopsy was performed, showing plasma cell infiltration without the typical findings of vasculitis. In the hypotesis of EGPA, high-dose corticosteroid therapy was initiated alongside biologic treatment with mepolizumab, with rapid clinical improvement and almost complete resolution of symptoms. Therefore, eosinophilia resolved, inflammatory markers normalized, and creatine kinase levels returned to baseline.Discussion Eosinophilic Granulomatosis with Polyangiitis (EGPA) is a rare ANCA-associated vasculitis, characterized by asthma, nasal polyps, blood eosinophilia and multiorgan systemic involvement. Muscular manifestations are unusual and rarely associated with elevated creatine kinase levels and myalgias. This case highlights the importance of considering EGPA even in case of atypical presentation such as predominant muscular symptoms and elevated creatin kinase levels.The absence of histologically confirmed vasculitis associated with elevated serum IgG4 and the response to biologic treatment suggest the diagnosis of EGPA and a possible overlap with IgG4-related disease.

ABSENCE OF CILIARY ARTERY OCCLUSION DOES NOT EXCLUDE ARTERITIC ANTERIOR ISCHEMIC OPTIC NEUROPATHY (A-AION): DIAGNOSTIC AND PATHOPHYSIOLOGIC IMPLICATIONS

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Introduction: Giant Cell Arteritis (GCA) is the most common vasculitis in the elderly. Ocular involvement by GCA occurs in up to a quarter of subjects, resulting in persistent visual loss in about 80% of them. This represent a medical emergency due to the high risk of progression to complete blindness and bilateral involvement, which high-dose steroids can prevent.
The most common site suffering from ischemia in ocular GCA is the optic nerve head, resulting in a condition known as Arteritic-Anterior Ischemic Optic Neuropathy (A-AION). Ocular ischemia frequently ensues in the early disease course, before a diagnosis of GCA has been made. Moreover, ocular involvement occurs in the absence of other GCA symptoms in about 20% of patients and may be a clue for diagnosing vasculitis and beginning therapies. However, AION is not specific for GCA. Rather, "non-arteritic"-AION (ie, NA-AION, which occurs in patients without GCA) is ~6 times more frequent than A-AION. Therefore, differentiation between the two, NA-AION and A-AION, is crucial for therapeutic implications. Traditionally, NA-AION and A-AION are believed to have different pathophysiology. At the optic nerve head, nervous fibres cross the inextensible fibrous envelope of the eye at the lamina cribrosa: in the case of a highly crowded crossing due to anatomical features, a transient hypoperfusion causing fibre swelling may trigger a compartmental syndrome, resulting in NA-AION. On the contrary, A-AION is believed to derive from the vasculitic occlusion of the posterior ciliary arteries. Thus, differential diagnosis of NA-AION and A-AION is based on semeiotic features of severe optic nerve ischemia and of ciliary arteries occlusion, which are considered as markers of A-AION and therefore of GCA. Recent reports have suggested that this may not always be true.
Using one of the largest ocular-GCA cohorts in the world, we aimed to i) verify if A-AION can occur in the absence of signs of ciliary artery occlusion, and ii) assess the frequency of such disease phenotype.
Methods: Monocentric observational cohort study on the incident patients with GCA and AION at ASST Fatebenefratelli-Sacco in Milan from January 2019 to April 2025. All patients met the 2022 ACR/EULAR classification criteria for GCA and were characterized by systemic and ophthalmologic features (ie, visual acuity, fundus semeiotic, fluorescence angiography, and optic coherence tomography -OCT). AION was recognized on the basis of fundus and OCT features. A-AION subjects without evidence of ciliary artery occlusion were defined by the absence of any of the following: chalky white optic disk at fundus and delayed choroidal perfusion at indocyanine green angiography.
Results: Among 126 eyes in 98 ocular GCA patients, 83 (66%) eyes in 65 (66%) patients were associated with AION. Of these, 9 eyes (11%) in 8 patients (12%) had no evidence of ciliary artery occlusion. These subjects had an ophthalmologic presentation indistinguishable from NA-AION and presented with an altitudinal visual field defect. Sex and age were similar between A-AION with or without evidence of arterial occlusion (p=0.369 and 0.148, respectively). A-AION was preceded by amaurosis and/or diplopia in 2/9 eyes without arterial occlusion (22%) and in 12/74 (16%) yes with ciliary artery occlusion (p=0.583). Despite proven vasculitis (by total body MR/PET, echo or temporal artery biopsy), the sensitivity of temporal artery biopsy tended to be lower in the subjects without evidence of ciliary arterial occlusion (29% vs. 73%, p=0.135). Moreover, A-AION subjects without ciliary artery occlusion had lower plasma levels of C-reactive protein [5.3 (2.7 to 16.3) vs. 40.5 (18.25 to 90.75) mg/L, p<0.001], erythrocyte sedimentation rate [53 (38 to 74) vs. 89 (55 to 115) mm/h, p=0.030] and platelet count [262 (231 to 307) vs. 433 (336 to 469)*10^9/L, p=0.002]. Plasma fibrinogen levels and leukocyte count were similar in subjects with or without ciliary artery occlusion. Fundoscopy showed signs of risk of developing a compartmental syndrome in the optic nerve head (ie, a small/crowded optic disk) in all subjects without evidence of ciliary artery occlusion.
Conclusions: A-AION is not always caused by ciliary artery occlusion, which occurs in 85-90% of cases. In the remaining cases, ophthalmologic features are indistinguishable from NA-AION, and GCA was revealed by elevation of inflammatory markers and imaging/biopsy and/or clinical symptoms. We conclude that all patients with AION should undergo GCA screening (at least clinical symptoms and inflammatory markers). In the case of suspected GCA without ciliary artery occlusion, imaging of large-vessel vasculitis is suggested, as temporal artery biopsy might be less sensitive than in typical cases. The mechanism of AION without ciliary artery occlusion is likely a compartmental syndrome due to optic nerve hypoperfusion because of sub-occlusive arteritic involvement.

EFFICACY OF A MULTIDISCIPLINARY CLINIC IN IMPROVING CARDIOVASCULAR AND LIVER OUTCOMES IN METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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Background: Cardiovascular disease (CVD) is the leading cause of mortality in metabolic dysfunction-associated steatotic liver disease (MASLD) patients. Guidelines recommend a multidisciplinary approach, but real-world data are limited.
Aims: This study aimed to assess the efficacy of a multidisciplinary MASLD clinic in optimising control of metabolic comorbidities and liver injury markers.
Method: We conducted a retrospective analysis of 465 patients seen in a multidisciplinary MASLD clinic from June 2014 to June 2024. All participants were evaluated by both a hepatologist and an expert in cardiovascular disease. Patients were referred directly from primary care or through the Camden and Islington MASLD Pathway (London, UK), which involved a FIB-4 and, if needed, an ELF score.
Each patient received a comprehensive hepatological assessment, cardiovascular risk assessment and management, and, where required, dietary counselling by a dietician. Diagnostic criteria for comorbidities, including hypertension, type II diabetes, dyslipidaemia, and obesity, were based on recognised clinical guidelines. Cardiovascular risk was assessed using the QRISK-3 Score, with statins recommended for patients with a ≥10% 10-year CVD risk or a history of cardiovascular events. Baseline and follow-up data on anthropometry, blood pressure, and laboratory values were collected.
Primary endpoints were changes in liver injury markers (transaminases, LSM) and metabolic comorbidities (e.g., blood pressure, HbA1c, lipid profile, and QRISK-3 Score).
Results: The mean age of 465 patients was 57 ± 12 years, 56% were males, and 54% Caucasian. Hypertension, diabetes, and dyslipidaemia were present in 66%, 56%, and 84% of patients, respectively.
At baseline, 65% had abnormal ALT, while LSM, measured in 95% of patients, had a median of 7.9 kPa. Of 190 liver biopsies ,79% showed steatohepatitis, with bridging fibrosis in 29% and cirrhosis in 14%. At a 15-month median follow-up, 61% of patients remained under secondary care, with significant improvements observed in ALT ($p<0.001$), AST ($p<0.001$), GGT ($p<0.001$), total cholesterol ($p<0.001$), LDL-c ($p<0.001$), TG ($p=0.007$), systolic and diastolic blood pressure ($p<0.001$ and $p=0.001$), weight ($p<0.001$), BMI ($p<0.001$), LSM ($p=0.020$), and QRISK-3 Score ($p=0.002$). Waist circumference decreased significantly in obese patients, with 12% achieving ≥10% weight loss.
Therapy adjustments improved metabolic markers, notably HbA1c, blood pressure, and lipid profile in patients with diabetes, hypertension, and dyslipidaemia, respectively.
Conclusion: A multidisciplinary approach to MASLD effectively improves liver and CV risk markers. Long-term collaboration between primary and secondary care is crucial to achieve and maintain these health improvements.

LOMITAPIDE-INDUCED FATTY LIVER IS A REVERSIBLE CONDITION: EVIDENCE FROM A CASE OF FAMILIAL CHYLOMICRONEMIA SYNDROME

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Familial chylomicronemia syndrome (FCS) is a rare autosomal recessive disorder caused by biallelic loss-of-function variants in genes coding for lipoprotein lipase (LPL) enzyme and its co-factors (APOC2, APOA5, LMF1, and GPIHBP1) (1). These genetic defects lead to severe impairment of hydrolysis of triglyceride-rich lipoproteins (TRLs), mainly of those of intestinal origin (chylomicrons). This causes severe hypertriglyceridemia (sHTG) with levels commonly exceeding 2000 mg/d. Clinically, FCS is characterized by recurrent episodes of acute pancreatitis (AP), a potentially life-threatening condition, as well as hepatosplenomegaly, lipemia retinalis, and other metabolic complications. Conventional TG-lowering therapies (eg. Fibrates, omega-3) are poorly effective in FCS, thus requiring the search of novel treatments.
Lomitapide, an inhibitor of microsomal triglyceride transfer protein (MTP), has demonstrated efficacy in reducing TG levels in FCS. MTP is a key protein involved in the assembly and secretion of apolipoprotein B-containing lipoproteins, such as very-low-density lipoproteins (VLDL) in the liver and chylomicrons in the intestine. By blocking MTP activity, lomitapide reduces the hepatic and intestinal output of triglyceride-rich lipoproteins, leading to a marked decrease in circulating TG levels. However, this mechanism also impairs lipid export from hepatocytes, causing intracellular lipid accumulation and, consequently, hepatic steatosis. For this reason, its long-term use requires close and regular liver monitoring.
Here we present a case study of a 71-year-old female patient with genetically confirmed FCS, a baseline TG level of 2300 mg/dl (25.97 mmol/L) and a history of AP, who was treated with lomitapide for almost 5 years. The treatment allowed a marked reduction of TG (about 90%) and no recurrence of AP. Throughout this prolonged exposure, lomitapide therapy maintained average TG values around 322 mg/dl (3.64 mmol/L), with the lowest value recorded being 24 mg/dL. However, hepatic monitoring during treatment revealed a progressive worsening of liver fat accumulation as detected by MRI, which was associated with a pronounced increase in liver transaminases (ALT 104 U/L, AST 121 U/L) and liver stiffness (up to 15 kPa). Despite the absence of symptoms or signs of systemic decompensation, and in the context of stable body weight, these findings prompted the precautionary discontinuation of lomitapide. An MRI scan repeated after 70 days of drug withdrawal revealed complete resolution of fatty liver disease associated with normalization of liver stiffness (4.1 kPa) and liver transaminases (ALT 36 U/L, AST 42 U/L).
This case uniquely demonstrates that even advanced lomitapide-induced hepatic steatosis and increased liver stiffness are reversible upon timely interruption of therapy. It underscores the need for rigorous and regular hepatic surveillance in patients undergoing long-term MTP inhibitor treatment. Furthermore, this observation raises mechanistic questions regarding the different hepatic responses to lomitapide in FCS compared to other lipid disorders, such as homozygous familial hypercholesterolemia (HoFH), and highlights the importance of identifying predictive markers of hepatic susceptibility. Importantly, the abrupt rise in TG levels (>2400 mg/dl) after drug discontinuation highlights the clinical dilemma and therapeutic gap in managing FCS patients intolerant to both lomitapide and volanesorsen.
In conclusion, this case supports the long-term effectiveness of lomitapide in TG control and AP prevention in FCS, while offering reassuring evidence that hepatic complications associated with its use may be fully reversible. Given the limited therapeutic alternatives and the high clinical burden associated with uncontrolled hypertriglyceridemia in FCS, this observation contributes meaningful insights to the safety profile of lomitapide and underscores the need for individualized, closely monitored long-term treatment strategies. Moreover, it addresses a key gap in the current literature and may serve as a reference for clinicians facing similar therapeutic dilemmas in this rare and challenging condition.

CORRELATION BETWEEN LDL CHOLESTEROL BURDEN AND CORONARY ATHEROSCLEROSIS IN PATIENTS WITH HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA (HEFH)

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Introduction and state of the art: Heterozygous Familial Hypercholesterolemia (HeFH) is an autosomal dominant disorder causing high LDL cholesterol and increased risk of premature atherosclerosis and cardiovascular disease. LDL cholesterol burden (CB) is key in developing atherosclerosis, though its exact relationship with atherosclerotic burden (AB) remains uncertain. Computed tomography coronary angiography (CCTA) is a valuable tool for assessing AB. Recent studies indicate that early lipid-lowering therapy reduces coronary plaque volume, linking CB to plaque size.
Aim of the study: The main aim of this study is to investigate the association between CB and AB in patients with genetically confirmed HeFH. Secondary objectives include the evaluation of the impact of lipid-lowering on the reduction of BA. Methodology The is a retrospective-prospective, observational, non-randomized study on 250 patients with molecularly confirmed HeFH carrying pathogenic variants in LDLR, included in the LIPIGEN study and undergoing CCTA for routine clinical practice. Among these patients, 92 have already undergone CCTA and will be included in the present preliminary analysis. Medical records were retrospectively revised to collect clinical, biochemical, pharmacological and imaging data. BA was estimated by a com-

prehensive assessment of plaque phenotype, assessment of the degree of coronary stenosis by Coronary Artery Disease-Reporting and Data System (CAD-RADS score from 0 to 5) and evaluation of calcium quantity by Agatston score (expressed in HU, Hounsfield Units)]
Preliminary results: The cohort of patients undergoing CCTA (n=92, 59.8% male) had a mean LDL-C levels of 150,22 mg/dl corresponding to a CB equal to 6276 mg-year/dl (4769.25 - 8636.25). 44.6% (n=41) had a CAD-RADS score of 0, while more than half of the patients (n=51, 55.5%) had a CAD-RADS ≥1. The entire cohort of patients also had a median Agatston score of 8.85 (0 - 125.3). Regression analyzes highlighted a positive correlation between CB and CAD-RADS (Beta = 0.26, P = 0.009) which remained significant even after adjustment for major confounding factors, such as sex, BMI and smoking habits (Beta = 0.33, P = 0.001). Furthermore, the CB emerged as a predictor of the increase in the Agaston score (Beta=0.25 P=0.016), even after adjustment for confounding factors (Beta =0.27 P=0.008). At the time of drafting the present abstract, 30 patients have been included in the prospective phase by undergoing CCTA and the CT images are currently being processed at a dedicated referral center.
Conclusions: This preliminary analysis confirmed a positive correlation between cholesterol burden and atherosclerotic burden. Further investigation will enable us to assess whether pharmacological modulation of LDL cholesterol can lead to a significant reduction in atherosclerotic plaque burden.

PORTAL VEIN PULSATILITY INDEX: A VALUABLE POCUS TOOL FOR THE MANAGEMENT OF ASCITES IN LOW-RESOURCES SETTINGS

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Background: Ascites is a frequent cause of admission in medical wards in sub-Saharan Africa, being associated with a great burden of morbidity and mortality. The etiologies of ascites could be classified depending on the prevalent pathophysiological mechanism. In some cases, due to pathophysiological overlap, a univocal diagnosis is difficult to achieve. Nonetheless, a correct etiological diagnosis of ascites is crucial to initiate adequate therapeutic management. To date, besides clinical evaluation, the most accurate item to obtain an etiological diagnosis of ascites is represented by sero-ascites albumin gradient (SAAG), which can accurately predict the presence of portal hypertension, and total protein test on ascitic fluid performed on paracentesis sample. Unfortunately, in low-resources settings these laboratory tests are rarely available. On the contrary, ultrasound (US) equipment is often accessible in those settings, providing a valuable tool to individuate the cause of the ascites. US can be significantly helpful to determine the presence of cirrhosis or heart failure, which have been suggested to be the two main non-inflammatory causes in sub-Saharan African countries. More specifically, the increased pulsatility index (PI) of the portal vein flow assessed through pulse wave (PW) Doppler has been associated with the presence of heart failure. The easy reproducibility and feasibility of this measurement makes it a useful point-of-care ultrasound (POCUS) tool in low-resources settings. To date, to our knowledge, increased PI of portal vein flow has not yet been directly associated with the cardiac etiology of ascites. The aim of this pilot study is to evaluate the accuracy of an increased PI of the portal vein flow for distinguishing cardiogenic ascites from other etiology in a hospital of the Southwest Shoa Zone, Oromia Region, Ethiopia.
Methods: Among the adult patients admitted to the Emergency Outpatients Department (EOPD), those with a US diagnosis of ascites have been recruited. After anamnesis collection and physical examination, the patients underwent cardiac and abdominal US, with grading of ascites, portal vein maximum velocity (Vmax), minimum velocity (Vmin), mean velocity, and pulsatility index (PI), portal vein diameter, inferior vena cava (IVC) diameter, liver morphology, margins, and echotexture, spleen longitudinal diameter. Laboratory tests have been performed according to National and Hospital's Guidelines and include plasmatic creatinine, albumin, and total protein, urinalysis with evaluation of albuminuria and other signs of glomerular damage (casts or microhematuria presence). Once the diagnostic work-up has been completed, a definitive clinical diagnosis of the cause of the ascites was formulated by the Hospital Medical Ward physicians.
Results: The trial is ongoing. To date 11 patients have been recruited. Our preliminary data confirmed the high prevalence of cardiogenic ascites in this setting (40%), followed by ascites due to liver cirrhosis (20%), and nephrotic syndrome (20%). A cut-off of 0.6 was used for portal vein PI showing a high accuracy in differentiating cardiogenic ascites from other etiologies (sensitivity > 0.9 and specificity > 0.9).
Conclusions: In conclusion, portal vein PI assessment can distinguish with good sensitivity and specificity ascites with a cardiogenic origin. If further confirmed, these data can suggest the precious value of this measurement for the management of patients with ascites, providing an easy and reproductible POCUS tool, available from the first patient evaluation in EOPD, to drive the appropriate diagnostic and therapeutic management.

IL RUOLO DEL TEST DA SFORZO CARDIOPOLMONARE NELLA VALUTAZIONE DEI PAZIENTI AFFETTI DA PATOLOGIA DI ANDERSON-FABRY

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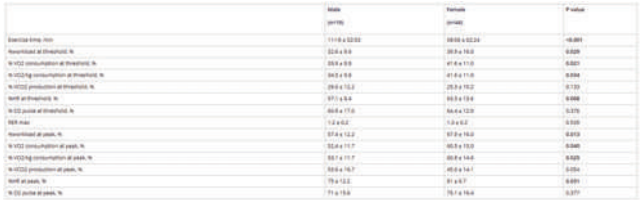
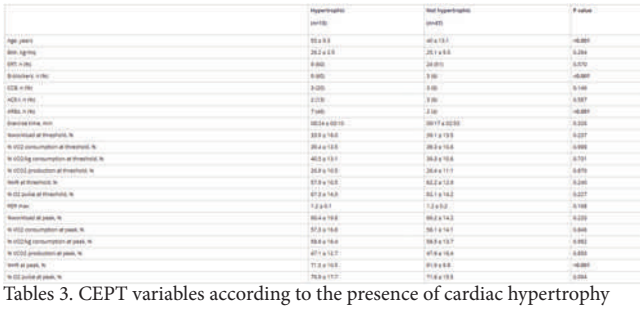
Background e scopo: La malattia di Fabry (FD) è una patologia rara da accumulo lisosomiale a trasmissione X-linked, determinata da mutazioni del gene GLA, codificante per l'enzima a-galattosidasi. Clinicamente, il sintomo più frequente è l'astenia e la ridotta tolleranza allo sforzo, che viene spesso considerata come il risultato del coinvolgimento multiorgano della patologia, e dell'ipertrofia cardiaca. Tuttavia, il sintomo è comune sia a maschi che a femmine affette da FD, anche se per la lionizzazione del cromosoma X il coinvolgimento multiorgano è spesso assente presso la popolazione femminile. In questo studio abbiamo studiato la tolleranza allo sforzo in pazienti FD attraverso il test da sforzo cardiopolmonare (CPET)
Metodi: Da marzo 2024 a febbraio 2025 abbiamo arruolato 63 pazienti affetti da FD (età media 44 ± 14 anni, 68% donne), di cui il 54% era in terapia sostitutiva enzimatica. La tabella 1 riassume le caratteristiche generali della nostra popolazione ed i principali risultati ottenuti al CPET.

Tables 1. General characteristics and CPET variables in the study cohort

Per meglio valutare l'impatto determinato dal coinvolgimento multiorgano sul CPET, abbiamo diviso la popolazione in uomini e donne, normalizzando i parametri CPET rispetto al risultato predetto per età e sesso. Come si evince dalla tabella 2, gli uomini raggiungevano carichi di lavoro minori rispetto all'atteso, sia al raggiungimento della soglia anaerobica sia al picco dell'esercizio, spesso con test sotto-massimali rispetto alla percentuale di frequenza cardiaca (FC) raggiunta. Inoltre, i pazienti di sesso maschile, presentavano minori valori di VO2/kg sia alla soglia anaerobica che al picco, rispetto alle donne. La produzione di CO2 è tendenzialmente maggiore rispetto alle donne sia alla soglia che al picco dell'esercizio.



Tables 2. CEPT variables according to sex



Tables 3. CEPT variables according to the presence of cardiac hypertrophy

Infine, suddividendo i pazienti in base alla presenza di ipertrofia ventricolare sinistra (IVS) all'ecocardiogramma, tuttavia, non si denotano differenze nei parametri CPET considerati (dati non mostrati).
Conclusioni: I pazienti FD presentano una ridotta tolleranza allo sforzo che è maggiore nei pazienti maschi rispetto alle femmine, indipendentemente dalla IVS. I nostri dati quindi mostrano che il maggiore determinante della ridotta tolleranza allo sforzo sia da attribuirsi al coinvolgimento del muscolo striato.

EFFECTS OF SARS-COV-2 INFECTION ON RESPIRATORY FUNCTION IN COPD

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Background: COPD is one of the most frequent diseases in the West world. Its prevalence progressively increases over the last decades. The SARS-CoV-2 infection, in particular associated to lung pneumonia, could have negatively influenced the respiratory function, in individuals with COPD.
Aim of the study: We aimed to evaluate the impact of the Sars-Cov-2 infection, with or without association with pneumonia, on the respiratory function of COPD patients.
Methods: A retrospective study was carried out on three Groups of COPD patients: Group 1 was composed by COPD who, during the pandemic, did not contract the Covid19 infection; Group 2 was made by COPD subjects who developed COVID19 infection, without clinical and radiological signs of pneumonia; Group 3 consisted of COPD patients who developed COVID19 infection with clinical and radiographical evidences of pneumonia. Indexes of respiratory function, collected the year previous the pandemic, were compared to those measured in the post-pandemic period, in order to establish the impact of Sars-Cov-2 on respiratory decline function in COPD patients.
Results: In Group 1, mean FEV1 decreased by 2.8% and Tiffenau index (FEV1/FVC %) by 1.4% ($p<0.001$ vs basal). In Group 2, mean reduction of FEV1 was of 3.5% and for Tiffenau index was 1.73% (p=ns vs basal). The decline observed in COPD without pneumonia was similar as compared to that measured in COPD patients who were not affected by COVID19. In Group 3, mean reduction of FEV1 was 7.8% and for Tiffenau index 3.8% ($p<0.001$ vs basal and vs Group 1 and Group 2).
Conclusions: Covid-19, associated with pneumonia, generated a more pronounced deterioration of respiratory function in COPD patients, as compared to the natural history of the COPD, or to patients with COVID-19 infection, without pneumonia.

STARTING FROM FEVER: A SHORT JOURNEY INTO GCA

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Background: giant cell arteritis (GCA), also known as Horton's disease, is one of the most common forms of systemic vasculitis. It typically affects individuals over 50 years of age, with peak incidence in the seventh decade. It involves medium- and large-sized vessels (aorta, carotid arteries and their branches, such as the temporal arteries; less commonly, the iliac or coronary arteries), leading to a broad spectrum of clinical manifestations. These may include fever of unknown origin, new-onset headache, jaw claudication, visual disturbances or vision loss, and signs of vascular involvement such as differential blood pressure or weak peripheral pulses. Vascular lesions are characterized by inflammatory infiltrates consisting of T cells, macrophages, histiocytes, and multinucleated giant cells.Suspicion should arise in patients over 50 presenting with one or more of these symptoms and/or elevated ESR or CRP, as included in the 2022 ACR classification criteria. Diagnostic confirmation is based on color Doppler ultrasound (CDUS) and/or temporal artery biopsy. Treatment typically includes high-dose glucocorticoids.
Case presentation: a 75-year-old man presented to our emergency department with a 7-day history of fever (38.5°C) and diffuse arthralgia, without other organ-specific symptoms. His medical history included ischemic heart disease treated with PCI and stenting, and known mild aortic stenosis (last cardiology follow-up several years prior). No recent travel was reported. On examination, the patient was febrile with a systolic murmur as the only relevant finding. Blood and urine cultures were collected (urine culture was negative), and blood tests showed elevated inflammatory markers (WBC 10,470/mm^3, CRP 209.6 mg/L). Chest X-ray was negative.On admission to the internal medicine ward, due to the lack of evidence for an infectious cause, no empirical antibiotic therapy was initiated.
Further investigations included urinary antigens for *Legionella and Streptococcus pneumoniae* (negative), serologies for viral and atypical pathogens (HBV, HCV, CMV, HSV-1/2, toxoplasmosis, VZV, EBV, parvovirus B19, *Chlamydia, Mycoplasma, Borrelia*), all negative for acute infection. Quantiferon was negative. Autoimmune testing revealed only low-titer ANA positivity (1:80); ESR was elevated.
A transthoracic echocardiogram (TTE) was initially performed to rule out endocarditis, and two additional sets of blood cultures were collected during febrile peaks. The diagnostic hypothesis of endocarditis was subsequently dismissed, as all blood cultures (two sets collected in the ED and two more in the ward) returned negative, and the echocardiographic findings were non-diagnostic for vegetations, showing only calcific degeneration of the aortic valve with mild stenosis and regurgitation.
A contrast-enhanced chest and abdominal CT scan was done and revealed reactive periaortic fat stranding and prominent subcentimetric intra-aortocaval and para-aortic lymph nodes, interpreted as suggestive of aortitis. Rheumatologic ultrasound of the temporal arteries was done, that showed borderline thickening of the bilateral common superficial temporal artery branches (0.55 mm on the left, 0.4 mm on the right) and of the right orbital branch. A diagnosis of GCA was therefore considered highly probable, and steroid therapy with prednisone 50 mg/day (with subsequent tapering) was initiated, resulting in rapid resolution of fever and normalization of inflammatory markers.The patient denied acute visual symptoms but was evaluated by ophthalmologists, who found bilateral optic nerve subatrophy suspected to be vascular in origin, stable at follow-up. MR angiography of the neck, chest, and abdomen revealed contrast-enhancing vascular wall abnormalities in the thoracic and abdominal aorta, consistent with large vessel vasculitis (LVV).
After discharge, a whole-body scintigraphy was performed as part of the diagnostic work-up, which showed no uptake at the level of the previously identified periaortic and intra-aortocaval lymph nodes on CT. However, increased uptake was noted diffusely in the gastrointestinal tract, suggestive of an inflammatory process, and further investigations are currently ongoing.Due to the gastrointestinal evidences (under investigation), weekly subcutaneous tocilizumab (162 mg) was added to the steroid regimen in detapering. At rheumatologic follow-up, the patient remained clinically stable, continued tocilizumab, and successfully tapered off glucocorticoids. Monotherapy with tocilizumab is now ongoing.
Early initiation of glucocorticoids (40–60 mg/day of prednisone equivalent or higher in the presence of visual symptoms at the diagnosis) is associated with better prognosis in GCA by reducing the risk of vision loss and vascular complications. In selected patients at high risk for steroid-related toxicity (as in our case) or with relapsing disease the use of glucocorticoid-sparing agents such as tocilizumab allows for an effective steroid-sparing strategy to achieve good disease control.

UNVEILING CARDIOVASCULAR RISK IN MASLD AND METALD: A CROSS-SECTIONAL ANALYSIS OF METABOLIC PROFILES AND PREDICTIVE MARKERS

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Background: and aims: Steatotic liver disease (SLD) is a major component of metabolic dysfunction and is strongly linked to Atherosclerotic Cardiovascular Disease (ASCVD). This study analyzed a large cohort of dysmetabolic patients with SLD, classified under the novel MASLD framework, to assess gender differences, metabolic risk factors, and lifestyle habits.
Methods: A total of 400 patients (mean age: 58.6±0.9 years; BMI: 29.0±0.3 kg/m^2; M/F: 222/178) were enrolled at a metabolic/CVD outpatient clinic. Physical exams, anthropometric measurements, and blood tests were performed. Lifestyle factors, including adherence to the Mediterranean diet (MD) and physical activity, were assessed by validated questionnaires. Liver steatosis and

atherosclerotic plaques were detected by ultrasonography. Patients were subclassified into MASLD and MetALD (MASLD with high alcohol intake). Metabolic and liver indices were calculated, and a 10-year ASCVD risk was estimated.
Results: Among participants, 35.0% had diabetes, 59.5% hypertension, 41.3% obesity, 83.0% dyslipidemia, and 43.3% metabolic syndrome. SLD was detected in 65.5% (MASLD 93.9%, MetALD 6.1%), with higher prevalence in males, who also exhibited greater smoking, alcohol consumption, and CVD events. MASLD and MetALD patients had similar dysmetabolic profiles, but MetALD patients showed a higher prevalence of family history for cardiovascular diseases, atherosclerotic plaques, and ASCVD risk. In patients with SLD, waist circumference but not adherence to MD was directly associated with ASCVD risk. TyG emerged as more accurate than FLI, HSI, and MAF-5 to predict ASCVD risk in patients with SLD with low risk of fibrosis and without previous major cardiovascular events, after considering the role of possible individual confounders.
Conclusion: The cardiovascular risk in patients with SLD can be influenced by a number of possible individual confounders. A systematic screening for CVD risks in patients with MASLD and an accurate phenotype characterization of patients are needed. In the determination of cardiovascular risk, a relevant role is played by waist circumference. The role of adherence to MD (at least in subjects with medium adherence) is poor, and the TyG index might be useful to predict ASCVD risk in patients with low risk of liver fibrosis and without previous major cardiovascular outcomes.

THE NOVEL ALTOGRANO® BREAD ENHANCES SATIETY BUT NOT EARLY COLONIC FERMENTATION. A SUSTAINABLE DIETARY SOLUTION FOR DYSPEPTIC PATIENTS?

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Background: In the context of the ongoing global crisis, the WHO-Sustainable Development Goals 2-3 () recommend access to healthy, safe, and sustainable food. In this respect, there is an urgent need for scientifically validated products that are both nutritious, green, and sustainable.
Aim: We evaluated the nutritional properties, sensory profile, and gastrointestinal function in response to a novel and a standard bread.
Methods: Altograno Bread® (AGB) (Next Generation Food, Casillo, Corato, Italy) is a novel bread assembled to enhance nutritional value and sustainability. It contains wheat flour enriched with 10% recovery from wheat by-products, resulting in higher levels of polyphenols, fiber, and protein, along with a reduced carbohydrate content. A standard commercial white control bread (COB) served as control. Twenty-four asymptomatic lean healthy volunteers on a prior carbohydrate-free diet and fasting overnight randomly consumed 80 g of either AGB (n=11; mean age: 29.9 ± SEM2.0 years; BMI: 23.1 ± 0.8 kg/m²) or COB (n=13; age: 25.0 ± 1.1 years; BMI: 22.4 ± 0.9 kg/m²). During 120-minutes, we measured organoleptic domains (visual aspect, smell, taste, texture), gastrointestinal symptoms (nausea, vomiting, bloating, epigastric pain, belching, flatus), appetite and satiety responses on a Visual Analogue Scale (VAS mm, 0=absent -100=max). Time-dependent gastric and gallbladder motility were monitored by functional abdominal ultrasonography. Orocecal transit time (OCTT) and colon fermentation capacity were assessed simultaneously via the lactulose hydrogen (H2) breath testing upon ingestion of 10g (15 mL) lactulose added to 200 mL of water and registration H2 levels (ppm) in exhaled air. In a pilot study, another 12 subjects complaining of functional dyspepsia (bloating, nausea, belching and negative EGDS) were tested up to 4 hrs postprandially with AGB (n=6) and COB (n=6) to monitor symptoms and crude colonic fermentation (H2) without the osmotic lactulose.
Results: Acceptance as taste VAS was higher in AGB than COB (83 vs 70, respectively; p<0.05). Gastrointestinal symptoms were absent with either bread. AGB induced significantly greater satiety than COB (AUC120min 7203 vs 4101 VAS×120 min; p<0.05). Gastric and gallbladder emptying kinetics, and OCTT were comparable between AGB and COB (Stomach: respectively max antral area 12.8 vs. 11.4 cm²; half-emptying time 59.5 vs 43.7 min; final antral area 4.9 vs 4.7; p=ns. Gallbladder respectively ejection volume 45% vs 48%; emptying rate –0.16 vs –0.10 mL/min, half-emptying time 32.1 vs 33.6 min; p=ns; OCTT 92 min vs 89.5 min; p=ns; peak H_2 production 53.6 vs 26.5 ppm; p<0.05). In the pilot study over 240 min, both AGB and COB induced a slow, mild colonic fermentation (<15 ppm), but only AGB did not generate dyspeptic symptoms.
Conclusions: Altograno Bread (AGB), enriched with wheat by-products, has favorable sensory qualities, induces enhanced satiety, and provides good gastrointestinal tolerability, without causing H2 peaks when ingested alone. Besides its beneficial nutritional effects, AGB may be particularly suitable in individuals with functional gastrointestinal disorders such as dyspepsia or meteorism. AGB is a promising food to be included as a component of the healthy and sustainable Mediterranean-style diets.

ENHANCED MEDITERRANEAN DIET WITH LOCAL PRODUCTS BOOSTS SATIETY AND REDUCES CALORIC INTAKE IN OVERWEIGHT ADULTS

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Background: The Mediterranean diet (MD) is widely recognized for promoting a healthy lifestyle and reducing the risk of several chronic metabolic diseases. Vegetables and fiber, in particular, are key components of MD. Thus, we explored whether enriching the MD with specific local Apulian vegetable products could further enhance MD impact on appetite regulation, satiety, and metabolic parameters.
Methods: This study compared the effects of similar hypocaloric traditional Mediterranean diet (MeD) versus enhanced Mediterranean diet (MeD(v+)) enriched with 120 g of *cucumis melo* "Barattiere" (BAR) and Microgreens (young seedlings of the broccoli plant) (MG). Overweight or obese individuals (n=47, median age: 55.0 years; median BMI: 29.6 kg/m²; 57.4% male) were randomized to MeD (n=23) or MeD(v+) (n=24). Subjects were instructed to eat weekly freshly-provided BAR and MG before a standard meal, over a 90-day intervention. Dietary adherence, lifestyle habits, and physical activity levels were assessed using validated questionnaires on a weekly basis. Appetite, satiety, and hedonic aspects of food intake (liking, wanting, learning) were evaluated using a 100-mm visual analogue scale (VAS). Anthropometric measurements (BMI, waist, abdominal, and hip circumference) were recorded, and subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), and liver steatosis were assessed via ultrasonography.
Results: Adherence to MD significantly improved in both groups (p<0.05). Both BAR and MG had high VAS-liking scores (BAR 95; MG 77.5) leading to high compliance during 90 days. All participants in the MeD(v+) group (100%) reported increased satiety after meals, compared to only 56.5% in the MeD group. Similarly, a greater proportion of MeD(v+) subjects (91.7%) reported reduced appetite, compared to 52.2% in the MeD group (p<0.005).
Total caloric intake decreased in both the MeD group (-9.0%, p=0.004) and more markedly in the MeD(v+) group (-15.7% vs. baseline, p=0.0002), irrespective of physical activity levels. Body weight and abdominal circumferences decreased significantly vs. baseline (weight MeD -2.3%, p=0.02; MeD(v+) -3.0%, p=0.001, abdominal circumference MeD: -2.8%, p=0.01; MeD(v+) -3.2%, p<0.02.
Conclusion: A Mediterranean diet further enriched with local vegetable products such as *Barattiere* and Microgreens (MeD(v+)) provides beneficial outcomes, i.e., enhances satiety, reduces appetite, and contributes to greater caloric reduction. The effects on decrease of weight loss might require longer observation times. There is a potential role for regionally tailored diet enhancements to improve dietary compliance and metabolic outcomes as well. Further studies are warranted to explore long-term benefits and their implications for metabolic health and disease prevention.

POLIPROTECT® PRESERVES GASTROESOPHAGEAL EPITHELIAL INTEGRITY AGAINST ACID AND BILE INJURY: AN EX VIVO STUDY FROM HUMAN ESOPHAGEAL BIOPSIES

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Background: The integrity of the gastroesophageal epithelium plays a crucial role in protecting against gastric reflux and heartburn, particularly in patients with gastroesophageal reflux disease (GERD), GERD-like symptoms, or functional dyspepsia.
Aim: This study evaluated the protective effects of Poliprotect® (PPRO), a CE-marked natural medical device, on gastroesophageal epithelial integrity using ex vivo models. Specifically, we investigated whether PPRO prevents damage induced by hydrochloric acid (HCl) and bile acids (taurodeoxycholic acid, TDCA) in esophageal and gastric tissues, simulating GERD and acid-related gastric injury.
Methods: A total of 47 esophageal and 20 gastric biopsies were collected from individuals undergoing routine esophagogastroduodenoscopy. Tissues were mounted in Ussing chambers, pretreated with PPRO, and then exposed for 20 minutes to HCl (pH 2 for esophagus, pH 1.5 for stomach) alone or combined with TDCA (2 mM). Epithelial integrity was assessed by measuring transepithelial resistance (Rt, Ohm/cm²). Morphological changes were evaluated through histological staining with Periodic Acid-Schiff (PAS) and hematoxylin-eosin (H&E).
Results: In esophageal samples, exposure to HCl and HCl+TDCA led to Rt reductions of -10.5% and -33%, respectively. Pretreatment with PPRO at 50 and 100 µg/mL significantly preserved epithelial integrity against both types of damage ($p < 0.001$). At 1 mg/mL, PPRO continued to offer protection against HCl+TDCA even after a 60-minute wash ($p < 0.001$). In gastric tissues, exposure to TDCA+HCl reduced Rt by -45.8%, an effect significantly mitigated by PPRO pretreatment at 5 mg/mL (-28.3%, $p < 0.05$). Histological analysis confirmed that PPRO reduced mucosal injury and preserved epithelial structure in both esophageal and gastric tissues.
Conclusions: PPRO effectively protects the gastroesophageal mucosa, likely through the formation of a protective adherent barrier that shields against acid and bile-induced epithelial damage. These results support its potential use in reinforcing mucosal defenses and alleviating GERD-related symptoms.

INFLAMMATORY, ADRENERGIC AND CYTOKINES PATTERN IN CRITICAL SEPSIS PATIENTS

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La sepsi è una condizione pericolosa per la vita che si verifica quando la risposta del corpo a un'infezione provoca danni ai tessuti, insufficienza d'organo o addirittura la morte. Nel reparto di emergenza, il rapido riconoscimento, la diagnosi e il trattamento della sepsi sono fondamentali per migliorare gli esiti clinici dei pazienti. Diversi scores numerici sono disponibili per agevolare e rendere più oggettiva la valutazione della disfunzione d'organo di questi pazienti. Gli scores maggiormente utilizzati sono il qSOFA, il SOFA, il NEWS2. L'obiettivo del presente lavoro è valutare il possibile ruolo di alcuni marcatori di infiammazione e di risposta adrenergica per l'accuratezza nella diagnosi e prognosi della sepsi.
Sono stati arruolati 71 pazienti ricoverati presso il DEA del Policlinico Umberto I con diagnosi di sepsi.
Sono stati registrati i parametri vitali, esami ematologici ed ematochimici ed è stata inoltre effettuata una emogasanalisi. In tutti i pazienti sono stati valutati i seguenti marker specifici oggetto di questo studio: IL-6, GDF-15 e metanefrine plasmatiche.
I livelli di questi marcatori sono stati quindi correlati alla presenza della patologia settica così da valutare la loro sensibilità rispetto alla presenza di questa.
Le concentrazioni dei marker studiati, hanno dimostrato una correlazione significativa con i parametri dell'emogas, con i parametri di infiammazione sistemica e di danno d'organo. Le curve ROC valutate per il SOFA score in combinazione con i risultati delle concentrazioni di IL-6, GDF15 e metanefrine hanno dimostrato un miglioramento sia quando utilizzato per valutare la richiesta di inotropi che per la mortalità intraospedaliera. In particolare. il SOFA score modificato con i marcatori per valutare le richieste di inotropi arriva a valori dell'area sotto la curva ROC (AUC) superiori 0.95, laddove il SOFA riporta un AUC=0.88. Per la mortalità si un aumento del AUC da 0.75, quando il SOFA score non è modificato, a valori di AUC=0.86 quando lo score considera anche i marcatori
I marcatori analizzati hanno dato promettenti risultati sia per un miglioramento della diagnosi che della terapia. I valori di metanefrine misurati hanno dimostrato come la risposta adrenergica eccessiva sia un fattore prognostico negativo molto sensibile e specifico.

PLASMAPHERESIS: IN THE MANAGEMENT OF COMPLEX THROMBOPHILIA

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Case presentation: A 49-year-old male presented with acral lesions at the level of the 4th finger of the right hand. Previous medical history included kidney transplant due to complicated diabetes mellitus type I and retinopathy since he was 11. Liver fibrosis associated with portal thrombosis and cavernoma. Thalassemic trait. Thrombophilia due to mutation of factors VII, IX, and X. In 2021, the patient developed multiple episodes of necrotic cutaneous lesion of the first finger of the left foot, necessitating amputation of the tip of the finger and revascularization, while in 2022, the same lesion developed on the opposite foot, which was surgically treated with partial resolution, and a recurrent lesion appeared on his second tip of finger of the same right foot, requiring an intravenous infusion of autologous monocytes in April 2023. The patient was admitted to our ward for the resurgence of another lesion of the 4th distal phalange of the right hand. Upon physical examination, additional ulcerations were discovered on the index and 2nd finger of the left hand. Blood work revealed Creatinine 1.47mg/mL (n.v. 0.67 – 1.17), eGFR 55 ml/min (n.v. >90), Lipoprotein a 49 mg/dL (n.v. <30), hyperhomocysteinemia 23.7 umol/L (n.v. 3.2 – 10.7). To investigate the reasons behind the recurrence as in the case of vasculitis, we performed a complete autoimmune panel (normal RF, reduced C3, normal C4, negative ANA, AMA, ANCA, anti-dsDNA, anti-CCP, lupus anticoagulant test), additional serological tests that excluded HBV and HCV infection. The coagulation test, which exhibited a decrease in plasminogen activator inhibitor-1 (PAI) and an increase in IX and VIII factors, supported the initial suspicion of thrombophilia. Genetical test with real time PCR showed homozygous genotype of the MTHR C677T. The capillaroscopy demonstrated nonspecific alteration but concluded for diabetic micro-angiopathy. Considering the blood work, instrumental and previous patient history (recent admission to a nephrological ward in December 2023 for nephrotic syndrome, and a renal biopsy revealed focal segmental glomerulosclerosis and diabetes glomerulopathy class III), a nephrological consult was requested and plasmapheresis was advised to treat the microcirculation disorders.
Discussion: Thrombophilia is a condition that makes blood more likely to form clots, which can lead to several complications. This condition results from an imbalance in blood-clotting factors, increasing the risk of thrombosis (blood clots in blood vessels). It can be hereditary or acquired due to cancer, surgery or pregnancy. The most common complications include pulmonary embolism, renal failure and cardiovascular disease. The patient showed clinical improvement after undergoing the first plasmapheresis session, it could be associated with the blood removal of procoagulant molecules. Plasmapheresis leads to the elimination of tumor necrosis factor (TNF), lipoprotein-a (Lpa) and the reduction of coagulation factors, fibrinogen and von Wilibran factor resulting in improved clinical outcomes. Although PAI decrease is associated with hemorrhagic diatesis in our patient thrombophilic disorders occurred, this could be explained by a more complex procoagulant microenvironment rather than the lack of singular factor. The MTHFR 667C>T contributes to an increase cardiovascular risk by the enhancing endothelial oxidative damage and shifting the environment toward a prothrombotic state. Following discharge, folate supplements were added to domiciliary medication to minimize hyperhomocysteinemia. Maintaining terminal parts of body warmer was another advice given to the patient to promote blood circulation by stimulating vasodilatation and so reducing necrosis of tips. In addition to clopidogrel/acetylsalicylic acid, cilostazol was added to domiciliary therapy to minimize thrombotic issues, along with mycophenolate and tacrolimus were confirmed as immunosuppressive medication.
Conclusion: This case highlights the multifactorial nature of thrombophilia in a complex patient with diabetic microangiopathy, genetic predisposition, and post-transplant status. The integration of nephrological, vascular, and hematological assessments was essential for identifying the underlying pathophysiological mechanisms driving recurrent acral ischemic lesions. Plasmapheresis proved to be a valuable therapeutic option, likely through the reduction of circulating procoagulant and proinflammatory mediators, with associated clinical benefit. The presence of homozygous MTHFR C677T mutation and elevated homocysteine levels further supported the need for adjunctive metabolic correction and antiplatelet therapy. This case underscores the importance of a personalized, multidisciplinary approach in managing thrombotic disorders with atypical presentations. Future efforts should focus on pre- and post-apheresis biomarker monitoring to better understand the pathogenesis of thrombophilia and optimize individualized treatment strategies.

EFFECT OF THE SODIUM-GLUCOSE CO-TRANSPORTER-2 (SGLT2) INHIBITORS ON PLATELET ACTIVATION AND LIPID PEROXIDATION: RESULTS OF A PILOT STUDY

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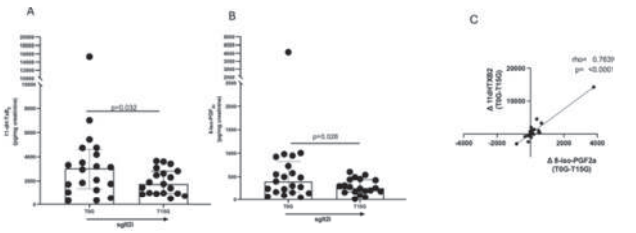
Background: Sodium–glucose co-transporter-2 inhibitors (SGLT2i), or gliflozins, represent the most recent class of antihyperglycemic agents and have been shown to confer significant cardioprotective effects in patients with and without type 2 diabetes (T2D).
Thromboxane (TX)-dependent platelet activation and lipid peroxidation—reflected *in vivo* by urinary excretion of 11-dehydro-TXB_2 and 8-iso-prostaglandin (PG)F2α—play a critical role in the development of atherothrombosis in type 2 diabetes mellitus (T2DM)
Aim: Since oxidative stress and platelet activation play a key role in the development of atherothrombotic complications, we hypothesized that gliflozins may exert modulatory effects on these pathways.
Methods: We conducted a pilot prospective observational study in diabetic patients naïve to gliflozins, in whom these drugs are prescribed according to clinical indications, before–after initiation of SGLT2i in 20 patients with T2D receiving background therapy with metformin. Oxidative stress and platelet activation, were evaluated at baseline and after 15 days of treatment. To exclude any potential interaction of glycaemic control central improvement and since metabolic on haemodynamic effect of SGLT2i occur as early as 15 days after after the prescriptions treatment in clinical studies.
Results: In patients treated with gliflozins, we observed significant reductions in markers of platelet activation and oxidative stress: 11-dehydro-TXB_2 ($p = 0.032$) (figure, panel A), 8-iso-prostaglandin (PG)F2α ($p= 0.026$) (figure, panel B). Delta 8-iso-prostaglandin (PG)F2α was directly correlated with delta 11-dehydro-TXB_2 (rho=0.7639, $p <0.001$) (figure, panel C). The decrease in 8-iso-prostaglandin (PG)F2α ($p=0.006$) and 11-dehydro-TXB2 ($p=0.057$) was significantly higher in those on beta-blockers therapy despite no significant differences at baseline.
Conculsions: These findings suggest that gliflozins possess antiplatelet and antioxidants properties, as reflected by 11-dehydro-TXB_2 and 8-iso-prostaglandin (PG)F2α downregulation. This mechanism may contribute to the cardiovascular benefits observed with SGLT2i therapy in patients with and without T2D.



EARLY DETECTION AND MANAGEMENT OF PICC-RELATED THROMBOSIS IN ONCOHEMATOLOGIC PATIENTS THROUGH SERIAL ULTRASOUND MONITORING: A PROSPECTIVE OBSERVATIONAL STUDY

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Introduction: The use of central venous catheters (CVCs) is well established in clinical practice for the management of both chronic and acute conditions. They are essential for the administration of intravenous therapies such as chemotherapy or parenteral nutrition, as well as for frequent blood sampling in patients with poor peripheral venous access or for intensive hemodynamic monitoring. Among CVCs, peripherally inserted central catheters (PICCs) are particularly suited for patients requiring medium- to long-term venous access—typically ranging from four weeks to six months—as is often the case in oncology and oncohematology. In oncohematologic patients, however, the presence of a PICC represents a significant risk factor for thromboembolic complications at the catheter site, compounded by the underlying disease-related hypercoagulable state. Diagnosis of PICC-related thrombosis may be prompted by clinical signs and symptoms such as limb edema, erythema, localized warmth, and pain, but it can also be incidentally discovered in asymptomatic patients—either due to catheter malfunction or during routine imaging. In this context, compressive ultrasound (CUS) and color Doppler sonography emerge as valuable, non-invasive, and cost-effective tools for clinicians. Requiring only minimal operator training, these imaging techniques allow for the early detection of in situ thrombosis, even before clinical manifestations arise.
Purpose of the study: This prospective study is based on the monitoring of oncohaematology patients undergoing PICC placement via serial CUS, with the aim of assessing the occurrence of thrombotic complication, the timing with which it occurs and the correlation between it and biomarkers or possible predisposing factors, such as platelets count, leucocytes count, coagulation status (PT, aPTT and fibrinogen) at the time of insertion, underlying pathology, presence in lymphoproliferative diseases of axillary adenopathies, mediastinal adenopathies or bulky mediastinal masses, presence in therapy of antiplatelet or anticoagulant prophylaxis before the thrombotic event.Collaterally, in the presence of a PICC-related thrombotic event not yet clinically manifest, it will be assessed whether the early initiation of anticoagulant therapy will avoid removal of the PICC with contextual placement of an alternative CVC.
Methods: The study population comprises patients with oncohematological diseases requiring PICC placement for therapeutic purposes. Catheter insertion is performed using ultrasound-guided techniques by a team of specialized nurses, with correct positioning subsequently confirmed by chest X-ray. After PICC placement, patients undergo serial monitoring with compressive ultrasound (CUS) along the catheter's trajectory, as far as assessable (typically up to the subclavian vein), irrespective of clinical signs or catheter malfunction. In cases where compression alone does not allow a reliable evaluation of venous patency, color Doppler ultrasound is employed as an adjunct. Ultrasound assessments are scheduled between day +3 and day +7 post-insertion, and then every 14 to 21 days thereafter, depending on the frequency of the patient's chemotherapy cycles. In cases where a thrombotic event is detected—regardless of clinical symptoms—anticoagulant therapy with therapeutic-dose low molecular weight heparin (LMWH) will be initiated.
Results: Currently 30 patients have been enrolled (20 patients with lymphomas, 4 with multiple myeloma, 6 with acute leukemia). The incidence of PICC-related thrombosis is approximately 30% (9 cases) in the absence of clinical manifestations, with only one case of overt thrombosis. Notably, early initiation of anticoagulant therapy appears to be particularly beneficial. In all observed cases, the use of serial CUS enabled the early detection of thrombosis at the PICC site—prior to the onset of clinical symptoms. Initiation of therapeutic-dose low molecular weight heparin (LMWH) at this subclinical stage allowed 100% of affected patients to retain the catheter without malfunction or the need for removal. No bleeding manifestations were observed.
Conclusions: The preliminary findings of this study suggest that oncohematological patients undergoing PICC placement represent a population at increased risk of catheter-related thrombosis. Identifying clinical or laboratory predictors of thrombosis could guide the selection of high-risk individuals who may benefit from targeted prophylactic anticoagulation. Moreover, the systematic use of serial compressive ultrasound offers a valuable, non-invasive strategy for the early detection of asymptomatic thrombotic events. Early initiation of anticoagulant therapy in these patients may significantly reduce the need for catheter removal and associated treatment delays, ensuring continued vascular access and improving overall care continuity. If validated in larger cohorts, this approach could inform future guidelines for PICC surveillance and thromboprophylaxis in oncohematological settings, with the potential to enhance both patient safety and therapeutic outcomes.

AN UNUSUAL TANGLE: A RARE CASE OF VENOUS THROMBOSIS

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Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT)

and pulmonary embolism (PE), is a significant complication in Internal Medicine (IM) departments and accounts for 5–10% of deaths in hospitalized patients(1). Typically, venous thrombosis occurs in the lower limbs; more rarely, it appears in atypical sites (e.g., upper limb, splanchnic, cerebral veins) with heterogeneous clinical presentations(2). We present the case of a patient with recurrent DVT in suprapubic circles and abnormal symptom onset.

A 55-year-old man with a history of recurrent right lower limb DVT (first episode at age 2 after immobilisation for thoracic burns), never pharmacologically treated. Last DVT confirmed by ultrasound examination (ECD) in May 2022 before orthopedic surgery: right iliac-femoral axis occlusion with vicariant suprapubic venous circulation. Comorbidities: hypertension, dyslipidemia, overweight (112 kg, H 202 cm). In September 2022, he presented to the Emergency Department (ED) with hypogastric swelling, pain, right limb dysfunction and fever. Labs showed slight CRP and D-dimer elevation (2192 ng/mL). Admitted to IM department, venous ECD revealed residual thrombosis of the right iliac vein due to post-thrombotic syndrome and ongoing thrombosis of suprapubic vicariant collaterals. No signs of acute DVT in the lower limbs. A contrast-enhanced CT showed right segmental/subsegmental PE, thrombosed suprapubic epigastric collaterals, focal thrombosis in the right inguinal vein and internal iliac collaterals bilaterally. Thrombophilia screening revealed slightly elevated factor VIII (153.4%). Following initial therapy with low molecular weight heparin (LMWH 8000 IU BID), the patient was switched to rivaroxaban 20 mg/day on 20 September 2022, which remains his current treatment. The patient is undergoing angiological follow-up, with partial recanalization of the suprapubic collateral veins observed.

VTE is linked to long-term complications, worse prognosis, longer hospitalization, and higher healthcare costs(1). It is also a preventable cause of morbidity in inpatients(3). Treatment involves anticoagulants to prevent progression and PE. For typical sites, Direct Acting Oral Anticoagulants (DOACs) or parenteral anticoagulants are recommended, with duration based on recurrence risk and condition, supported by international guidelines(4). For atypical sites, treatment is less standardized: LMWH or unfractionated heparin followed by vitamin K antagonists (AVK) remain first-line (5). However, these therapies are less tolerated by patients. Our case raises questions about classifying the recurrence site as typical or atypical, influencing therapy choice (AVK vs DOACs). In terms of treatment duration, the presence of recurrent episodes supports a consensus toward long-term anticoagulation. Considering DOACs therapy, determining the appropriate long-term dosing after the initial VTE treatment phase poses a clinical challenge. In this case, full-dose rivaroxaban was selected, taking into account the patient's body weight, history of prior events, the presence of pulmonary embolism and a low bleeding risk (ACCP guidelines). Rivaroxaban plasma levels were measured and found to be within the therapeutic range.

Given the predictability of most morbidity and mortality related to VTE, it is essential to implement preventive measures in all patients, particularly in internal medicine patients. Treating VTE can often be very complex in this population due to multiple comorbidities and clinical frailty, which in most cases necessitate a personalized therapeutic approach.

References:

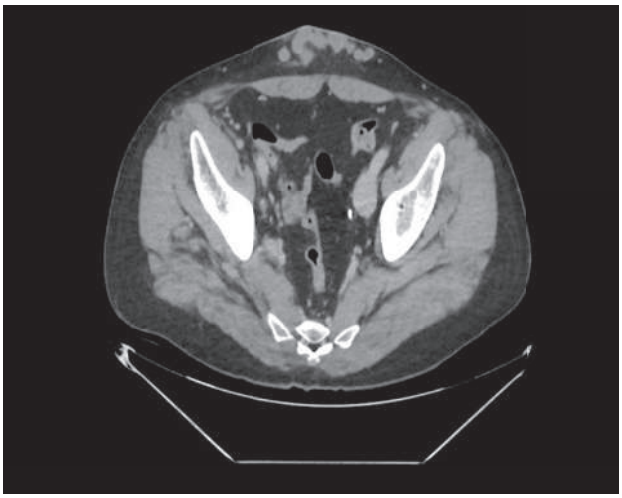
(1) Magna A. et al. Rate and Predictors of Thromboprophylaxis in Internal Medicine Wards: Results From the AURELIO Study. Thrombosis Research. 2024;243:109148.

(2) Lussana F. et al. Venous thrombosis at unusual sites and the role of thrombophilia. Semin Thromb Hemost. 2007 Sep;33(6):582-7.

(3) Peter K. Henke et al. Call to Action to Prevent Venous Thromboembolism in Hospitalized Patients: A Policy Statement From the American Heart Association; AHA|ASA Journal. May 2020; Vol 141 n24 https://doi.org/10.1161/CIR.0000000000000769

(4) Kearon C. et al. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. Chest. 2016 Feb;149(2):315-352.

(5) Abbattista M. et al Treatment of Unusual Thrombotic Manifestations. Blood. 2020;135(5):326-334.



URINARY POC TESTING FOR MEASUREMENT OF DOAC IN AN EMERGENCY CLINICAL SETTING: REAL WORLD DATA

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Background: and Aims: Oral anticoagulation therapy (OAT) reduces the risk of ischemic stroke (IS) and systemic embolism (SE) by 60–70% in patients with atrial fibrillation (AF). However, due to the limited scientific evidence available, major international guidelines do not provide clear recommendations for managing adverse events during OAT. While plasma levels of direct oral anticoagulants (DOACs) can be assessed through routine laboratory methods, the threshold values to exclude an anticoagulant effect remain debated. Since DOACs are significantly excreted in urine, point-of-care (POC) tests for urinary detection have recently been introduced, demonstrating good correlation with plasma concentrations. The aim of our study was to determine the feasibility and clinical utility of measuring DOAC levels by an urinary POC test which provides rapid and qualitative results. For this purpose, we repeated "a posteriori" a DOAC measurement by a quantitative standardized assay on plasma samples collected at the same time.

Methods: In the period between January 2024 and March 2025, patients admitted to the Emergency Department and Short and of the University Hospital of Careggi, Florence, for haemorrhagic, ischemic or thromboembolic and post-traumatic events, for whom clinicians requested the rapid assessment of DOAC levels, were recruited for this study. DOAC levels were determined by DOASENSE (Heidelberg, Germany) dipstick on urine and by commercial kits (Werfen) on plasma.

Results: We included 60 patients (mean age was 84±7 years old, 53% female). The most commonly encountered comorbidities are atrial fibrillation (91%) and high blood pressure (73%). A significant frequency of diabetes mellitus was found in patients on edoxaban compared to Dabigatran and Rivaroxaban (p 0.027), and a history of ischaemic stroke in patients on Dabigatran (43%) and Rivaroxaban (37%) (p 0.043). Vital parameters taken at the patient's admission to the emergency room and laboratory test values showed only one significant variable: aPTT, which was more prolonged in dabigatran patients than in the other patient groups (p 0.032). The majority of patients enrolled in the study had atrial fibrillation as an indication for DOAC therapy (93%), while only 7% were on direct oral anticoagulant therapy following pulmonary embolism or deep vein thrombosis. The patients enrolled were tested to determine the presence of DOAC both by urinary Dipstick and plasmatic assay. 9 out of 60 patients (15%) were excluded: 4 for "creatinine levels low", 3 for undeterminate values (due to a hyper-dilution of the sample) and 2 for hematuria. As regards as the remaining 51 patients, 45 (88%) were positive and 6 (12%) were negative. Table 1 shows the concordance between the two methods: 43 are true positives (TP), 3 false negatives (FP), 2 false negatives (FN) and 3 true negatives (TN). The 3 False Positive (FP) samples on anti-Xa may be ascribed to concentrated urine during d ehydration. In the 3 False Negative

(FN), we detected anti-Xa plasma levels close to the cut-off value of 30 ng/mL. Overall, the qualitative urine test was evaluable in 90% of cases, demonstrating good sensitivity (96%) with a specificity of 50% in predicting therapeutic plasma levels of DOAC.
Conclusion: In an emergency clinical practice (about 15%), the technical features of the test made it not usable in a non-negligible proportion of patients. In the remaining cases, our experience confirmed that it is a simple and effective way to rapidly detect the presence of clinically relevant DOAC levels. However, in 3 FP cases the quantitative dosage would have led to different clinical choices. These findings highlight the need for further real-life studies with larger patient cohorts.

	Plasma dosage		Total	*P value*
Urinary dosage	>30 ng/mL	<30 ng/mL		
Positive	43 (TP)	3 (FP)	46	
Negative	2(FN)	3 (TN)	5	*0,009*
Total	45	6	51	

CLINICAL FEATURES AND SURVIVAL OUTCOMES OF T-CELL AND B-CELL PRIMARY INTESTINAL LYMPHOMAS: A MULTICENTRE STUDY

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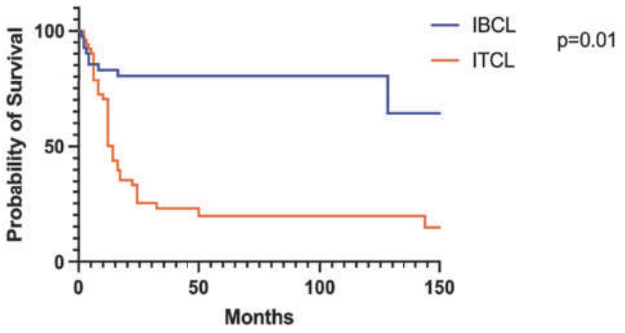
Background: and Aims: Primary intestinal lymphomas, a rare and still partially understood subset of gastrointestinal non-Hodgkin lymphomas, are classified into T-cell (ITCL) and B-cell (IBCL) subtypes. This study aimed to evaluate the clinical features and survival outcomes of primary intestinal lymphomas, with a focus on comparing ITCL and IBCL histotypes.
Methods: This multicentre, retrospective study included 94 patients (53 ITCL and 41 IBCL) diagnosed between 2001 and 2024. Diagnoses were established using Dawson's criteria, with histopathological classification following the 5th edition of the WHO Classification of Haematolymphoid Tumours, independently confirmed by two experienced haematopathologists. Clinical, laboratory, and survival data were collected. Univariate and multivariate analyses were performed to identify factors differentiating ITCL from IBCL. Survival analysis was conducted using Kaplan-Meier estimates.
Results: Among ITCLs, enteropathy-associated T-cell lymphoma (EATL) was the most frequent subtype (79%), followed by monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL, 9%), ITCL not otherwise specified (5.7%), and indolent T-cell lymphoma of the gastrointestinal tract (ITCLGT, 5.7%). IBCLs mainly comprised diffuse large B-cell lymphoma (DLBCL, 44%), follicular lymphoma (27%), marginal zone lymphoma (15%), and mantle cell lymphoma (7%). ITCL predominantly involved the small bowel (68%), while IBCL mostly affected the colon (39%). Coeliac disease was strongly associated with ITCL (81% vs. 7%, p<0.01), especially with EATL and MEITL. Weight loss was significantly more common in ITCL (60% vs. 27%, p<0.01). ITCL patients also presented more frequently with stage IV disease (30% vs. 5%, p<0.01), higher lactate dehydrogenase (LDH) and β2-microglobulin (β2MG) levels (p<0.01). Treatment regimens differed: (R)-CHOP was more commonly used in IBCL (73% vs. 40%, p<0.01), while ITCL patients more often required more aggressive therapies. Survival outcomes were markedly worse for ITCL, with a median overall survival of 12 months compared to 56 months for IBCL (p<0.01; Figure 1). Multivariate analysis identified coeliac disease (p<0.01), elevated LDH (p=0.03), and β2MG (p<0.01) as significant differentiating factors.
Conclusions: ITCL and IBCL display distinct clinical and prognostic profiles, highlighting the importance of tailored diagnostic and therapeutic strategies, particularly for the aggressive ITCL subtype.



APPROACH TO FEVER OF UNKNOWN ORIGIN: A COMPLEX CASE OF MPO-POSITIVE MICROSCOPIC POLYANGIITIS AND PRIMARY SCLEROSING CHOLANGITIS

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Fever of unknown origin (FUO) remains a challenging diagnostic entity requiring a systematic and multidisciplinary approach, particularly in elderly patients with multiple comorbidities. Autoimmune diseases are an important cause of FUO, often requiring integration of immunological, imaging and histopathological data for diagnosis.
Case presentation: . A 79-year-old female was referred to the FUO outpatient clinic of hospital San Paolo due to persistent evening fever for five months. She was treated with two courses of antibiotic therapy without any benefit. Moreover, the patient complained of systemic symptoms (fatigue, general malaise, myalgias, muscle fatigue) and mild nonspecific abdominal tenderness. Over the prior three months, she had also developed dependent edema, cough, exertional dyspnea, and an itchy erythematous rash on the lower limbs. The diagnostic work-up performed by the FUO outpatient clinic (Table 1) was remarkable for an increase in acute phase reactants (erythrocyte sedimentation rate, C reactive protein, thrombocytosis), ANCA anti-MPO positivity (60 U/mL, n.v. < 5 U/mL) with negative anti-PR3, increased cholestasis [gamma-glutamyl transferase 171 U/L (n.v. 6-40 U/L), alkaline phosphatase 767 U/L (n.v. 35-105 U/L)] and renal impairment [eGFR 32 mL/min/1.73 m^2, progressive urinary sediment abnormalities with proteinuria (zenit 590 mg/day) and microscopic hematuria].
The patient was then hospitalized in the Internal Medicine department for further diagnostic evaluation.
MRI cholangiography was performed revealing dilatation of the intra- and extrahepatic bile ducts due to common bile duct stricture at the level of the ampulla of Vater. Consequently, endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP) were performed, with brushing and biopsies at the ampulla and subsequent placement of a biliary stent. Histological examination of the biopsies showed an inflammatory pattern consistent with a systemic inflammatory disease with no signs of malignancy, which, together with suggestive ultrasound findings (echogenic portal triads, areas of segmental biliary duct dilation) [1], raised the suspicion of primary sclerosing cholangitis associated with an ANCA-associated MPO-positive small vessel vasculitis (microscopic polyangiitis, MPA).
The case was discussed in a multidisciplinary meeting also with a nephrologist and a rheumatologist. It was decided to initiate systemic steroid therapy with methylprednisolone 250 mg daily for three consecutive days, because the risks of a renal biopsy were thought to outweigh the potential diagnostic and therapeutic benefits.
Following corticosteroid initiation, the patient experienced a gradual improvement in overall clinical status with resolution of the fever and a progressive reduction of inflammatory markers. Moreover, induction therapy with intravenous (IV) rituximab was initiated at the standard dose of 375 mg/m2 weekly for 4 consecutive weeks. After the initiation of ursodeoxycholic acid (UCDA) 300 mg twice daily there was a gradual decrease in cholestasis markers up to normalization. Corticosteroid therapy was then gradually tapered until suspension after 12 months of therapy. As maintenance therapy, IV rituximab 500 mg was administered 2 weeks apart every six months. During the follow-up period, no emergent disease was detected.
Discussion: We have described a case of FUO with a final working diagnosis of MPO-positive MPA associated to primary sclerosing cholangitis which has

been successfully managed with high-dose corticosteroids, rituximab and chronic UCDA treatment. This case provides some useful learning points: (1) the integrated diagnostic approach of the FUO outpatient clinic in a teaching hospital in Milan; (2) the successful treatment of a debilitating and potentially life-threatening condition in a frail elderly patient with multiple comorbidities [2]; and (3) the intriguing overlap of these two autoimmune conditions involving the bile ducts [3].

References:

1. PMID: 6384229
2. PMID: 37433067
3. PMID: 35800183

Table 1. Results of the diagnostic work-up performed for fever of unknown origin (FUO)

	Test	Result
Immunology	Complement (C3, C4)	In range
	ANA	1:80 (fine speckled pattern)
	ANCA-MPO (n.v. < 5)	61 U/L
	ANCA-PR3	Negative
	ENA screening	Negative
Microbiology	Serial urine cultures	Negative
	C. pneumoniae serology	Positive IgG, negative IgM
	M. pneumoniae serology	Positive IgG, negative IgM
	Cytomegalovirus serology	Positive IgG, negative IgM
	Epstein Barr Virus serology	Positive IgG, negative IgM
	Parvovirus B19 serology	Positive IgG, negative IgM
	Treponema pallidum serology	Negative
	C. burnetii serology	Negative
	HIV serology	Negative
	HBV serology	Negative
	HCV serology	Negative
	Quantiferon test	Negative
Imaging	Abdominal ultrasound	Mild dilation of the biliary excretory system
	Chest computed tomography	Emphysematous microbullous cystic changes in the upper lung lobes; small subcentimetric mediastinal lymph nodes
	Positron emission tomography (PET)	No clinically relevant uptakes
Biochemistry	White blood cells (n.v. 4400-11300/mm^3)	8580 cells/mm^3
	Platelets (n.v. 150000-350000/mm^3)	642000 cells/mm^3
	Hemoglobin (n.v. 11.6-16.1 g/dL)	8.4 g/dL
	C-reactive protein (n.v. < 5 mg/L)	43 mg/L
	Erythrocyte sedimentation rate (n.v. 1-30 mm/h)	66 mm/h
	Gamma-glutamyltransferase (n.v. 6-40 U/L)	171 U/L
	Alkaline phosphatase (n.v. 35-105 U/L)	767 U/L
	24-hour proteinuria	425 mg/day
	24-hour albuminuria	118 mg/day

Abbreviations: ANA, antinuclear antibodies; ANCA, anti-neutrophil cytoplasmic antibodies; MPO, myeloperoxidase; PR3, proteinase 3; ENA, extractable nuclear antigens.

ASYMPTOMATIC CAROTID ATHEROSCLEROSIS: GENDER DIFFERENCES AND IMPLICATIONS IN CARDIOVASCULAR PREVENTION

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Abstract: Carotid atherosclerosis is a pathological condition associated with a high risk of ischemic stroke, which accounts for approximately six million deaths annually. While men have a higher incidence of stroke, women display greater rates of disability and mortality. This discrepancy is often attributed to the more atypical presentation of symptoms in women—such as headache, fatigue, or dizziness—which leads to delays in diagnosis and treatment. We present two clinical cases, one female and one male, both with asymptomatic carotid stenosis, to highlight gender differences in risk factors and plaque characteristics.

Case F: A.B.a 50-year-old woman, was referred for routine vascular screening. She was neurologically asymptomatic, reporting only occasional presyncopal episodes. She had a history of poorly controlled hypertension, dyslipidemia (LDL 100 mg/dl), impaired glucose tolerance, and a strong family history of cardiovascular disease. She was a former smoker. Carotid duplex ultrasound revealed a fibrocalcific atherosclerotic plaque at the right carotid bifurcation with 50% stenosis. Treatment included an angiotensin receptor blocker, aspirin, and high-dose statin therapy, along with lifestyle modifications.

Case M: B.C. a 64-year-old man, was evaluated during a routine vascular follow-up. His clinical background was similar, with hypertension, dyslipidemia, impaired glucose tolerance, and a history of smoking. He was already on aspirin and statin therapy. A brain CT scan showed signs of chronic small vessel ischemic disease. Carotid ultrasound revealed a hypoechoic plaque with 50% stenosis. Ezetimibe was added to his regimen to achieve an LDL target <70 mg/dl.

Despite comparable degrees of stenosis and similar cardiovascular risk profiles, differences in plaque morphology and response to therapy were notable. Women tend to develop larger, but more stable, plaques (fibrocalcific) with fewer inflammatory cells. Estrogen may play a protective role by preserving endothelial function, reducing foam cell formation, and promoting plaque stability. However, postmenopause, this protection diminishes and histological features become more similar to those observed in men.

Optimal medical therapy (OMT) is now the mainstay of treatment for asymptomatic carotid stenosis. Surgical options, such as carotid endarterectomy or stenting, are more selectively indicated—especially in women, who are at higher perioperative risk. Adherence to pharmacological therapy and aggressive control of modifiable risk factors (hypertension, hyperlipidemia, and glucose metabolism) remain crucial. However, women are less likely to receive statins and antihypertensives despite evidence showing greater stroke risk reduction in females.

In conclusion, these two cases emphasize the importance of a gender-tailored approach to cardiovascular prevention. Sex-based differences should be considered when assessing risk, selecting therapy, and planning follow-up in patients with asymptomatic carotid atherosclerosis. Supporting gender-specific cardiovascular prevention strategies is crucial to improving outcomes and achieving equity in vascular health.

CURRENT USE OF PROTON PUMP INHIBITORS MAY BLUNT THE CLINICAL EFFICACY OF ORAL BISPHOSPHONATES

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Proton pump inhibitors (PPIs) are commonly used drugs for acid-related disorders that decrease acid secretion in the stomach by blocking H+/K+ ATPase enzyme. Recently, the risks and benefits of long-term PPI use were questioned and many studies suggested an increased risk of fragility fractures, especially in the older persons. Oral bisphosphonates (BPs) are highly effective bone antiresorptive agents able to prevent fragility fracture. They represent the first line treatment for the management of osteoporosis in several settings. The aim of our research was to investigate the modifications of bone mineral density as a surrogate marker of bone strength in BPs users according to the use of PPIs.

A retrospective cohort study was conducted in postmenopausal women at high risk of fracture who were on PPIs (i.e. omeprazole, esomeprazole, lansoprazole, pantoprazole and rabeprazole) for at least 12 months and who were naïve at BPs (alendronate, risedronate, ibandronate) treatment.

180 women (mean age 61.2 yr; n=60 patients on PPIs) were recruited. After a median follow-up of 24 months, the concurrent PPI and BPs use was associated with a significantly lower mean percent BMD change at lumbar spine [-0.17 ± 7.4 vs 2.8 ± 6.8 %]. At a stepwise multiple regression analysis, PPI use was also independently associated with BMD change at lumbar spine (ß=−2.87, SE 1.34, p=0.03).

Long term PPIs use in postmenopausal women may blunt the response to oral BPs in severe osteoporosis. Physicians should be aware of this risk and consider PPIs deprescription when applicable.

EVOLUTIONARY ASPECTS OF MULTI-DISTRICT ATHEROSCLEROSIS: ANALYSIS AND CORRELATION OF FUNCTIONAL, BIOMOLECULAR AND GENETIC FACTORS IN TEN YEARS ULTRASONOGRAPHIC FOLLOW-UP

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Background: Atherosclerosis is a chronic, degenerative, multifocal disease that affects the intima and media layers of medium- and large-caliber arteries through the formation of atheromatous plaques composed of fibro-calcific tissue and lipid material. It is a progressive process and typically becomes clinically apparent in middle to older age. Although atherosclerosis can affect any vascular territory, certain arterial beds are more frequently involved (e.g. coronary arteries, arteries of central nervous system and arteries of lower extremities). Interestingly, atherosclerosis tends to affect specific sites within each vascular bed (e.g. the proximal segment of the left anterior descending coronary artery, or the carotid bifurcation); these predilections are partially attributed to local hemodynamic factors, but individual variability in lesion distribution suggests the influence of additional systemic and possibly genetic factors. Emerging evidence indicates that specific cardiovascular (CV) risk factors may influence the localization and progression of atherosclerotic lesions; among these, endothelial dysfunction and low-grade inflammation seems to be associated with certain plaque localization and with the entity of its progression over time.
ENDPOINT The aim of our study is to evaluate the evolutionary aspects of multi-territorial atherosclerosis by analyzing the potential role of morphological, biomolecular, and genetic factors in the progression of atherosclerotic lesions, in a ten-year ultrasound follow-up.
Materials and methods: This prospective longitudinal study was conducted on patients previously enrolled in the research study (protocol no. 14725/2014) carried out in our Angiology Department and re-evaluated ten years later. Patients were interviewed regarding their family and medical history, CV risk factors and current therapies. In addition, each participant underwent a comprehensive ultrasonographic assessment, including Ankle-Brachial Index (ABI), carotid-vertebral and lower limb duplex ultrasound. In the ultrasonographic evaluation, we employed the scoring system outlined in the aforementioned protocol (Ultrasonographic Lower Limb Atherosclerosis – ULLA), assigning a score to each vascular district based on the extent of atherosclerotic damage, and subsequently calculating a total atherosclerotic burden score. The newly collected data were then compared with baseline data from ten years prior to assess the progression of atherosclerotic lesions and their correlation with specific risk factors.
Results: Preliminary data analysis confirmed an association between the localization of atherosclerotic plaques and specific CV risk factors. In particular, cigarette smoking and dyslipidemia were associated with atherosclerotic progression of the extracranial carotid arteries and the iliac-femoral axis, while diabetes mellitus showed a stronger correlation with distal atheromatous progression in the lower limb arteries. Additionally, a greater progression of atherosclerotic lesions was observed in patients with a history of CV events. Regarding the potential role of genetic factors, ongoing investigations are assessing the relationship between specific osteoprotegerin (OPG) polymorphisms and the progression of atherosclerotic disease. Notably, over a ten-year follow-up period, patients with non-stenotic atherosclerotic lesions in the lower limb arteries exhibited disease progression, as indicated by an increase in the ULLA score, despite no significant changes in the ABI.
Conclusions: Preliminary findings from the study underline of the association between specific CV risk factors and progression of atherosclerotic plaques over time. Comparative ultrasonographic data in patients without clinically diagnosed peripheral artery disease (PAD) revealed the presence and progression of subclinical atherosclerotic plaques in the femoro-popliteal segment, even in absence of changes in the ABI. These results suggest that ABI, while routinely used for PAD screening, may fail to capture relevant information in patients with subclinical forms of atherosclerosis.
Ongoing statistical analyses are investigating the potential role of inflammation and specific genetic polymorphisms in influencing the distribution and progression of atherosclerotic disease. The study of genetic polymorphisms associated with atherosclerosis could, therefore, provide further interpretative elements for this phenomenon and, in clinical practice, could lead to new screening methods that may, in the future, help determine which vascular territory is at higher risk in individual patients.

A RARE CASE OF DIARRHEA

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Background: Adult-onset autoimmune enteropathy (AIE) is a rare and often underdiagnosed condition characterized by persistent diarrhea, severe malabsorption, small intestinal villous atrophy, and symptoms mimicking refractory celiac disease. AIE is often seen as cause of villous atrophy in children with T-cell dysregulation but now it is emerging diagnosis in adult as well. This case report focuses on adult-onset AIE and highlights the challenges in diagnosing and managing this condition due to its complex clinical and pathological presentations.
Case report: A 69-year-old patient with hypertension on Olmesartan was admitted for chronic non-bloody diarrhea, abdominal pain and weight loss of 15 kg in a few months. Serology for celiac disease was negative. ARBs were immediately discontinued on suspicion of Olmesartan-related enteropathy. However, rapid worsening of conditions with MOF due to malnutrition, persistence of diarrhea and acute kidney failure, required ICU monitoring. Antibiotic therapy was ineffective leading to high-doses of Methylprednisolone approach due to severity of illness. CT scan ruled out stricture or enhancement suspicious for IBD, showing non-specific thickening of ileal walls. EGD and colonoscopy showed severe atrophy in ileum and duodenum. Histology showed chronic inflammatory infiltrate with lymphocytes, plasma cells and eosinophils and intraepithelial enterocytes in association with villous blunting, severe villous atrophy and crypt hyperplasia. Atypical Crohn's disease, celiac disease and a rare form of enteropathy (i.e., AIE) were considered. Common immunodeficiency, AIDS, T lymphoma associated enteropathy, CMV overinfection or intestinal giardiasis were excluded according to lab tests. Search for anti-enterocyte antibodies was negative. Hospitalization was long and rich of complications (including repeated Candidemias and total parenteral nutrition while admitted). However, gradual improvement of clinical condition was seen. Based on symptoms of chronic secretory diarrhea, endoscopic and histological remission of villous atrophy and clinical improvement after steroids, diagnosis of adult-onset autoimmune enteropathy was made.
Conclusion: Adult AIE is a rare disease with very limited retrospective data consisting mostly of case reports and few small case series of 13-30 patients. Diagnostic criteria include chronic diarrhea, malabsorption, specific histological findings and absence of other causes of villous atrophy. Gut-specific antibodies are no longer required for diagnosis. Medications (i.e. Olmesartan, NSAID) can trigger secondary forms. AIE is a diagnosis of exclusion. Diagnosis remains challenging, but it should be considered in the differential diagnosis of malabsorption syndromes associated with villous atrophy without positive celiac serology.

PYOGENIC LIVER ABSCESSES: CLINICAL CHARACTERISTICS, MICROBIOLOGICAL FEATURES AND INDICATORS OF THERAPEUTIC FAILURE

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Background: Pyogenic liver abscesses (PLA) are suppurating infections of the hepatic parenchyma, which develop most commonly as complications of adjacent biliary tract infection but can also be seeded through portal circulation from intestinal sources, through systemic circulation or via penetrating trauma and surgery. Early diagnosis and treatment is a crucial step in the management of these patients, since the presentation may be subtle and not specific (abdominal pain, fever, nausea, and vomiting), so currently constitutes a challenge for physicians: a high index of suspicion is the cornerstone of prevention for misdiagnosis and improvement of prognosis.
Aim: The aim of this study is to review the experience of the Santa Croce and Carle Hospital (A.O. S. Croce e Carle) in Cuneo in the management of pyogenic liver abscesses over a period of approximately 23 years, identifying in a Northern Italian population the clinical, etiological, and microbiological characteristics, treatment choices, in-hospital mortality, and predictive factors of therapeutic failure.
Methods: The population included in this retrospective study consists of a consecutive series of patients diagnosed with PLA admitted to the Santa Croce and Carle Hospital of Cuneo over a period of twenty-three years, from January 1, 2000, to December 31, 2023. PLA cases were identified through the analysis of discharge diagnosis codes (code 572.0, according to the ICD9 - 1997 classification) related to hospital admissions. Using this method, the medical records of 210 patients were retrieved and reviewed.
Results: The majority of patients presented with fever (70%), right upper abdominal pain (65.7%), vomiting and nausea (19.8%). Increased C-reactive protein levels was the most common laboratory abnormality (98% of cases). Abdominal ultrasound was the diagnostic investigation in 38.3% of cases; CT scan and MR imaging were performed in 54% and 7.6% of cases respectively. We observed blood or pus culture study in 197 cases of which only 56.3% came with positive microbial reports. Early antibiotic treatment was started on all patients and 67.1% of cases required different approaches, such as percutaneous abscess drainage which was performed on 142 patients (66.6%).PLA is a diagnostically challenging problem due to nonspecific presenting characteristics.

Once recognized, percutaneous drainage and antibiotic treatment are the mainstay of management for PLA.
Conclusion: The study attempts to show our first-hand real, original experiences in this field and to provide useful information. In practice, clinicians should maintain a high index of suspicion for PLA in patients who present with risk factors, such as hepatic-pancreatic-biliary system pathologies, and clinical scenarios of fever, right abdominal pain, increased levels of C-reactive protein and white blood cell count. Prompt diagnosis of liver lesion, administration of antibiotics and percutaneous drainage can conduce to successful treatment.

ERADICATE STUDY: EPIDEMIOLOGY OF OCCULT INFECTION OH HEPATITIS C VIRUS IN HOSPITALIZED PATIENTS BORN BEFORE 1969: A SPONTANEOUS SCREENING

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Hepatitis C infection is one of the leading causes of acute and chronic infectious liver disease globally, with a significant morbidity and mortality associated risk due to development of liver cirrhosis and hepatocellular carcinoma. The highest number of individuals acquiring HCV infection in Europe are between 25 and 44 years old, mainly due to parenteral drug use or unprotected sexual activity. However, also individuals born between 1945 and 1968, the so-called "baby boomers", have a higher prevalence of chronic HCV infection. This is understandable considering that they may have acquired the infection before virus identification. In the 2020-2021 biennium, the Italian government funded a free screening program targeting all individuals born between 1968 and 1989 and higher-risk populations, such as individuals followed by the Public Addiction Services and prisoners. However, individuals born before 1968 were not included, thereby underestimating the prevalence of chronic HCV infection among these people, who may currently be experiencing complications and spread HCV infection. Based on these data, we performed a screening to all individuals born before 1968 admitted to the medicine and surgery departments of Fondazione Policlinico A. Gemelli (FPG) IRCCS. The aim of the study was to evaluate the presence of HCV infection in a large cohort of elderly patients not suitable for anti HCV screening campaign in a tertiary center in central Italy, and eventually further management in patients with a new diagnosis of HCV infection. The primary endpoint was assessment of the prevalence of anti-HCV antibodies. Secondary endpoints were description of the demographic and clinical characteristics of the patients, assessment of the prevalence of patients in whom HCV-RNA was sought; assessment of the prevalence of patients referred for hepatology visits; assessment of the prevalence of patients who started antiviral therapy for HCV. The target population consisted in individuals born before January 1 st 1968 admitted between January 1, 2023 and December 31, 2024 in the medical departments of Policlinico Universitario Agostino Gemelli IRCSS, without previous diagnosis of HCV acute or chronic infection and/or previous determination of HCV antibodies on blood samples available in their medical records at the time of the enrollment. Patients underwent POC serological testing on capillary blood obtained by fingertip puncture. For positive patients, quantitative HCV-RNA testing was performed; if positive, the patient was referred to the hepatology outpatient clinic for further diagnostic evaluation and begin antiviral treatment. Results: 2000 patients were enrolled and tested with anti HCV POC from January, 1st 2023 and December 31, 2024. Patients were mostly Caucasians and born in Italy. Dividing the population according for the decade of birth, 32.45% were born between 1958 and 1967, 34.8% between 1948 and 1957 and 26.05% between 1938 and 1947; only 135 patients were born before 1937. Point of care resulted positive in 16 patients (0.8% of the overall population). The majority of them were male (68.75%). Median age of this group was 70 years. Antibodies against HCV resulted expressed in 100% of the patients who tested positive for the point of care test. Non viremic patients were 3 (18.75%), while 13 resulted viremic (81.25%). Concerning direct antiviral treatment for viremic patients, 3 patients received glecaprevir/pibrentasvir, while 4 patient received sofosbuvir/velapatasvir (2 patients for 12 weeks, 2 patients for 24 weeks). Of the remaining patients, excluding the 3 who were non viremic, 1 patient died before the start of the treatment due to oncological comorbidy, 2 patients resulted too sick for the beginning of the treatment (candidate for best supportive care due to comorbidities) while 3 patients did not show up for the scheduled outpatient hepatological visit. Conclusion: Hepatitis C virus (HCV) infection remains a significant public health challenge, particularly among older populations who were not included in recent screening programs. Our findings, although limited to a hospital-based population, confirm that a non-negligible proportion of elderly individuals still harbor undiagnosed HCV infection. Our findings are consistent with previous epidemiological studies, which reported varying but often higher prevalence rates among older cohorts, particularly those born before widespread implementation of blood screening and harm reduction strategies. Our data also highlight a critical care gap in the HCV continuum: despite identification and referral, not all viremic patients initiated antiviral therapy. In conclusion, our study demonstrates that HCV infection remains present and underdiagnosed in individuals born before 1968. These data support reconsidering screening policies to include older cohorts and strengthen post-diagnosis care pathways to ensure that diagnosed patients are effectively linked to and retained in care. Expanding screening to this population may represent an important step toward achieving the WHO goal of HCV elimination by 2030.

A NOVEL HIMEA FUNCTIONAL TEST FOR THE DIAGNOSIS OF HEPARIN INDUCED THROMBOCYTOPENIA

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Background and Aims: Heparin induced thrombocytopenia (HIT) is a rare adverse effect of heparin therapy due to the production of IgG antibodies against heparin-platelet factor 4 (H-PF4) complexes, resulting in platelet activation and in decreased platelet count. The diagnosis is suspected based on the 4T pre-test probability score (4Tscore) and required the detection of antibodies against heparin/PF4. The combination of immunological assay (CLIA, ELISA) with functional test (HIPA) improves the accuracy of HIT, however HIPA test is technically demanding and time-consuming. The aim of our study was to estimate the Heparin induced Multiplate® electrode aggregation (HIMEA) cut-off for the detection of HIT positive patients by evaluating platelet aggregation in presence of platelet-activating IgG antibodies, as an alternative of functional test.
Methods: We included 62 patients with a clinical suspicion of HIT (4Tscore 4.8±1.6) and a positivity by an immunological test (CLIA), in whom we performed the HIPA functional test according to our clinical routine. In addition, we performed HIMEA test. Citrate whole blood was collected from healthy donors and incubated with patient's serum; platelet aggregation in response to unfractionated heparin (0.5 U/ml and 100U/ml) was evaluated by Multiplate® analyzer. HIT-positive serum induced platelet aggregation in presence of 0.5 U/mL heparin, while aggregation was inhibited with 100 U/mL heparin. 14 out of 62 patients (22%) were excluded from analysis for undeterminable results in HIMEA test.
Results: 48 patients [25 M/23F; mean age: 70.1±12.1] were analyzed by chemiluminescence immunoassay (CLIA), (Acustar IgG, Werfen, Italy >1 U/mL-median 14.43 U/mL [2.27-40.06]) and then evaluated with Heparin-induced platelet Activation-HIPA to confirm the ability of antibodies to induce platelet activation. HIPA positive test was found in 37 out of 48 samples (77.1%). In 89.2% of HIPA positive patients the 4T score was ≥4.
Previous studies identified a cut-off regarding the Area Under the Curve (AUC) with low-dose heparin ≥30 by considering the following criteria: typical sigmoid curve reflecting platelet aggregation, AUC of sample incubated with 0.5 U/mL heparin >30 U, AUC for high-dose heparin <50% of the low-dose heparin AUC and AUC < 30 U without heparin. Patients of our cohort who fulfilled all the mentioned criteria were 30 out of 37 HIPA positive patients (81,08%), 7 HIPA positive patients resulted negative by HIMEA and 11 patients were negative by both HIPA and HIMEA test. The sensitivity and specificity resulted 81.1% (64.8- 92%) and 100% (71.5-100%) respectively.
A ROC curve analysis correlating the AUC with low-dose heparin and HIPA produced a cut-off of 42.5 U; the sensitivity of the test was 81.1% (64.8- 92%) and the specificity 100% (71.5- 100). 30 out of 37 HIPA positive patients (81.08%), 7 HIPA positive patients resulted negative by HIMEA and 11 patients were negative by both HIPA and HIMEA test.
Considering the AUC ≥42.5U in sample incubated with 0.5U/ml Heparin as the only criterion, we achieved a sensitivity of 91.9% (78.1-98.3) and a specificity of 81.8%.
Moreover, correlating the results of the aggregation in HIMEA with the HIPA assay by ROC curve analysis, we established a cut-off of 21.5% (AUC 0.984, p<0.001) unlike the cut-off found in literature (60%). HIMEA assay with our cut-off yields a sensitivity of 73% (55.9-86.2) and a specificity of 100% (71.5-100). By setting the cut-off 21.5% the HIMEA results were concordant with HIPA assay (Cohen's kappa coefficient = 0.943, p<0.001): 36 patients had both test positive, 11 both test negative, and only 1 patient had a discordant result (false negative).
Conclusions: The combination of an immunological assay with a functional test improves the accuracy of HIT, but functional assays are limited to few,

expert laboratories. The combination of CLIA and HIMEA could simplify the diagnosis in suspected HIT patients. 22% of patients in our cohort were excluded due to ambiguous HIMEA test results. In the remaining 48 patients we found that a reasonable limit to exclude HIT in patients with a HIT clinical suspicion could be considering the AUC >42,5 U as the only criterion or in alternative the percentage of inhibition <21.5%.

LONG-TERM ANTITHROMBOTIC STRATEGIES FOR PERIPHERAL ARTERY DISEASE AND UNPROVOKED VENOUS THROMBOEMBOLISM: AN ITALIAN SURVEY

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Introduction: Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is conventionally treated with anticoagulant therapy (ACT), with long-term ACT recommended for unprovoked cases. Atherosclerotic cardiovascular diseases (ASCVD)-such as coronary artery disease and peripheral artery disease (PAD)—are typically managed instead with antiplatelet therapy (APT). VTE and ASCVD share several risk factors, and patients with one condition may develop the other. However, no high-quality evidence currently guides optimal antithrombotic management in patients affected by both ASCVD and unprovoked VTE. To address this knowledge gap, we conducted a nationwide survey aimed at assessing current prescribing patterns in Italy, with a specific focus on patients with symptomatic PAD.
Materials and methods: We designed an internet-based survey distributed among members of the Italian Society for Angiology and Vascular Medicine (SIAPAV). The survey was conducted between December 2023 and February 2024 and included four clinical scenarios:
Case 1: A 50-year-old man with intermittent claudication and unprovoked proximal DVT.
Case 2: A 50-year-old woman with unprovoked intermediate-high risk PE.
Case 3: A 50-year-old man with PAD treated with revascularization and stenting one year earlier, who
develops unprovoked proximal DVT.
Case 4: A 50-year-old woman with the same PAD history as case 3, but with unprovoked
intermediate-high risk PE.
In all cases, APT for PAD had been discontinued at the time of VTE diagnosis, and DOAC therapy was initiated. The primary question was which antithrombotic regimen to choose after 6 months of ACT, assuming normal kidney function and no bleeding complications. Each scenario was modified by patient age (>75 years), sex, and high bleeding risk, to evaluate their impact on treatment decisions.
Results: A total of 174 physicians completed the survey, representing approximately 30% of SIAPAV members. The majority were specialists in internal medicine (46%) or vascular medicine/angiology (36%), with more than 76% reporting over 10 years of clinical experience. All respondents had experience managing patients with PAD. In the default versions of the scenarios, the most frequently selected regimen was the combination of APT and low-dose DOAC (chosen by 45.3%, 36.4%, 40.0%, and 40.8% of respondents in cases 1 to 4, respectively). A smaller proportion opted for full-dose DOAC monotherapy (13.3%, 37.1%, 14.6%, and 28.8%), while APT combined with rivaroxaban 2.5 mg twice daily was selected by 31.3%, 14.3%, 36.1%, and 16.8% of respondents, respectively. The additional patient variables influenced decision-making differently.
Gender had little influence on decision-making, but age >75 years significantly increased the preference for APT alone (rising from 8.0% to 23.3% in case 1; 1.4% to 11.4% in case 2; 4.6% to 20.0% in case 3; and 4.0% to 12.1% in case 4). High bleeding risk had the most pronounced effect, making APT alone the most frequently chosen option (60.7%, 35.7%, 56.9%, and 42.4%, respectively).
Conclusions: This survey highlights substantial heterogeneity in antithrombotic prescribing patterns among Italian vascular specialists for patients with PAD and concomitant unprovoked VTE. The combination of APT with low-dose DOAC was the preferred therapy by many physicians in most cases. However, in older patients or those at high risk of bleeding, more conservative strategies such as APT alone were preferred. Of note, none of these choices is based on high-quality evidence, since the net clinical benefit of these regimens in the set of patients considered in this survey is unknown. Our findings underscore the need for more targeted research to help clinicians to optimize antithrombotic strategies and improve the outcomes of patients with PAD and concomitant unprovoked VTE.

A RARE CASE OF RFX6-RELATED MODY

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Il diabete MODY (Maturity Onset Diabetes of the Young) è una forma di diabete mellito monogenico dovuto a mutazioni legate a disfunzioni delle β-cellule pancreatiche. Rappresenta circa il 5% delle diagnosi di diabete mellito al mondo. Ad oggi sono conosciute e dettagliate circa 14 mutazioni diverse che sono responsabili di 14 forme di MODY; tra queste, le più frequenti sono legate a mutazioni dei geni HFN1A, HNF1B e GCK. Negli ultimi anni sono state identificate nuove mutazioni, alcune delle quali ancora non ben caratterizzate, tra cui rientra la mutazione del gene che codifica per il Fattore Regolatorio X6 (RFX6), un fattore che regola la differenziazione e funzione delle β-cellule pancreatiche. Un difetto omozigote di tale gene dà vita alla sindrome di Mitchell-Riley, caratterizzata da diabete neonatale, ipoplasia pancreatica, atresia intestinale e agenesia della cistifellea. Mutazioni in eterozigosi di RFX6 determinano uno specifico MODY, più incidente nelle regioni scandinave e con penetranza ridotta, caratterizzata da carenza di autoanticorpi anti-isole e ridotta secrezione di Polipeptide Insulinotropico Glucosio-Dipendente (GIP) in risposta all'ingestione del glucosio. Qui descriviamo il caso di una paziente eterozigote per mutazione RFX6 ed affetta da diabete mellito.
Caso clinico: T.G., donna di44anni, normopeso (BMI25kg/m^2) con familiarità per diabete mellito (padre, madre e sorella gemella), patologie cardiovascolari e autoimmuni (madre affetta da psoriasi). In anamnesi, ipotiroidismo in trattamento sostitutivo con Levotiroxina sodica in attuale eutiroidismo, ed ipercolesterolemia in trattamento ipolipemizzante con Atorvastatina10mg. Diagnosi di diabete mellito da circa20aa, trattato in precedenza con Metformina e Acarbosio, sospesi successivamente per *disconfort* gastrointestinale. Nel2023la paziente si sottopone ad esami genetici prima di sottoporsi a FIVET. In tale occasione, viene individuata l'eterozigosi per gene RFX6, caratteristico per diabete MODY variante RFX6. Durante la gravidanza la paziente ha praticato solo dietoterapia e la gravidanza, condotta a termine, esitava in parto eutocico in assenza di macrosomia. La paziente giungeva alla nostra osservazione per inquadramento della patologia diabetica. Al momento dell'osservazione, HbA1c5.6%, C-peptide0.77nmol/L e negatività agli autoanticorpi GAD, IA, ICA. LDL-C70,8mg/dL, Lipoproteina (a)44mg/dL. Allo screening delle complicanze croniche del diabete, assenza di malattia renale associata al diabete (eGFR calcolata con CKD-EPI109ml/min, microalbuminuria assente). L'esame ECD-TSA mostrava un ispessimento medio-intimale carotideo bilaterale (fino a1,6mm) senza evidenza di stenosi emodinamicamente significative. L'ECG era nei limiti e l'ecoscopia cardiaca documentava una funzione ventricolare sinistra conservata (FE >65%), con spessori parietali nei limiti e solo lievi insufficienze valvolari. Non segni di retinopatia diabetica o altre patologie oculari. Inoltre, FIB4ed ecoscopia addominale risultavano nei limiti della norma. Veniva inoltre approfondito il quadro di calcolosi renale riferito durante la raccolta anamnestica, con valutazione del metabolismo calcio-fosforo e del rischio fratturativo (la paziente portava in visione esame DEXA del2023con evidenza di osteopenia marcata). Lo studio del turn-over osseo, mostrava un aumento dei valori di CTX, motivo per il quale si indirizzava la paziente a visita specialistica ginecologica al fine di avviare terapia estro-progestinica preventiva.
Sulla scorta degli esami effettuati, si poneva quindi diagnosi di "Diabete MODY variante RFX6, ipotiroidismo in eutirodismo farmacologico, dislipidemia e iperLipoproteinemia(a), osteopenia con aumento del turnover osseo". Venivano quindi somministrati consigli nutrizionali per la gestione della patologia diabetica e indicazione a proseguire terapia ormonale sostitutiva e ipolipemizzante. In conclusione, è stato qui riportato raro caso di MODY con eterozigosi al gene RFX6. L'ottimo compenso glicemico, mantenuto con la terapia nutrizionale in assenza di complicanze croniche dopo oltre 20 anni dalla diagnosi di diabete conferma la scarsa penetranza di tale forma, così come riportato nei rari casi presenti in letteratura.

A COMBINATION OF TWO RAPID IMMUNOASSAYS IMPROVES HIT DIAGNOSIS

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Background and Aim: Heparin induced thrombocytopenia (HIT) is an

immune adverse drug reaction induced by the exposure to heparin which leads to the production of IgG antibodies against heparin-platelet factor 4 (H-PF4) complexes. Despite progress in understanding the underlying immunological mechanisms, the diagnosis of HIT remains challenging as it requires a combination of clinical criteria and specific laboratory tests. However, a rapid diagnosis is essential for prevention of potentially catastrophic thrombotic events. HIT diagnosis is suspected based on a clinical evaluation with the 4T pre-test probability score (4Tscore) and required the detection of circulating antibodies bound to heparin/PF4 complexes by immunological and functional assays. Immunological assays are based on different techniques such as, chemiluminescent IA (CLIA), latex immune- turbidimetric assay (LIA), enzyme-linked immunosorbent assays (ELISA). They are easy to perform, widely available and show high sensitivity. Functional assays are the gold standard for HIT diagnosis after a positive immunological test. Serotonin release assay (SRA) has been replaced by heparin induced platelet aggregation (HIPA). However functional tests are technically demanding, time-consuming and limited to few, expert laboratories. This study aims to evaluate the performance of a combination of two automated rapid immunoassays -LIA and CLIA -with respect to the gold standard: an immunoassay -CLIA- followed by functional test -HIPA- for HIT diagnosis.

Material and methods: This observational retrospective study investigated 100 patients (42 F; 58 M; mean age was 70.5 years ± 14.6) from Azienda Ospedaliera Careggi and other hospitals across or outside Tuscany, for whom clinicians requested Heparin-PF4 antibody detection for HIT suspicion. 4T pre-test probability score was assessed by clinicians: for 22% of patients a low risk probability (0-3), 62% had an intermediate risk probability (4-5) and 16% a high-risk probability (6-8).

Citrate whole blood and serum were collected and all samples were analyzed by CLIA assay at the time of sample submission. Subsequently we performed HIPA test, LIA and CLIA test on ACL TOP 970 on all 100 samples.

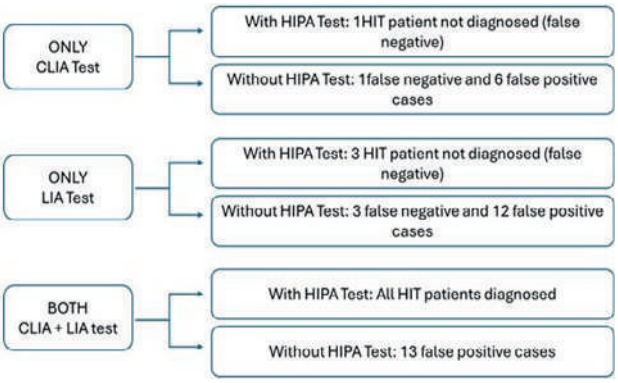
Results: As regard as CLIA test: 68 patients out of 100 (68%) were negative (<1U/mL) and 32 (32%) were positive (>1U/mL). As CLIA test was performed by both Acustar™ system and ACL TOP 970 CL, we found concordant results. The functional test confirmed HIT diagnosis in 26/32 patients and excluded HIT in 6/32 patients. Based on these results, CLIA method showed a sensitivity of 93.30% and a specificity of 91.78%. The Positive Predictive Value was 81.25% and the Negative Predictive Value of 98.53%.

As regard as LIA test: 64 out of 100 patients (64%) were negative (<1U/mL) and the remaining 36 (36%) were positive with a result equal or greater than 1U/mL. The HIPA tested 24/36 positive patients and 12/36 negative patients; only 3 out of 64 LIA negative patients were diagnosed as HIPA positive while 61 patients were confirmed as negative. LIA test displayed a sensitivity of 88.89% and specificity of 83.56%. The Positive Predictive Value was 66.67% and Negative Predictive Value of 95.31%.

HIPA functional test was performed on all 100 patients and confirmed HIT diagnosis on a total of 27 patients (27%), 23 patients were positive on both CLIA and LIA test, 1 patient was negative on CLIA and positive on LIA test while 3 patients resulted positive on CLIA and negative on LIA. By combining CLIA and LIA methods, a sensitivity of 100% and a specificity of 82.2% have been achieved.

The positive predictive value was 67.5% and Negative Predictive Value 87%. Among the 100 patients, the combination of CLIA and LIA tests allowed us to categorize 27 true positive, 13 false positive, 0 false negative and 60 true negative patients.

Conclusion: Our results allowed us to evaluate the role of the combined CLIA/LIA test both in laboratories with or without available HIPA functional test. By analyzing all possible scenarios, the combination of CLIA and LIA test improved HIT diagnosis identifying all HIT positive patients achieving a 100% sensitivity In conclusion, our study demonstrates how combined LIA/CLIA testing optimizes diagnostic sensitivity, with progressively greater probability of detecting platelet-activating antibodies with higher assay reactivity that reaches 100% when both automated assays yield moderate or strong results.



NEUTROPHIL-LYMPHOCYTE RATIO AND SUBCLINICAL ATHEROSCLEROSIS IN ESSENTIAL HYPERTENSIVE PATIENTS

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Arterial hypertension plays significant role in promoting the development of organ damage and atherosclerosis; Neutrophil-Lymphocyte Ratio (NLR) is an accessible and cost-effective biomarkers, strongly associated to adverse outcomes in patients with coronary artery disease and chronic heart failure. Study aimed disease to evaluate the clinical utility of NLR as surrogate of subclinical atherosclerotic damage in patients with essential hypertension.

From January 2024 to November 2024, we have consecutively enrolled 346 patients with essential hypertension. In all patients, webiochemicalbiomarkera the evaluated history, anthropometric data, biochemicals analysis and subclinical organ damage with 24-h urinary excretion of μ-albuminuria, carotid intima-media thickness, transthoracic echocardiography. We have excluded patients with arterial hypertension, coronary artery disease, cerebrovascular or peripheral artery diseases.

In our study, we found that patients with higher NLR was related with high blood pressure values, the assumption of more than 3 anti-hypertensive drugs, high prevalence of dyslipidemia and obstructive sleep apnea syndrome. Moreover, NLR values were correlated to higher prevalence of subclinical organ damage (left cardiac ventricular mass, carotid atherosclerosis and higher μ-albuminuria values). Our study shows that in essential hypertensive patients, the NLR is significantly correlated with some cardiovascular comorbidities and subclinical organ damage.

SEVERE BILATERAL EXOPHTHALMOS AS THE ONSET OF ORBITAL METASTATIC MELANOMA IN A PATIENT WITH METABOLIC SYNDROME

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ARNAS Civico Di Cristina Benfratelli

Introduzione: L'esoftalmo bilaterale rappresenta un segno clinico spesso associato a patologie di natura endocrina, infettiva, infiammatoria o neoplastica. In questo caso, l'approccio multidisciplinare ha consentito di diagnosticare un quadro atipico e raro di metastasi orbitarie da melanoma maligno, inizialmente non noto, in paziente affetto da plurime comorbilità.

Presentazione del caso: Paziente di 65anni, contadino, ex fumatore, affetto da sindrome metabolica (ipertensione arteriosa, diabete mellito di tipo 2, ipercolesterolemia, obesità viscerale), gozzo multinodulare ad estrinsecazione retrosternale normofunzionante con autoimmunità negativa. Giungeva presso gli ambulatori di " Malattie della Tiroide" della nostra UOC di Medicina Interna per esoftalmo bilaterale severo ingravescente con chemosi e papilledema in parziale risposta a terapia steroidea sistemica.

Indagini diagnostiche precedentemente effettuate (TC encefalo, TC collo/torace, RM orbite ed encefalo) evidenziavano:

Durante la degenza sono state eseguite:

;Una **TC addome con mdc** ha sollevato il sospetto di patologia sistemica linfoproliferativa per la presenza di pseudonoduli epatici, splenici, surrenalici e renali, multiple linfoadenopatie e versamento ascitico, quadro compatibile con **"omental cake"**. La **PET-TC** confermava la presenza di aree di aumentato me-

tabolismo in più distretti e la **RM addome** ha rafforzato il sospetto di patologia infiltrativa o neoplastica sistemica. La citofluorimetria ha mostrato inversione del rapporto CD4/CD8 ed incremento del rapporto kappa/lambda.
In tale contesto, nel sospetto di coinvolgimento infettivo, è stata inoltre intrapresa terapia empirica con antibiotici ad ampio spettro e con antimicotici, con scarso beneficio.
Diagnosi: Decisivo nel processo diagnostico è stato l'esame istologico del **grasso periorbitario dell'occhio destro** che ha evidenziato un' **infiltrazione neoplastica da melanoma maligno**. È stata pertanto effettuata valutazione specialistica dermatologica e biopsia di una lesione cutanea dorsale sospetta, già nota al paziente e sottoposta a precedente valutazione da parte di altro specialista dermatologo che aveva posto diagnosi di "Granuloma Piogenico". L'esito dell'esame istologico ha confermato invece la presenza di **Melanoma Nodulare polipoide**. Indagini di biologia molecolare hanno evidenziato **mutazione BRAF positiva** e mutazione PDL1 negativa.
Discussione: La metastatizzazione orbitale da melanoma è un evento raro, più frequentemente diagnosticato in fase avanzata. Il presente caso è peculiare per: L'approccio multidisciplinare ha permesso un inquadramento completo e l'avvio della corretta strategia terapeutica.
Conclusioni: Il caso sottolinea l'importanza di un sospetto clinico allargato nei quadri atipici di esoftalmo, specialmente in presenza di comorbidità ed indagini iniziali non dirimenti. L'infiltrazione orbitaria da melanoma metastatico può essere la prima manifestazione clinica della malattia, e il ruolo della biopsia rimane cruciale per la diagnosi definitiva.

UNLOCKING THE PREDICTIVE POWER OF NUTRITIONAL SCORES IN SEPTIC PATIENTS

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Sepsis is a critical condition characterized by severe immune dysregulation, ranking among the leading causes of morbidity and mortality in intensive care and internal medicine units. Nutritional status plays a pivotal role in modulating these responses, as when inadequate it can compromise immune defenses, the body's ability to handle stress and inflammation, and the clinical course. Malnutrition is frequently observed in septic patients and is strongly associated with worse clinical outcomes, including increased mortality, prolonged hospital stays, and greater complication rates. In this context, nutritional scoring systems have emerged as valuable tools to evaluate patients' nutritional status and predict clinical trajectories.
Objectives: Given the absence of a direct comparison of their performance in an internal medicine setting, this study aimed to assess the effectiveness of various nutritional scores as predictive tools for clinical outcomes in septic patients, emphasizing their application within the field of internal medicine.
Methods: and Results: A retrospective analysis was conducted on 143 patients diagnosed with sepsis or septic shock who were admitted to an internal medicine unit. Key variables included clinical and laboratory parameters, comorbidities, and nutritional scores at the time of diagnosis. The modified Glasgow Prognostic Score (mGPS), the Prognostic Nutritional Index (PNI), the Controlling Nutritional Status (CONUT) score, the modified Nutrition Risk in Critically Ill (mNUTRIC) score, and the blood urea nitrogen-to-albumin ratio (BAR) were evaluated in forecasting mortality and clinical outcomes in patients with sepsis. Among them, the mNUTRIC score emerged as the strongest independent predictor of in-hospital mortality, with a good performance and a reasonable threshold for risk stratification.
Conclusions: The study highlights the mNUTRIC score's practicality and reliability in assessing nutritional and inflammatory risks in septic patients, particularly in non-ICU settings. These findings suggest its potential utility in guiding nutritional interventions and improving clinical outcomes, emphasizing the importance of integrating nutritional assessment into sepsis management.

IMPACT OF RECOMBINANT ERYTHROPOIETIN ON ANEMIA, PHYSICAL FUNCTION AND COGNITIVE ASSESMENT IN HOSPITALIZED OLDER ADULTS.

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Anemia in elderly individuals is a significant clinical issue that often deteriorates quality of life and increases the risk of complications. Anemia is defined as a hemoglobin (Hb) level of less than 12 g/dL in elderly women and less than 13 g/dL in elderly men. In this study, we evaluated the effectiveness of erythropoietin (EPO) in treating anemia in patients over the age of 65, examining not only hematologic parameters but also its effects on physical and cognitive functionality.
A total of 156 elderly patients with confirmed anemia based on blood tests were enrolled.
The patients were randomized into three treatment groups: the first group received a single weekly dose of 40,000 units of EPO, the second group received 4,000 units three times a week, while the third group was treated according to standard guidelines with blood transfusions as necessary.
All patients underwent comprehensive geriatric assessments at the start of the study and at regular intervals during the observation period.After 12 weeks of treatment, results indicated that in the EPO-treated groups, hemoglobin levels increased on average by approximately 2 points, representing a significant improvement compared to the transfusion group.
Additionally, patients demonstrated a marked improvement in balance and walking ability, as evidenced by Tinetti test scores increasing from an average of 18 to 21 points. The time taken to stand up and walk (Timed Up and Go Test) also significantly improved, decreasing from 14 to around 11 seconds.Cognitive functions, assessed using the Mini-Mental State Examination (MMSE), increased by an average of 2 points, as did the ability to perform daily activities. Particularly noteworthy was the 42% reduction in fall episodes, which is a critical concern in the elderly population.Statistical analysis revealed that while anemia did not show a direct correlation with overall mortality, it was associated with an increased risk of cardiovascular events such as heart failure and syncope.
This suggests that EPO treatment may offer benefits that extend beyond mere correction of anemia, substantially enhancing the daily lives of elderly patients. The study demonstrates that EPO is a valid therapeutic option for anemia in the elderly, with positive effects on both hematologic and physical and cognitive parameters. However, further studies are needed to evaluate the duration of these benefits over time and to identify any potential long-term side effects.
These results open interesting prospects for improving the quality of life in the geriatric population and indicate that correcting anemia involves significant improvements in functional activity and cognitive abilities in elderly individuals.

A CASE OF AUTOIMMUNE AMEGAKARIOCYTIC THROMBOCYTOPENIA PROMOTED BY ENTEROCOCCUS FAECIUM UROSEPSIS

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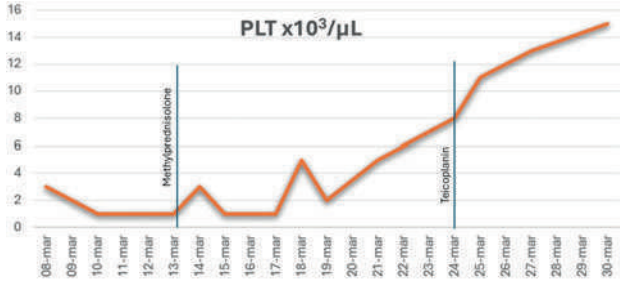
Background: Severe thrombocytopenia with life-threatening bleeding in elderly patients presents a diagnostic and therapeutic challenge, particularly when multiple comorbidities and potential immune or infectious triggers coexist.
Case presentation: A 77-year-old male with a history of HFpEF, atrial fibrillation on apixaban, pacemaker for complete AV block, MGUS (IgG-k 0.4 g/dL), and hypothyroidism due to autoimmune thyroiditis, was admitted at emergency with acute hematemesis, melena.
Initial examinations revealed microcytic anemia (Hb 6.7 g/dL), critical thrombocytopenia (PLT = 2,000/μL), neutrophilia (11.040/ul), and elevated CRP (166.8 mg/L). An urgent EGDS was performed, describing multiple hemorrhagic foci of gastric mucosa. The peripheral blood smear excluded the presence of schistocytes; hence an autoimmune thrombocytopenia was hypothesized and intravenous Immunoglobulins (IVIG) at 400 mg/kg/day × 5 days were started. Steroids were initially avoided because of the recent gastric bleeding. However, despite transfusions and IVIG therapy, a severe thrombocytopenia persisted with platelets number ranging between 500 and 1,000/μL.
Management and Outcome: A bone marrow aspirate and biopsy (BOM) were performed. FISH testing was negative for myelodysplastic syndromes, and karyotype analysis showed no cytogenetic abnormalities, ruling out clonal hematologic disorders. In contrast, a total absence of megakaryocytes was detected. Thyroid function confirmed severe hypothyroidism (TSH = 118.6 μU/mL, fT4 = 0.26 ng/mL, and positivity for anti-tireoperoxidase antibodies).
Considering the persisting very severe thrombocytopenia, methylprednisolone 1 mg/kg/day.
Of note, antibiotics were not prescribed at admission since the absence of clinical signs of infection except for generic increase of CRP. However, three

blood cultures and one urine colture revealed the presence of enterococcus faecium which was eradicated with antibiogram-based therapy with teicolplanin.
After introducing steroids, a progressive platelet increase occurred from 1,000 to 4,000/μL within 14 days with a final number of 15,000/ul after 3 weeks, when the patient was dismissed.
Conclusion: This case underscores the diagnostic complexity of secondary immune thrombocytopenia in elderly patients with multifactorial comorbidities. Here, we might conclude that a urosepsis caused by Enterococcus *faecium* promoted an autoimmune amegakariocytic thrombocytopenia in a patient with immune dysfunction (MGUS and autoimmune thyroiditis).
Bone marrow evaluation was critical to exclude underlying clonal or myelodysplastic processes. PLT x103/ μL



DIRECT ORAL ANTICOAGULANT FOR VENOUS THROMBOEMBOLISM IN PATIENTS WITH FACTOR V LEIDEN AND/OR PROTHROMBIN GENE MUTATION: A RETROSPECTIVE COHORT STUDY

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Background: The risk of clinically relevant outcomes during anticoagulation with direct oral anticoagulants (DOACs) in patients with venous thromboembolism (VTE) and thrombophilia is not well known. The aim of our study is to evaluate the effectiveness and safety of DOACs for VTE in patients with factor V leiden (FVL) and/or prothrombin gene mutation (PGM).
Methods: In this retrospective cohort study, patients on DOACs for VTE were included between 2014 and 2024. Baseline characteristics and presence of mutations (i.e., FVL and PGM) were collected. The primary effectiveness outcome included on-treatment recurrent VTE. The secondary effectiveness outcome comprehends acute arterial events. Safety outcomes included major and clinically-relevant non-major bleedings. Cumulative incidence with Kaplan-Meier curve was calculated for primary effectiveness outcome. The other outcomes were descriptively reported.
Results: A total of 192 patients were included of which 35 with FVL, 18 PGM, 10 FVL and/or PGM, and 123 wild-type. Characteristic of the two subgroups are reported in Table. Mean age was significantly lower in patients with FVL and/or PGM (64 versus 71 years). A similar proportion of patients between groups had a personal or family history of VTE. Most of patients had lower extremity deep vein thrombosis with/without pulmonary embolism and a small proportion an atypical site thrombosis with similar proportions between subgroups.
Treatment duration with DOACs was 42 months and 40 months in patients with and without thrombophilia. During DOACs, the cumulative incidence of recurrent VTE was 16.5% (95% confidence intervals – CI –, 4.7%-34.7%) in patients with FVL, 19.4 (95% CI, 4.1%-43%) in patients with PGM, and 3.3% (95% CI, 0.9%-8.7%) in wild-type patients. No recurrencies occurred in patients with FVL and PGM. A similar proportion of patients with and without thrombophilia had arterial events (3.2% versus 2.4%), major (1.6% versus 3.3%), clinically-relevant non-major bleedings (6.3% versus 2.4%).
Conclusions: Incidence of recurrent VTE during DOACs was significantly higher in patients with FVL and/or PGM than wild-type patients. The incidence of arterial events and of bleeding complications was similar between the two subgroups of patients. Future studies will be needed to assess the best therapeutic management of these patients.

Table. Baseline characteristics of included patients

Overall	Wild type N = 123	Fattore V Leiden e/o Mutazione gene protrombina N = 68	p-value
Mean age, years (SD)	71 (16)	64 (17)	0.006
Female sex, n (%)	64 (52.0)	28 (44.4)	0.410
Mean BMI, kg/m2 (SD)	27 (4)	28 (5)	0.234
VTE risk factors			<0.001
Persistent, n (%)	90 (49.7)	45 (37.5)	
Transient, n (%)	23 (12.7)	21 (17.5)	
Unprovoked, n (%)	68 (37.6)	54 (45.0)	
Previous TEV, n (%)	35 (30.4)	24 (42.9)	0.152
Family history of TEV, n (%)	12 (11.7)	6 (11.8)	0.779
Previous bleeding, n (%)	4 (3.5)	6 (10.5)	0.138
Site of VTE			0.343
PE	38 (30.9)	13 (20.6)	
LEDVT	47 (38.2)	30 (47.6)	
LEDVT + PE	27 (22.0)	13 (20.6)	
UEDVT	4 (3.3)	3 (4.8)	
UEDVT + PE	2 (1.6)	0	
Atypical site thrombosis	3 (2.4)	3 (4.8)	
Other sites	2 (1.6)	1 (1.6)	
Type of thrombophilia			
FII	0	18 (28.6)	
FVL	0	35 (55.6)	
FVL e/o FII	0	10 (15.8)	
Outcomes			
Recurrent VTE, n (%)	3 (2.4)	7 (11.1)	0.032
Arterial events, n (%)	3 (2.4)	2 (3.2)	1.000
Bleeding, n (%) Major CRNM	4 (3.3) 3 (2.4)	1 (1.6) 4 (6.3)	0.342
Mean follow-up, months (SD)	40 (34)	42 (34)	0.751

EFFECT OF GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONISTS ON BLOOD PRESSURE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Glucagon-like peptide-1 receptor agonists (GLP1-RAs) have recently emerged as a new treatment option to reduce cardiovascular mortality and morbidity in obese patients with and without diabetes. Arterial hypertension is one of the main cardiovascular risk factors and is strongly associated with obesity. However, no evidence exists on the effect of GLP1-RAs on blood pressure reduction.
Purpose: To assess the efficacy of GLP1-RAs on systolic and diastolic blood pressure reduction, as well as weight reduction. All-cause mortality was also explored as an efficacy outcome, while hypoglycemia episodes and pancreatitis were assessed as safety outcomes.
Methods: RCTs published up to October 2024 were systematically retrieved from PubMed, ClinicalTrials.gov, and Embase. The inclusion criteria were: 1) RCT comparing a GLP1-RA with placebo; and 2) Reporting the outcomes of interest.To account for potential heterogeneity, both a random effect and a fixed effect model were used. Variables are reported as median and interquartile range [IQR] and effect sizes as risk ratio (RR) and 95% confidence interval (CI) or mean difference (MD) and 95% CI, as appropriate.
Results: After the literature screening, 79 RCTs were included, encompassing a collective cohort of 89,348 patients (57.7% in the treatment arm). Median follow-up was 7 months [IQR 6-14], median age of the enrolled population was 54.5 years [IQR 49-58.5], and 36% were female. At baseline, median weight was 94 kg [IQR 90-100], systolic blood pressure was 129 mmHg [IQR 127-133], and diastolic blood pressure was 80 mmHg [IQR 77-81].
Systolic blood pressure was significantly reduced with GLP1-RA (MD -3.2 mmHg, 95% CI -3.8, -2.7; I2 = 86%), as well as diastolic blood pressure (MD -0.8 mmHg, 95% CI -1.2, -0.4; I2 = 92%), and body weight (-4.5 kg, 95% CI -5.6, -3.4; I2 = 99%) (Figure 1). The high heterogeneity did not affect the results, but significantly influenced its magnitude.
All-cause mortality was also significantly reduced with GLP1-RA treatment (RR 0.82, 95% CI 0.75, 0.90; I2 = 0%). Regarding the safety outcomes, no significant effect on pancreatitis was noted (RR 0.81, 95% CI 0.59, 1.12; I2 = 0%), with inconsistent results for hypoglycemia episodes (RR 1.06, 95% CI 0.84, 1.34; I2 = 69%), likely due to the high heterogeneity (Figure 2).
Conclusion: The findings of this meta-analysis suggest that GLP1-RAs may be an emerging treatment strategy for arterial hypertension in obese patients, with a significant reduction in both systolic and diastolic blood pressure. Furthermore, their use was associated with a significant reduction in all-cause mortality, together with a favorable safety profile.

SPONTANEOUS ABDOMINAL HEMATOMAS AS COMPLICATIONS OF PARENTERAL ANTICOAGULANT THERAPY: ANALYSIS OF CHARACTERISTICS, MANAGEMENT, AND OUTCOME OF A COHORT OF PATIENTS IN TRENTO

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Introduction: Bleeding is the primary complication of parenteral anticoagulant therapy, occurring in various locations and with varying degrees of severity. Among these, spontaneous abdominal hematomas are rare but potentially life-threatening, making prompt recognition and treatment essential. The available literature mainly consists of case reports or studies with small sample sizes, and little attention has been given to the outcomes of patients after the diagnosis and treatment of these complications. The aim of this study is to share our experience with these complications and highlight their clinical significance.
Methods: We conducted a retrospective observational study on patients admitted to the Azienda Provinciale per i Servizi Sanitari (APSS) in Trento from January1,2019, to August31,2024. The study focused on patients who developed rectus sheath hematoma (RSH) or spontaneous retroperitoneal hematoma (SRH) during parenteral anticoagulant therapy. Recorded variables included age, gender, hospitalization duration, type and indication of anticoagulant therapy, comorbidities, concomitant medications that could increase bleeding risk (e.g., antiplatelet agents and/or other anticoagulants), hematoma location, and whether active bleeding was present. Clinical presentation, diagnostic imaging, treatment type, and outcomes were also collected. Laboratory values (plasma creatinine, eGFR, complete blood count) were recorded at the onset of the hemorrhagic complication and prior to the event.
Results: Fifty-one patients were included in the study,51% of whom were women, and96% were elderly (≥65years). The mean age-adjusted Charlson Comorbidity Index (CCI) was5.75. Most patients (78.4%) were treated with LMWH, primarily for thromboembolism prevention (56% of cases) in atrial fibrillation/flutter. Concomitant antithrombotic therapy was used in35.3% of cases, with acetylsalicylic acid, clopidogrel, and warfarin being the most common agents.Laboratory findings showed a mean reduction in estimated glomerular filtration rate (eGFR) of10.41mL/min and a mean hemoglobin decrease of4.15g/dL, with a maximum drop of9.2g/dL. Regarding hematoma location,52.9% involved the rectus abdominis,41.2% were retroperitoneal affecting the iliopsoas, and5.9% had both. Common clinical signs included abdominal pain (72.5%) and abdominal swelling (21.6%), with5.9% of patients being asymptomatic and diagnosed through acute anemia.Diagnosis was confirmed in98% of patients via contrast-enhanced abdominal CT, with82.4% showing active bleeding. Most patients (82.4%) underwent interventional treatment, including embolization (80.4%), surgical drainage (7.8%), or ureteral stent placement (3.9%). Forty-four patients received blood transfusions (mean5units).After the acute event,60.8% resumed anticoagulation therapy before discharge,9.8% restarted after one month, and29.4% did not resume therapy (3of whom died during hospitalization). Outcomes showed that5.9% of patients died during hospitalization,11.8% experienced new bleeding (6patients had a major bleeding, among these2died), and7.8% died later from unrelated causes.
Conclusions: SRH and RSH are rare but potentially serious complications of anticoagulant therapy. These conditions can significantly impact healthcare resources and patient outcomes, particularly in the case of retroperitoneal hematomas. They are most commonly observed in patients with multiple comorbidities, including renal insufficiency. During parenteral anticoagulant therapy, especially with LMWH, it is essential to monitor plasma creatinine and eGFR at the start of treatment to determine the correct dosage. Regular follow-up assessments are also crucial, particularly in complex patients undergoing polytherapy, as rapid deterioration may occur.When evaluating a patient on anticoagulant therapy who presents with acute anemia, it is important to consider the possibility of SRH or RSH, especially in the presence of abdominal pain, swelling, or symptoms of compression. Timely recognition and treatment are key to avoiding delays in diagnosis.Given the insidious nature of these complications and their potential for significant morbidity and mortality, it is vital to stay vigilant. Once the acute event is resolved and the patient returns to their baseline condition, the clinician must decide whether to resume anticoagulant therapy. Although no clear guidelines exist for this decision, our data—showing a low rate of major bleeding recurrence—suggest that resuming therapy can be done safely with careful consideration. However, the decision must weigh the risks and benefits for each individual patient.

IN-HOSPITAL MORTALITY IN PATIENTS UNDERGOING INFERIOR VENA CAVA FILTER PLACEMENT FOR ACUTE DEEP VEIN THROMBOSIS

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Background: Inferior Vena Cava Filters (IVCFs) are often used outside of established indications and many authors argue about their actual utility, especially in terms of survival. In this retrospective study, we measured in-hospital mortality among patients who underwent IVCF placement. The analysis was limited to the cases for which a correct indication to IVCF placement existed.
Methods: First, we retrospectively analyzed the electronic database of Fondazione Policlinico Universitario A. Gemelli IRCCS, searching for consecutive hospitalized patients who underwent IVCF placement. The search covered the period between 1 January 2010 and 31 December 2020. Next, we eliminated those cases for which a correct indication to IVCF placement was not clear. For correct indication to IVCF placement, we intended the following two situations: 1) patients with acute (<30 days) thrombosis of the proximal deep veins of the legs and concomitant absolute contraindication to therapeutic anticoagulation, 2) patients with acute (<30 days) thrombosis of the proximal deep veins of the legs and need to stop anticoagulation due to urgent non-deferrable surgery.
Results: The search resulted in the identification of 168 individuals. The reason for filter placement was an established contraindication to therapeutic anticoagulation in 116 cases (69.0%) and the need for urgent non-deferrable surgery in 52 cases (31.0%). A total of 24 patients (14.3%) died during the same hospital stay in which the IVCF was placed. Mortality rate was significantly higher in patients with a contraindication to anticoagulation than in patients who underwent IVCF placement because of urgent surgery (19.0% vs. 3.8%, OD 5.85 vs. 0.17). In-hospital mortality was also significantly higher among patients with chronic kidney disease and those who needed blood cell transfusion during hospitalization.
Conclusions: In-hospital mortality is high among patients who undergo IVCF placement, especially those with absolute contraindication to anticoagulation, chronic kidney disease, and need for blood cell transfusion. Further studies are needed to understand whether the placement of IVCFs is useful or futile in these situations.

MARKERS OF INFLAMMATION AND HYPOFIBRINOLYSIS ARE ASSOCIATED WITH COGNITIVE DYSFUNCTION AND MOTOR PERFORMANCES IN ATRIAL FIBRILLATION PATIENTS ON ORAL ANTICOAGULANT THERAPY: INSIGHTS FROM THE STRAT-AF STUDY

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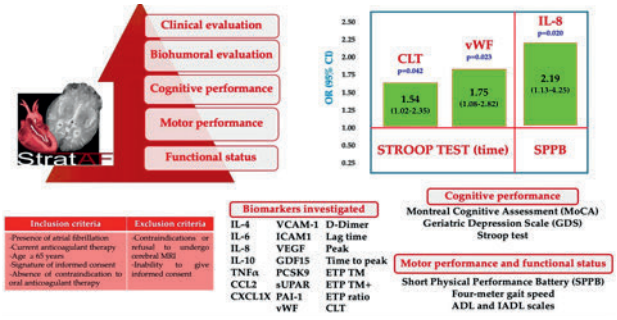
Background: Atrial fibrillation (AF) is the most common supraventricular arrythmia and one of the most commonly encountered heart conditions in clinical practice. Emerging evidence suggests a significant role of inflammation in the pathogenesis of AF. Population studies have also suggested an association between AF and cognitive impairment and dementia. The aim of this study is therefore to assess, in a population of AF patients on oral anticoagulant therapy, the association between circulating biomarkers involved in the pathogenesis of AF and the cognitive and motor performances of the enrolled patients.
Methods: The Strat-AF study is an observational, prospective, single-center, hospital-based study enrolling elderly patients with AF. Results refer to180subjects who underwent a complete clinical, biohumoral, cognitive, and functional evaluation.
Results: At multivariate logistic regression, Clot Lysis Time (CLT) and circulating levels of von Willebrand Factor (vWF) remained significantly associated with pathological performances at the Stroop test (expressed as execution time) [OR95% CI1.54(1.02-2.35), p =0.042and1.75(1.08-2.82), p =0.023, respectively]. With regard to the Short Physical Performance Battery (SPPB), the circulating levels of IL-8remained significantly associated with the clinical endpoint [OR95% CI2.19(1.13-4.25), p =0.020].
Conclusions: Our results suggest a potential innovative tool able to identify AF patients at risk of worse prognosis in terms of cognitive and motor per-

formances. The clinical relevance of these results is due to the fact that we have no efficient methods to predict a deterioration in the cognitive performance and, consequently, the possible onset of dementia in AF patients undergoing oral anticoagulant therapy.



TO TRANSFUSE OR NOT TO TRANSFUSE: THAT IS THE QUESTION

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Case report: In March 2024 a 42 y.o. woman with history of beta-thalassemia trait and frequent musculoskeletal pain episodes when exposed to low temperatures, presented to an Emergency departmente of an hospital of the Northern Italy because of fever, and back and left-sided thoracic pain. Lab tests showed severe microcytic anemia (hemoglobin 5.1 g/dL), thrombocytopenia, leukocytosis and hemolytic markers alteration with positive indirect Coombs test. She was transfused with 2 PRBC units with a further drop in hemoglobin levels. Given her worsening conditions she was transferred to the Intensive Care Unit of our Hospital, where she was found to have severe hemolytic anemia, with positive indirect Coombs test and high titer anti-E antibodies in concomitance to an acute infection by Parvovirus B19. Given to the medical history of the patient, a misdiagnosed Sickle-beta-thalassemia syndrome complicated by delayed hemolytic transfusion reaction (DHTR) was suspected, so High Performance Liquid Chromatography (HPLC) and genetic test were repeated and they confirmed the diagnosis of microdrepanocytosis. Due to the hyperhemolytic syndrome and concomitant alloimmunization, despite the severe anemia, the patient did not undergo further transfusions and, after high-dose steroid therapy and intravenous immunoglobulins, progressively returned to baseline Hb levels (Table 1).
Conclusion: . Hemoglobinopathies are the most frequent anemias requiring blood transfusions. Despite transfusion therapy plays a crucial role in the management of these diseases, it is burdened by complications, which could present as life-threatening conditions. This case highlights the importance of an accurate diagnostic process in order to reach the correct diagnosis, and of an individualized risk-benefit evaluation to ensure the best therapeutic strategy to the patient.

Table 1.

ACQUIRED HEMOPHILIA AFTER SARS-COV-2 IMMUNIZATION: A NARRATIVE REVIEW OF A RARE SIDE EFFECT

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Acquired hemophilia A (AHA) is a rare but severe hemorrhagic disorder characterized by the production of autoantibodies directed against coagulation factor VIII, which presents an increased risk of spontaneous bleeding and potentially life-threatening complications, primarily related to immunosuppressive treatment. The annual incidence is estimated at approximately 1.4 cases per million people. Clinical manifestations include: bruising, soft tissue hematomas, and mucosal bleeding. In recent years, particular attention has been directed toward the possible association between AHA and anti-SARS-CoV-2 vaccination, especially following the widespread administration of mRNA vaccines (BNT162b2 and mRNA-1273).
This review analyzes 18 publications, including 2 case series and 16 case reports, describing the onset of AHA in patients vaccinated against COVID-19. It was observed that most cases occurred in individuals aged between 67 and 86 years, often with a history of cardiovascular or metabolic diseases. Although the causal link between vaccination and AHA has not yet been definitively established, the most widely accepted pathogenic hypothesis suggests that the immune stimulation induced by the vaccine may trigger an autoimmune response directed against factor VIII in predisposed individuals.
Despite the serious hemorrhagic manifestations, the prognosis of patients with vaccine-related AHA has generally been favorable, with spontaneous resolution in some cases and a positive response to immunosuppressive and hemostatic therapies in others. However, timely recognition and treatment are crucial, especially considering the widespread deployment of COVID-19 vaccines.
Currently, no specific pharmacovigilance registries or dedicated prospective studies have been activated to systematically monitor cases of acquired hemophilia (AHA) potentially related to anti-COVID-19 vaccines. Further studies are needed to thoroughly elucidate the immunological mechanisms involved and identify any predisposing risk factors. Therefore, it is essential to implement clinical awareness programs regarding this potential hematological complication and to develop standardized diagnostic-therapeutic algorithms that balance the undeniable benefit of vaccination with the proper management of bleeding adverse events.
In conclusion, while anti-COVID-19 vaccines represent a crucial tool in the fight against the pandemic, their association with AHA requires further scientific investigation and a cautious clinical approach, especially in elderly and frail patients. The identification of predictive biomarkers will be fundamental for optimizing therapeutic strategies to ensure maximum safety in the use of these vaccines.

TOOTH LOSS, ORAL HYGIENE, AND CARDIOVASCULAR AUTONOMIC MODULATION: BASELINE INSIGHTS FROM AN OBSERVATIONAL STUDY IN HOSPITALIZED PATIENTS

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Background: Oral health has been increasingly linked to systemic conditions, including cardiovascular disease. Tooth loss and inadequate oral hygiene may influence cardiac autonomic regulation, which can be assessed through heart rate variability (HRV).
Objectives: To investigate the association between tooth count and cardiovascular parameters—including HRV and length of hospital stay—in hospitalized patients, through an observational study.
Methods: Patients admitted to the Department of Internal Medicine at Ospedale Maggiore Policlinico di Milano were invited to participate. Those who provided written informed consent (Ethics Committee approval: 0046157-U) were enrolled. A trained dentist conducted oral examinations, and participants were stratified by tooth count (≤15 vs. >15 teeth). Collected data included oral health status, frequency of hygiene practices, denture use, signs of oral inflammation, blood pressure, hospital stay duration, and HRV parameters. Statistical analysis was performed using the Mann-Whitney and Kendall's Tau tests ($\alpha = 0.05$).
Results: Nineteen patients were included (68.4% male; mean age 71.6±16.5 years; mean tooth count 12.4±10). Patients with ≤15 teeth had significantly longer hospital stays compared to those with >15 teeth (13.5±8 vs. 6.8±3 days, p=0.02), regardless of systemic comorbidities. Tooth count was negatively

correlated with hospital stay duration (r=-0.35, p=0.043) and positively with hygiene frequency (r=0.63, p=0.001). Poor oral hygiene (0.5±0.6 times/day) was more common among patients with fewer teeth and was inversely associated with oral inflammation (r=-0.59, p=0.007). Inflammation was strongly associated with prostheses use (r=1, p<0.001). HRV parameters showed no significant group differences (LF p=0.44, HF p=0.18, LF/HF p=0.19; symbolic indices 0V% p=0.48, 2UV% p=0.57). However, heart rate was inversely correlated with tooth count (r=-0.47, p=0.049) and hygiene frequency (r=-0.48, p=0.044), and positively with inflammation (r=0.48, p=0.045).
Conclusion: Tooth count, oral hygiene frequency, and signs of inflammation may serve as valuable clinical indicators in hospitalized patients. Individuals with fewer teeth experienced longer hospitalizations and poorer oral hygiene, with inflammation strongly linked to denture use. Although HRV metrics did not differ significantly, heart rate correlations suggest a link between oral status and autonomic regulation. These findings support the integration of oral health assessment into routine hospital screening and care.

IDIOPATHIC UPPER EXTREMITY DEEP VEIN THROMBOSIS: REAL WORLD DATA

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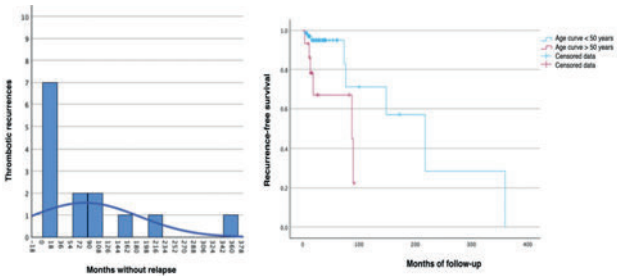
Background: Spontaneous deep vein thrombosis of the upper limbs are rare events with an incidence of 1-2 cases per 100000 inhabitants per year, and which have so far been poorly characterized in the literature. However, they often affect patients who are on average younger than those with lower limb events and with fewer comorbidities.
Methods: We retrospectively collected information about all patients with spontaneous thrombosis of the upper limbs followed by the Thrombosis Center of the AOU-Careggi. In particular, we studied the clinical-anamnestic characteristics of these patients, as well as the presence of thrombotic risk factors, such as thrombophilia, the use of estrogen-progestin therapy or thoracic outlet syndrome or strains/traumas preceding the event. We also compared the therapeutic regimens used, i.e. LWMH/VKA versus DOACs, in terms of efficacy and safety in the acute phase therapy of the event. Finally, we collected information about the rate of recurrence and the development of post-thrombotic syndrome during follow-up.
Results: We enrolled 92 patients with an average age of 38 years (± 13), with an equal male/female ratio. A third of the women were taking estrogen-progestin at the time of the event, while only in 15% of cases it was possible to identify a particularly intense effort prior to the event. Thoracic outlet syndrome was found in one third of patients, whereas only one fifth of patients had underlying thrombophilia. All events were unilateral and 12 cases were complicated by pulmonary embolism. No deaths were recorded. From the comparison between patients treated with LWMH/VKA (57) versus those treated with DOACs (35), no statistically significant differences emerged in efficacy and safety in terms of major or clinically relevant bleeding. The average follow-up was 49 months and in the total population only three patients developed a post-thrombotic syndrome at least moderate degree, measured on the basis of clinical criteria and the impact on the patient's life. In total, there were 14 relapses following suspension of anticoagulant therapy, of which 9 in the same location as the index event and 5 in the lower limbs. The overall relapse rate was 4.8%, with a peak of 6.4% within 18 months of the event. From a multivariate analysis for the clinical and anamnestic variables collected, only age over 50 years was found to be a risk factor for relapse with an OR of 5.2 (95% CI 1.5-18.7, p=0.010).
Conclusions: Despite the limitations of a retrospective study, we have collected a rather large population with characteristics in agreement with what has already been reported in the literature. From our data emerges the safety and effectiveness of DOAC therapy, which to date does not have a formal indication for this type of thrombotic events, but which is often used in common clinical practice. The rate of recurrence of events in these patients is rather low, so routine long-term anticoagulant therapy does not seem desirable. However, the location of the relapses, often in the lower limbs, suggests an increased systemic thrombotic risk and not an isolated predisposition at the level of the upper limb circulation. A greater characterization of these events is certainly desirable to select patients at greater risk of recurrence.



ELTROMBOPAG TREATMENT FOR THROMBOCYTOPENIA IN MYELODYSPLASTIC SYNDROMES: DIFFERENCES BETWEEN RESPONDING AND NON-RESPONDING PATIENTS - A PILOT STUDY

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Myelodysplastic syndromes (MDS) represent a heterogeneous group of hematopoietic cell disorders characterized by peripheral cytopenia, a variable rate of bone marrow failure, abnormal cellular maturation, and progression to acute myeloid leukemia (AML). Internists are particularly interested in this topic because patients with MDS often receive diagnoses in the hospital when admitted for complications such as infections or bleeding. Additionally, low-risk MDS patients typically require only supportive therapy and are managed in internal medicine wards.
Thrombocytopenia is one of the most common complications in patients with MDS, with a prevalence of 65% (range 23-93%). Severe thrombocytopenia in MDS can potentially increase the risk of hemorrhage and negatively impact the outcome of low-risk patients. The incidence of non-fatal bleeding as a complication of MDS is reported to range from 3% to 53%, with fatal bleeding reported at 14% to 24%. Unfortunately, reliable data on the consequences and incidence of thrombocytopenia in MDS are lacking.
For patients with MDS and a platelet count below 30 x 10^9/L, who have bleeding not responsive to platelet transfusions or antifibrinolytic therapy, treatment with thrombopoietin receptor agonists, such as Eltrombopag (ELTPO), is indicated. This category of drugs is generally reserved for low-risk MDS patients (< 5% blasts in the bone marrow). However, there is controversy regarding the use of TPO mimetics, which may potentially accelerate progression to AML. TPO mimetics can reduce bleeding and the need for platelet transfusions in a timely manner in patients with MDS.
In our 12-month pilot study, we evaluated 69 patients with MDS having platelet counts ≤ 30 x 10^9/L and bleeding unresponsive to platelet transfusions and antifibrinolytics, who were treated with Eltrombopag. Among these patients, 41 responded to the therapy, and they were compared with the 28 who did not respond to analyze differences in hematochemical parameters. Complete blood counts, liver profiles, and renal functions were monitored at baseline, weekly for the first 4 weeks, and every 15 days for the subsequent 8 weeks. After 12 weeks, patients who positively responded to therapy were monitored monthly, while the remaining participants were monitored biweekly for the duration of the study.
Inclusion criteria for the study were: age ≥ 18 years with a diagnosis of medium- or low-risk MDS with a stable platelet count (≤ 30 x 10^9/L) that were unresponsive or ineligible for platelet transfusion. Exclusion criteria included: primary chemotherapy-radiotherapy or previous treatment with TPO receptor agonists; monocytosis > 0.6 x 10^9/L, leukocytosis ≥ 10 x 10^9/L, bone marrow fibrosis > 3, Eastern Cooperative Oncology Group performance status > 3; serum creatinine > 2 times the upper limit of normal; AST and ALT > 3 times the upper limit of normal or bilirubin > 1.5 times the upper limit of normal; a pre-existing cardiovascular condition or arrhythmia associated with increased thromboembolic events.
The drug was administered orally at an initial dose of 50 mg/daily, titrated with increases of 50 mg every 2 weeks up to a maximum of 300 mg/daily or until achieving a complete platelet response defined as a count ≥ 100 x 10^9/L.
The first part of the study analyzed the response in terms of short-term efficacy, with a response considered as an increase in platelet count of approximately 100% in the absence of bleeding and without the need for platelet transfusions. The second part of the study assessed the long-term response and safety, including the stability of the platelet count values achieved in the initial phase

and the reduction of bleeding incidence.
Our study suggests that ELTPO reduces the risk of bleeding and decreases the requirement for platelet transfusions, allowing for early treatment in patients with MDS. The need for platelet and red blood cell transfusions is significantly reduced in these patients, likely due to not only the reduction in bleeding but also the effects of TPO mimetics on bone marrow function.

FONDAPARINUX FOR LONG-TERM TREATMENT OF VENOUS THROMBOEMBOLISM: RESULTS FROM THE START REGISTRY

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Background: and Aims: Fondaparinux is actually licensed for the first days of treatment of venous thromboembolism (VTE), but for some favourable characteristics it is sometimes used in specific subgroups also in the long-term treatment. Aim of this study was to evaluate the long-term effectiveness and safety of fondaparinux for the long-term treatment of VTE.
Methods: We performed a preliminary retrospective analysis on data from the START Registry about patients receiving long-term anticoagulation with fondaparinux (i.e., > 7 days). We evaluated as effectiveness outcome recurrent VTE and arterial events and as safety outcome major bleedings. Baseline characteristics of the enrolled population and outcome of interest are reported as descriptive statistics. Continuous variables were expressed as mean (standard deviation) or median (interquartile range – IQR –) values, according to data distribution after applying the Wilk-Shapiro test. Categorical variables were expressed as counts and percentages.
Results: We included a total of 133 patients receiving long-term fondaparinux. Table reported the baseline patients characteristics. Median age was 66 years (IQR, 55 to 76 years), 48.1% of patients were male, and median BMI was 27.3 kg/m2. Most of patients had a lower extremity deep vein thrombosis (72.2%), followed by pulmonary embolism (10.5%) and upper extremity deep vein thrombosis (9.0%). A small proportion of patients had atypical site thrombosis (2.3% splanchnic, 0.8% cerebral, and 0.8% caval vein thrombosis). Most of patients had an unprovoked vein thrombosis (46.7%). Median hemoglobin values was 13.1 g/dl (IQR, 11,8 to 14,7 g/dl), median platelet 226000/ul (IQR, 176000 to 296000/ul), and media creatinine value 0.85 mg/dl (IQR, 0.73 to 1.03 mg/dl). Median treatment duration was 34 days (IQR, 12 days to 112 days). One patient (0.8%) had an on-treatment recurrent VTE, two patients (1.5%) an on-treatment arterial event, and one patient (0.8%) an on-treatment major bleeding.
Conclusions: In this preliminary analysis, fondaparinux appeared to be an effective and safe therapy for the long-term treatment of VTE. Caution is needed for the interpretation of these results, which are limited by the small sample size of our cohort. Larger cohorts are needed to confirm these findings.

Table: characteristics of included population

Variables	Fondaparinux N = 133
Mean age, years (SD)	66.00 [55.00, 76.00]
Male sex, n (%)	64 (48.1)
Mean BMI, (SD)	27.30 [23.80, 30.90]
Site of thrombosis	
LEDVT	96 (72.2)
Pulmonary embolism	14 (10.5)
UEDVT	12 (9.0)
LEDVT & pulmonary embolism	5 (3.8)
Splanchnic vein thrombosis	3 (2.3)
Cerebral vein thrombosis	1 (0.8)
Caval vein thrombosis	1 (0.8)
UEDVT & pulmonary embolism	1 (0.8)
Risk factor of VTE, n (%)	
Unprovoked	50 (46.7)
Persistent	30 (28.1)
Transient	27 (25.2)
Mean Hb, g/dl (SD)	13.10 [11.80, 14.70]
Mean PLT, (SD)	226.00 [176.00, 296.00]
Mean clearance creatinine, (SD)	0.85 [0.73, 1.03]
Outcomes	
Major bleeding, n (%)	1 (0.8)
Recurrent VTE, n (%)	1 (0.8)
Arterial events, n (%)	2 (1.5)

ASSESSMENT OF PRESCRIBING APPROPRIATENESS USING STOPP/START CRITERIA IN A COHORT OF HOSPITALIZED PATIENTS

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Introduction: Inappropriate prescribing is commonly observed across all clinical settings in elderly patients dealing with multiple chronic conditions and polypharmacy. This issue is highly relevant to patient safety, as it significantly contributes to morbidity and mortality through adverse drug reactions. The STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert the Right Treatment) criteria are explicit tools developed to identify potentially inappropriate medications (PIMs) and potential prescribing omissions (PPOs). These tools are based on a thorough literature review and have been validated by a consensus from a panel of European experts. Their development was inspired by the Beers Criteria—first introduced in 1991 and subsequently updated in 2011 by the American Geriatric Society—which evaluate medications that may be inappropriate or require cautious use in older adults. Several recent studies conducted in varied clinical settings have confirmed the relevance of STOPP/START in improving prescribing practices. These findings emphasize the necessity for enhanced education of both patients and physicians regarding the risk-benefit balance of pharmacological treatments. They also highlight the importance of accurate and up-to-date medical documentation to avoid unnecessary or unsuitable recommendations.
Aims: This study primarily aims to assess the prevalence of PIMs and PPOs in patients admitted to our hospital. Additionally, we evaluate modifications made to patients' medication regimens, particularly focusing on the discontinuation of inappropriate drugs and the initiation of previously erroneously omitted medications.
Methods: Initially, we reviewed existing literature to understand the current application of the STOPP/START criteria. Subsequently, we extracted relevant information from the MED-Cli multipurpose prospective database, which contains clinical data from patients hospitalized in the Internal Medicine Departments of San Raffaele Hospital. All participants provided informed consent for inclusion in this registry. . We analyzed data from patients admitted between February 2024 and January 2025. For each patient, we evaluated the presence of PIMs and PPOs at the time of both admission and discharge. Due to practical limitations, we did not apply all STOPP/START criteria in our analysis: within the STOPP criteria, we excluded the first (i.e., any medication prescribed without a clear indication), and within the START criteria, we omitted the section on vaccinations. Descriptive statistical analysis was performed on the collected data.
Results: A total of 392 patients were included in the analysis. Approximately half of the patients (52,9%) were male and the median age was 73 years. This cohort is representative of older people with polypharmacy, with over 80% of individuals taking five or more regular medications. At admission, 30% of patients had at least one PIM as defined by STOPP criteria, which decreased to 25% at discharge. PPOs, as defined by START criteria, were identified in 50% of patients at admission and 20% at discharge. The most frequently observed PIMs at admission involved medications associated with an increased risk of falls. This was followed by drugs targeting the cardiovascular system, as well as neurological and psychotropic agents. The prevalent PPOs at the admission regarded cardiovascular medications, followed by treatments related to the musculoskeletal and respiratory systems, and analgesics. When comparing our findings to a previous study conducted on 304 patients admitted between November 2022 and April 2023 within the same department, we found no statistically significant differences. However, a clearer trend toward discontinuation of inappropriate drugs was evident.
Discussion and Conclusion: Our findings differ somewhat from other prevalence studies, especially concerning STOPP-defined PIMs, which were less frequently observed in our sample. In hospital-based settings, the reported prevalence of at least one PIM ranges from 35% to 77%, and PPOs from 51% to 73%. These discrepancies may be attributed to our selective exclusion of certain STOPP/START criteria during the analysis. Nevertheless, we observed a general improvement in prescribing quality by discharge, particularly regarding the correction of PPOs during hospitalization. Future research is essential to assess the long-term outcomes of these therapeutic modifications and to further explore the integration of these criteria into everyday clinical practice.

ABSTRACT: LESSONS FROM A CASE OF MULTIPLE COMPLICATIONS FOLLOWING FEMORAL ARTERY ACCESS AND THEIR TREATMENT

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Both local and systemic complications following diagnostic and interventional procedures are not so uncommon in clinical practice and sometimes their treatment exposes patients to even more harmful risks. Vascular complications such as arterial occlusion and pseudoaneurysm concern not only large-caliber vessels.
Presented is the case of a 90-year-old man with critical limb ischemia who underwent a double procedure of revascularization of the right lower limb (first attempt was unsuccessful) by selective catheterization and contralateral femoral access using a "cross-over" technique with a 5F sheath. In both revascularization procedures mechanical hemostasis was achieved using the MynxGrip5 extravascular closure device and application of the SafeGuard, inflated to 40 mL. The second attempt, although terminated with therapeutic success, was complicated by a pseudoaneurysm of the left femoral artery. Because of its anatomical features, the pseudoaneurysm was treated by thrombin injection. The Doppler ultrasound (DUS) examination performed within 24 hours after treatment documented a partial thrombosis of the common femoral vein and focal dissection of the adjacent common femoral artery. Anticoagulant therapy was undertaken, and the patient was started for follow-up.
Our case shows a succession of complications following interventional procedures using a large-caliber arterial access. Vascular closure devices (VCDs) have been developed to reduce complications and ensure hemostasis in large-bore accesses. They have also been shown to be non-inferior to manual compression. A recently published paper provides guidance on minimizing the risk of complications from large-caliber femoral accesses, such as by identifying the correct puncture site, new approaches (e.g., the Micropuncture kit [Cook Medical, Bloomington, IN]), and the proper management of VCDs. There is no consensus on the choice of VCDs. A meta-analysis by Tayyab Cheema et al. focused on the safety and effectiveness profile of MANTA and Perclose devices, currently the most widely used for closure of large-bore access. Perclose achieves hemostasis with a single monofilament suture at the vascular access site with a 92% success rate and a 4.4% complication rate. MANTA, instead, consists of an extravascular collagen structure held in place by an endoluminal polymer toggle, stainless steel element, and suture that achieves high technical efficacy with a low risk of vascular complications.
However, the use of MynxGrip has recently been investigated in the literature in two RCTs which show an advantage over manual compression in terms of faster hemostasis and earlier ambulation, without major adverse vascular events (MAVE).
The MynxGrip is a passive VCD designed to achieve femoral artery and vein haemostasis via delivery of an extravascular, water-soluble (hydrogel) and polyethylene glycol (PEG) sealant. A semi-compliant balloon is inflated intraluminally to serve as an anchor as the sealant is deployed over the arteriotomy. The balloon is deflated and removed, leaving the sealant over the arteriotomy, which expands upon contact with subcutaneous fluids and is resorbed within 30 days. There are no contraindications known for MynxGrip. Major possible complications include access-site-related bleeding requiring transfusion, vessel occlusion, pulmonary embolism, or death; while minor ones include pseudoaneurysm and hematoma.
To rule out their presence, DUS allows early detection of intra and postoperative adverse events with the advantages of being fast, non-invasive and readily available. However, it is operator-dependent and requires considerable expertise.
The randomized UNIVERSAL trial recently compared the safety of VCDs in patients undergoing US-guided vs non-US-guided femoral arterial access for coronary procedures, showing that US-guided access was associated with fewer bleeding and vascular complications. Another retrospective analysis of neurovascular cases performed with femoral access between Jan 2016 and Dec 2022 found no statistically significant difference in complication rate between the two groups. However, it proves beneficial in high-risk cases. Notably, interventional procedures, particularly endovascular treatment (EVT), use of larger sheaths, and dual antiplatelet therapy (DAPT), have been identified as independent predictors of femoral access site complications.
In such high-risk scenarios, ultrasound guidance plays a crucial role in minimizing access-site complications.
Our case highlights the usefulness and simplicity of post-procedural DUS evaluation in identifying early complications of vascular access. Although all EVTs were performed under US-guidance, it was not possible to prevent serious complications such as pseudoaneurysm, arterial dissection, and thrombosis. In this case, the MynxGrip did not prove significantly different from other VCDs studied in the past. This underscores the need to refine these techniques and to make ultrasonographic evaluation by an experienced operator a standard part of every procedure.

VITAMIN D STATUS IN PATIENTS ADMITTED TO THE INTERNAL MEDICINE UNIT AND ORTHOPEDICS UNIT OF THE AZIENDA OSPEDALIERO-UNIVERSITARIA SENESE

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Background: Vitamin D is essential for optimal bone health and muscle function. However, an alarming rate of hypovitaminosis D has been recently reported in the global population, without distinction of race, age, or ethnicity. The issue of vitamin D deficiency is of significant relevance within the Italian population. Hypovitaminosis D is often associated with frailty, leading to increased morbidity and mortality. Furthermore, vitamin D deficiency increases the risk of fractures and reduces the effectiveness of osteoporosis medication. Epidemiological studies show that vitamin D deficiency is indeed very frequent in the elderly and during the winter months. It is estimated that 86% of Italian women over 70 years of age have vitamin D levels below the normal range at the end of winter. This finding is particularly alarming in institutionalized individuals or those with other concomitant pathologies. The higher prevalence of hypovitaminosis D in Mediterranean countries compared to Northern Europe, which is significantly less sunny, is known as the "Scandinavian paradox." This is due to the long-standing practice of fortifying foods with vitamin D in Northern European countries. The increasing prevalence and incidence of hypovitaminosis D in Italy is also due to the aging of the population; in fact, the enzymatic system responsible for vitamin D synthesis becomes less efficient with age.
The aim of this study was to evaluate serum levels of 25-hydroxyvitamin D (25OHD) in patients hospitalized in orthopedics following a hip fracture and in an internal medicine unit.
Materials and methods: The subjects of our study were 272 patients hospitalized in the Orthopedics Unit (ORT) of the Azienda Ospedaliero-Universitaria Senese (A.O.U.Senese) following a hip fracture (mean age = 84.4 ± 9.2 years) and 222 patients (mean age = 79.6 ± 11.7 years) hospitalized in the Internal Medicine and Complexity Unit (MIC) of the A.O.U.Senese. Anamnestic data were collected from computerized medical records and the archive of the A.O.U.Senese information system. All patients underwent venous blood sampling for the evaluation of calcemia, phosphatemia, creatinine, alkaline phosphatase, parathyroid hormone (PTH), 25OHD, and bone-specific alkaline phosphatase isoenzyme (B-ALP). Comorbidity was measured in all patients using the Charlson Comorbidity Index (CCI).
Results: We observed that 25OHD levels were insufficient in both patients hospitalized in Orthopedics for hip fracture and those hospitalized in Internal Medicine Unit (13.8 ± 14.2 ng/mL and 14.8 ± 11.4 ng/mL, respectively). Furthermore, the prevalence of insufficient serum 25OHD levels was higher in patients with hip fracture hospitalized in ORT compared to those hospitalized in MIC (59.2% vs 47.5% respectively, $p<0.05$). As expected, patients hospitalized in MIC had significantly higher Charlson scores compared to those hospitalized in ORT (6.11 ± 3.31 and 2.25 ± 1.59, respectively). CCI values, when analyzed based on different 25OHD cut-offs, did not show significant differences between the two populations.
Conclusions: Our study highlights that hospitalized patients, regardless of the setting, present with insufficient 25OHD levels, with no evidence of differences based on age and comorbidities. Numerous confirmations from the literature indicate that low vitamin D levels represent a risk factor for BMD loss and fractures. Moreover, in recent years, a growing number of clinical studies have shown an association between low serum 25OHD levels and an increased risk of pathological conditions such as coronary artery disease, type 2 diabetes, cancers, and neurological diseases. This potential role of vitamin D has therefore generated increasing interest in studying the prevalence of hypovitaminosis D, in order to promote the achievement of 25OH D levels above 20 ng/mL in the general population and above 30-40 ng/mL in frail populations such as the elderly and at-risk individuals.

ADAMTS13, VON WILLEBRAND FACTOR, PLATELET MICROPARTICLES, FACTOR VIII, AND IMPACT OF SOMATIC MUTATIONS IN THE PATHOGENESIS OF SPLANCHNIC VEIN THROMBOSIS ASSOCIATED WITH BCR-ABL-NEGATIVE MYELOPROLIFERATIVE NEOPLASMS

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The pathogenesis of thrombotic manifestations in the context of myeloproliferative neoplasms (MPNs) is multifactorial and not fully understood. Key players in the thrombosis mechanism are considered to be the activation of leukocytes, erythrocytes, and platelets derived from a clonal hematopoietic population in the bone marrow. This activation is further complemented by the activation of the hemostatic system, evidenced by an increase in tissue factor (TF) deposited at the platelet level. Recent studies have highlighted an increase in endothelial adhesion molecules induced by various inflammatory mechanisms. Additionally, in JAK2-positive patients, increased erythrocyte adhesion to endothelial cells has been documented.
The incidence of thrombosis in MPNs varies from 3 to 10 times that of the general population. Arterial thromboses account for about two-thirds of thrombotic events and include stroke, myocardial infarction, and peripheral arterial occlusions. The frequency of arterial thrombosis ranges from 16% to 27%, with rates of 0.76% in polycythemia vera (PV), 18% in essential thrombocythemia (ET), and 4% in primary myelofibrosis (PMF). Venous thromboembolism (VTE) accounts for about one-third of thrombotic events in MPNs, affecting approximately 0.6% of patients with ET and pre-myeloid fibrosis, and 1% of those with PV; the clinical presentation includes deep vein thrombosis, pulmonary embolism, and splanchnic thrombosis (portal, splenic, mesenteric), as well as cerebral thrombosis. Cerebral and splanchnic thromboses represent typical sites of thrombotic occurrence in MPN-related thrombosis, and thromboses occurring in atypical sites may reflect concomitant MPN.
In this study, we evaluated the possible association of ADAMTS13, von Willebrand factor, platelet microparticles, and factor VIII in thrombotic events associated with myeloproliferative neoplasms in 36 patients with myeloproliferative neoplasm. The diagnosis of MPN was based on clinical features or demonstration of clonality through the detection of JAK2, CALR, or MPL mutations. Fifty patients with myeloproliferative syndrome without thrombosis and 50 healthy subjects were used as controls. In all subjects, complete blood count, ADAMTS13, von Willebrand factor, microparticles (MV), and factor VIII:C levels were evaluated.
Results: The JAK2 mutation was identified in 94% of patients with thrombosis, with none being triple-negative for JAK2 V617F, CALR, MPL, and exon 12 mutations. ADAMTS13 levels were significantly lower in patients with MPN. Factor VIII:C levels were significantly higher in patients with splanchnic vein thrombosis (SVT) compared to those without thrombosis ($p = 0.007$ and $p = 0.04$, respectively). Splenomegaly was present in 78% of patients with MPN and SVT, and in 30% of those without SVT ($p < 0.001$). The ADAMTS13/von Willebrand factor ratio was reduced in all patients but not in healthy blood donors ($p < 0.001$).
Conclusions: The significant increase in circulating microparticles, von Willebrand factor, and factor VIII:C in patients with MPN and those with thrombosis supports the role of endothelial damage in promoting thrombotic events. A significant increase in von Willebrand factor and factor VIII:C levels was observed in MPN patients with SVT.

PLEIOTROPIC EFFECTS OF ANTICOAGULANT THERAPY: IS THERE A DIFFERENCE BETWEEN AVK AND DOACS?

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Background: Atrial fibrillation (AF) is the most common supraventricular arrythmia in clinical practice. Emerging evidence suggests a significant role of inflammation in the pathogenesis and in the maintenance of AF, We hypothesize a different role of anticoagulant therapy (AVK. vs. DOACs) in reducing the levels of inflammatory biomarkers in AF. Methods: The Strat-AF study is an observational, prospective, single-center hospital-based study enrolling patients with atrial fibrillation, aged 65 years or older, and with no contraindications to undergo magnetic resonance imaging, referring to Center of Atherothrombotic Disease of our University Hospital (AOU Careggi) for the management of oral anticoagulation therapy. Recruited patients are evaluated by means of a comprehensive protocol, with clinical, cerebral magnetic resonance imaging and circulating biomarkers assessment. One of the main outcomes is the evaluation of the role of circulating biomarkers of inflammation (IL-6, IL-8, TNFα, IL-4, IL-10, CCL2, CXCL10, ICAM-1, VCAM-1, VEGF), haemostasis (PAI-1, CLT, vWF) and extracellular matrix remodeling (MMP-2, -7, -8, -9, -12, TIMP-1, -2, -3, -4) in relationship to the type of oral anticoagulant therapy. Results: The results refer to 170 subjects [mean age 77.7 ± 6.8 years, females n = 59 (34.7%)] enrolled in the Strat-AF Study. The subjects of the study were all on oral anticoagulant therapy: 30.6% (n = 52) were on VKA, whereas 69.4% (n = 118) were on DOACs. Regarding those who were on AVK, 81.3% (n = 39) of them had an adequate TTR (>60%), whereas, with regard to the patients anticoagulated with DOACs, we performed the dosage of each type of DOAC (apixaban, dabigatran, edoxaban, rivaroxaban) and discovered that in the majority of cases (>90%), the DOAC concentrations were in line with the average concentration reported in clinical studies. Patients treated with AVK had significantly lower circulating levels of IL-6 and of TNF-alpha (pro-inflammatory cytokines) and significantly lower circulating levels of IL-10 (anti-inflammatory cytokine) if compared to patients treated with DOACs [0.38 (0.30-1.21) pg/mL vs. 1.98 (1.42-3.58) pg/mL, p<0.001, 1.53 (0.59-2.28) pg/mL vs. 2.95 (1.51-5.00) pg/ml, p<0.001 and 1.45 (0.24-3.46) pg/mL vs. 3.29 (1.09-3.56) pg/mL, p=0.003, respectively]. The levels of ICAM-1 and VCAM-1 were significantly lower in AVK treated patients if compared to patients treated with DOACs [297.46 (247.84-385.63) pg/mL vs. 343.62 (273.42-601.88) pg/mL, p=0.023 and 1205.00 (971.11-1830.00) pg/mL vs. 1532.00 (1032.08-2148.13) pg/mL, p=0.036, respectively]. Moreover, in patients treated with AVK, PAI-1 levels and values of ETP (endogenous thrombin potential) ratio (TM+/-) were significantly higher than in patients receiving DOACs [11.33 (7.83-18.32) vs. 8.64 (6.83-12.53), p=0.020 and 0.87 (0.68-1.01) vs. 0.65 (0.41-0.90), p<0.001, respectively]. Lastly, the circulating levels of MMP-12 were significantly lower in AVK treated patients if compared to patients treated with DOACs [79.35 (45.01-93.91) vs. 450.10 (309.12-612.28), p<0.001]. Conclusions: These results from Strat-AF study may be an essential step towards the exploration of the role and the contribute of anticoagulant therapy in reducing inflammation-related biomarkers in AF patients. In particular, these results suggest a pleiotropic role of AVK: identifying a possible effect of these drugs on coagulation and inflammation pathways could pave the way for clinical-therapeutic scenarios.

AN UNUSUAL CASE OF SUBACUTE DYSPNEA IN INTERNAL MEDICINE: BREATHLESSNESS AND SKIN, TWO FACES OF THE SAME COIN

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Background: Dyspnea is one of the most frequent symptoms that lead patients to the Emergency Room. The rapid and prompt diagnosis of the cause of dyspnea is mandatory. We can distinguish cardiac, pulmonary or ENT causes of acute dyspnea. The related symptoms, clinical signs and anamnesis are the key for the diagnosis and management of dyspnea.
Case report: We describe a case report of a 50-year-old woman admitted in our Internal medicine ward for respiratory failure. She complained of worsening dyspnea with mild efforts associated with chest discomfort, pain and fever.
Her medical history recorded a diagnosis of Sjogren syndrome with Raynaud Phenomenon treated with hydroxychloroquine (HCQ) and a low dose of steroids. After a few months, she stopped the treatment for Adverse drug reaction to HCQ and was started on azathioprine, which was promptly discontinued due to liver injury. She had been admitted in hospital thrice in the last three years due to recurrent episodes of pleuropericarditis with pleural effusion. At the hospital admission, she was only on a low dose of methylprednisolone (8 mg per day).
She had no evident signs of ENT cause of dyspnea, no cough or fever at the moment of our observation, and her ABG was normal, SpO2 was >95% and she showed no clinical signs of pneumonia.
Some blood tests were run and she was found to be mildly anemic, WBC were normal, CRP was negative but we found hypocomplementemia. Moreover, she had recently underwent chest CT scan with evidence of fibrotic streaks and irregular fibrotic thickening of the pleural mantle.
To our first observation the patient showed a thin and small mouthline, pinched nose, facial teleangectasias, and puffy, red fingers. An ecocardiography was performed that confirmed the right cardiac overload with hypertrophy of right ventricle and severe raising in pulmonary pressure (TAPSE 14,1 mm,

PAPs 87 mmHg).
Right cardiac catheterization was suggested with finding of Type 1 APH (mean PAP 43 mmHg), normal pressure in right atrium and normal capillary wedge pressure.
Thus, a therapy with mycophenolate mofetil, phosphodiesterase-5 inhibitors and endothelin receptor antagonist was started.
The patient also performed a basal spirometry that showed restrictive deficit with mild end espiration fluxes limitation (MMEF 46%) and a global spirometry and pletismography that showed reduced TLC (74,6%) and DLCO 34% (vs 53% in 2022). She also performed 6MWT with a walked distance of 407,4 mt.
A complete autoimmune panel was run and she tested positive for U1RNP antibodies (85 U/ml), but SCL70 Ab and anticentromere Ab were negative, despite clear clinical signs of systemic sclerosis.
That led us to formulate the diagnosis of mixed connective tissue disease (MCTD), an overlap clinical condition between SLE and SSc.
Discussion: An overlap syndrome is a clinical condition in which features of at least two more widely recognized disorders are recognized. MCTD is an overlap autoimmune syndrome defined by the presence of U1RNP antibodies and Raynaud's phenomenon. The disease is characterized by the presence of at least two features commonly attributed to a well-defined connective tissue disease among SLE, SSc, polymyositis, dermatomyositis or rheumatoid arthritis. However, some authors consider MCTD as an early stage of another well-defined connective tissue disease, such as SSc or SLE.
In this case, the main symptom the patient complained of was dyspnea, for which MCTD is responsible, but she had much more problems that could be explained by MCTD, such as dysfonia, difficulty in grabbing objects and fatigue that often forced her to lose workdays.
Connective tissue disease-associated pulmonary arterial hypertension (CTD-PAH) is a life-threatening condition and systemic sclerosis-associated pulmonary arterial hypertension (SSc-PAH) has been proven to have a lower survival rate compared to systemic erythematosus lupus-associated PH (SLE-PH).
As regards to overlap syndrome, it has been reported that the MCTD group was significantly younger at diagnosis and more frequently developed PAH than the pure SSc group.
However, evidence suggest that the anti-U1RNP-positive group of SSc-PAH had a better survival rate than the negative group.
Conclusions: PAH is among the major causes of morbidity and mortality in patients affected by CTD and remains a dramatic condition despite many progresses were made in the last 20 years regarding early detection and risk stratification considering the clinical conditions, exercise tolerance, right ventricular function and hemodynamic components. This risk stratification also allows a step-by-step therapeutic approach based on combination drug therapies with PAH targeted therapies and the use of immunosuppressants in SLE- and MCTD-PAH with encouraging results. Much research is more to come in this field, but one thing is for certain: an integrative and multidisciplinary approach in reference center is necessary to diagnose and treat these complex diseases.

COMPARATIVE EFFECTIVENESS OF SGLT2 INHIBITORS, GLP-1 RECEPTOR AGONISTS, DPP-4 INHIBITORS, AND SULFONYLUREAS ON THE RISK OF MODERATE-TO-SEVERE COPD EXACERBATIONS IN PATIENTS WITH TYPE 2 DIABETES: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS OF OBSERVATIONAL STUDIES

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Background: Chronic obstructive pulmonary disease (COPD) commonly coexists with multiple comorbidities, among which cardiovascular diseases (CVD) are the most prominent, contributing to a syndemic interplay that worsens clinical outcomes, complicates treatment, and increases healthcare burden. Type 2 diabetes mellitus (T2DM) is a particularly relevant comorbidity in this context. The coexistence of COPD and T2DM is frequently encountered in clinical settings: around 10% of individuals with T2DM have COPD, while COPD patients face a 1.33-fold higher risk of developing T2DM compared to those without COPD. Importantly, T2DM independently worsens pulmonary outcomes in COPD, including faster lung function decline and more frequent and severe exacerbations.
Recent clinical evidence indicates that novel glucose-lowering agents—specifically sodium-glucose cotransporter-2 inhibitors (SGLT2i), glucagon-like peptide-1 receptor agonists (GLP-1 RAs), and dipeptidyl peptidase-4 (DPP-4) inhibitors—confer benefits beyond glycemic control, notably in reducing cardiovascular and renal events. Emerging data also suggest potential respiratory advantages, including improved airway inflammation, reduced bronchial hyperresponsiveness, lower systemic CO_2 levels, and overall metabolic enhancement. Nonetheless, direct comparisons of their impact on respiratory outcomes, particularly among individuals with coexisting type 2 diabetes mellitus (T2DM) and chronic obstructive pulmonary disease (COPD), remain scarce.
To address these evidence gaps, we conducted a systematic review and network meta-analysis (NMA) of observational studies comparing the effectiveness of SGLT2 inhibitors, GLP-1 receptor agonists, DPP-4 inhibitors, and sulfonylureas in preventing moderate-to-severe COPD exacerbations among patients with type 2 diabetes. This analysis aims to synthesize existing data, establish a clinically relevant comparative ranking of glucose-lowering therapies, and inform both clinical decision-making and future research priorities.
Methods: Studies were eligible for inclusion if they met the following criteria: (1) randomized controlled trials or observational studies; (2) enrolled adults (≥40 years) with diagnosed COPD and comorbid type 2 diabetes; (3) evaluated the association between initiation of glucose-lowering therapies—specifically SGLT2 inhibitors, GLP-1 receptor agonists, DPP-4 inhibitors, or sulfonylureas—and the outcome of interest; (4) included an active comparator; and (5) reported on moderate-to-severe COPD exacerbations. The primary endpoint was a composite of moderate or severe COPD exacerbations. Secondary outcomes included the individual components of the composite endpoint. We conducted a NMA to simultaneously compare the efficacy of all interventions of interest, integrating both direct and indirect evidence across the included studies. Treatment rankings were calculated using P-scores, a frequentist analogue of SUCRA, which quantify the certainty that a given treatment is among the most effective. P-scores range from 0 to 1, with higher values indicating higher rank.
Results: Our literature search initially yielded 1039 results. After removing duplicates (n=134) and inelegible studies based on title/abstract inspection (n=888), we fully reviewed 17 studies. We finally included 9 studies in the systematic review and quantitative analysis.
Across all models, sulfonylureas were consistently associated with a higher risk of moderate-to-severe and severe COPD exacerbations compared to SGLT2 inhibitors, GLP-1 receptor agonists, and DPP-4 inhibitors. SGLT2 inhibitors and GLP-1 RAs demonstrated the most favorable profiles. Network estimates suggest a potential advantage of SGLT2i and GLP-1 RAs over DPP-4 inhibitors as well.

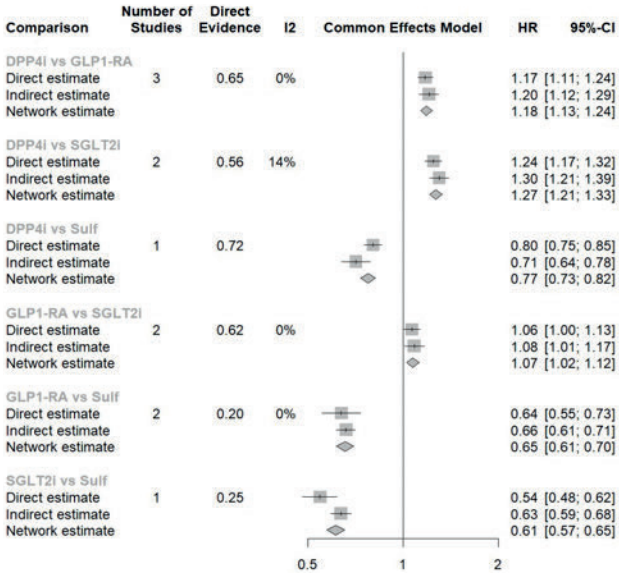

Figure 1. NMA results for "moderate or severe" exacerbation of COPD

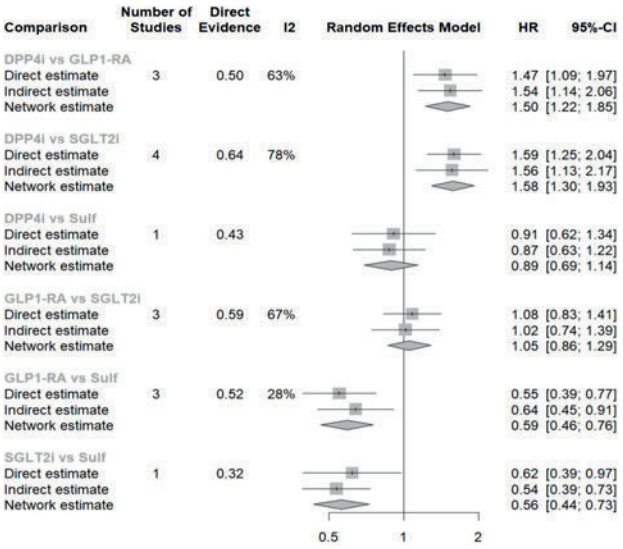

Figure 2. NMA results for "severe" exacerbation of COPD

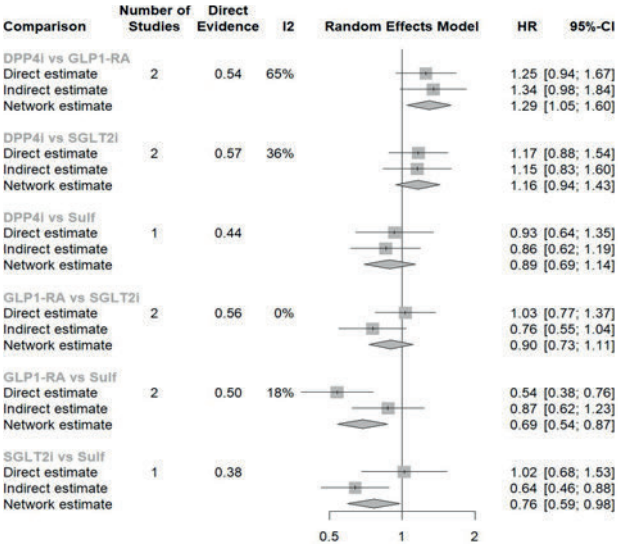

Figure 3. NMA results for "moderate" exacerbation of COPD

Conclusion: In this network meta-analysis of observational studies, newer glucose-lowering agents—particularly SGLT2 inhibitors and GLP-1 receptor agonists—were associated with a lower risk of moderate-to-severe COPD exacerbations in patients with comorbid type 2 diabetes, compared to sulfonylureas and, to a lesser extent, DPP-4 inhibitors. These findings suggest that the clinical benefits of cardiometabolic therapies may extend beyond traditional endpoints to include mitigation of cardiopulmonary risk. This highlights the evolving paradigm in which cardiometabolic and respiratory health are increasingly recognized as interconnected, particularly in multimorbid patients. Preferential use of agents with both metabolic and pulmonary benefits may represent a more holistic approach to reducing the burden of disease in individuals with coexisting T2DM and COPD. Further prospective studies are needed to validate these associations and clarify the mechanisms underpinning this expanded therapeutic potential.

THE POWER OF STEROIDS: CENTRAL HYPOSURRENALISM IN HYPOPITUITARISM

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Introduction: Hypopituitarism is defined as the partial or complete deficiency of anterior or posterior pituitary hormones and it results from compromised pituitary production or from an impaired pituitary stalk. This condition could lead to central hypoadrenalism, central hypothyroidism, hypogonadotropic hypogonadism and arginine vasopressin deficiency, depending on the hormones affected. Hypopituitarism is rare and likely to be underdiagnosed. It is typically classified based on onset of hormone deficiency and whether such deficiency results from structural extra-gland injury or pituitary or hypothalamic dysfunction. Overall, the most common cause is compressive sellar or suprasellar lesion. Clinical features vary with the time of onset, the cause and the number of pituitary axes disrupted. However, the treatment aims at replacing of deficient hormones.

Case Study: A 90-year-old woman presented to the ED due to progressive functional decline, impaired gait, aphasia and hemianopsia.

The woman's medical history included a previous surgical removal of a meningioma in the anterior cranial fossa, with resulting hemianopsia (followed up stopped 6 years before), hypertensive cardiomyopathy, renal insufficiency, parkinsonism, early cognitive decline, and gastroesophageal reflux disease.

In the ED the patient was initially alert but poorly responsive, able to follow simple commands and hypothermic. Laboratory tests revealed a possible septic state, renal insufficiency (creatinine 1.33 md/dL, GFR sec CKD-EPI 38mL/min/1.73m2), hypernatremia (Na 148 mmol/L) and hyperkalemia (K 6,1 mmol/L) which was corrected with buffered glucose solution. Subsequently, the patient experienced seizures during a hypoglycemic event, likely iatrogenic, in the context of sepsis and severe electrolyte imbalance. She then went into coma.

A brain CT scan showed marked dilation of the right lateral ventricle (ex vacuo) and a coarse right frontal hypodensity in the context of previous craniotomy. A large bilobed solid mass with calcifications was also observed in the suprasellar region. Chest CT revealed multiple bilateral pulmonary consolidations, likely of inflammatory or infectious origin. Empiric antibiotic therapy was initiated, and the patient was admitted to our department for further management and supportive care.

During hospitalization antibiotic therapy and correction of electrolyte imbalances were continued. Anyway the neurological status didn't improve. Given the overall clinical picture and the findings on brain CT and the previous neurosurgery, even in the absence of specicic hormonal assessment, steroid therapy was started ex-iuvantibus on suspicion of central adrenal insufficiency. After two days of therapy, a progressive improvement in the level of consciousness was observed, culminating in the complete restoration of alertness. These findings supported our diagnostic hypothesis, and upon endocrinological recommendation, further hormonal blood tests were performed (TSH 0.42 mU/L, fT4 13.8 pmol/L, fT3 2.6 pmol/L, FSH 5.3 U/L, IGF1 42 mcg/L, PRL 33 mcg/L, macroPRL neg, PTH 125 ng/L, vitD 25-OH 10 mcg/L). These results allowed us to diagnose hypopituitarism secondary to an anatomical alteration of the suprasellar region, leading to central adrenal insufficiency, growth hormone deficiency, and hyperprolactinemia likely due to hypothalamic-pituitary disconnection. Concurrently, hormonal investigations also revealed a picture consistent with secondary hyperparathyroidism due to vitamin D deficiency and chronic kidney disease.

Conclusions: Based on the established diagnosis, chronic steroid therapy with cortisone acetate was continued, with a recommendation to increase the dose in case of stress conditions such as fever, infections, or surgical procedures.

It is of particular interest that the prompt initiation of corticosteroid therapy most likely led to a marked improvement in patient's prognosis. Althought the resolution of sepsis and electrolyte imbalances, without hormone replacement therapy we couldn't have restored patient's cognitive and motor functions. The patient, despite advanced age and comorbidities, experienced resitutio ad integrum, we could compleately restore her pre event clinical condition.

THROMBOINFLAMMATION AND ROS ACCUMULATION IN INDIVIDUALS WITH HIGH LIPOPROTEIN(A) LEVELS

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Lp(a) is considered one of the strongest genetically determined and independent risk factors for cardiovascular disease (CVD) through mechanisms associated with increased atherogenesis, inflammation, and thrombosis. Elevated Lp(a) levels have been associated with increased cardiovascular risk even in individuals with low LDL cholesterol concentrations. Despite growing evidence, therapeutic strategies targeting Lp(a) remain limited, with no effective treatments currently available, particularly for primary prevention. Platelets are key mediators of thrombosis and vascular inflammation, and emerging evidence suggests that elevated Lp(a) levels may influence platelet reactivity. However, the physiological

effect of Lp(a) on platelets activity is still unclear. To gain deeper insight into this interaction, proteomic analysis may represents a powerful approach: by profiling the platelet proteome in individuals with elevated Lp(a) levels, it could be possible to identify alterations in signaling contributing to the increase cardiovascular risk in these patients. Proteomic analysis could also help to elucidate the mechanisms linking Lp(a) to prothrombotic states and potentially reveal novel biomarkers or therapeutic targets for individuals at high cardiovascular risk.
Objectives: To investigate the platelet proteomic profile of patients with elevated Lp(a) levels, with the aim to evaluate how Lp(a) modulates molecular pathways involved in platelet production and turnover, inflammation, oxidative stress, and in regulation of thrombotic processes.
Methods: In a cross-sectional study, we enrolled donors referring to the Blood Transfusion Service of Pescara Hospital with levels of Lp(a) above (n=20) or below (n=20) 50 mg/dL patients with higher (n=20) and lower (n=20) levels of Lp(a). Blood and urine sampling was performed. A proteomic analysis was performed on pooled samples of platelet pellets from 5 patients with the highest and lowest Lp(a) levels, Pool A and Pool B respectively, selected from a population of blood donors and stratified according to Lp(a) levels (cut-off: 50 mg/dL). For validation, circulating and platelet MRP-8/14 protein levels were analysed by ELISA assay and Western blotting analysis, and urinary 8-iso-PGF2a excretion levels were measured.
Results: Proteomic and bioinformatic analysis showed an activation of pathways related to "Inflammation of organ" and "accumulation of ROS" in patients with elevated Lp(a) levels. As a validation, circulating and platelet MRP-8/14, involved in both the pathways, was higher in patients with elevated Lp(a) levels (p=0.064, p= 0.041) than in patients with low Lp(a), thus confirming proteomics. The urinary excretion rate of the F2-isoprostane 8-iso-PGF2α (p=0.039), *in vivo* marker of lipid peroxidation, was higher in subjects with elevated Lp(a) levels.
Conclusions: Our findings suggest that individuals with elevated Lp(a) levels exhibit increased thromboinflammatory activity and pro-oxidative state, as reflected by proteomic analysis of inflammatory and ROS pathways and higher levels of 8-iso PGF2a, but also higher circulating and platelet-derived levels of MRP-8/14. These results support the hypothesis that Lp(a) contributes to a pro-oxidative and pro-inflammatory milieu, potentially through modulation of platelet activation and function. These findings highlight the need for further investigation into Lp(a)-mediated platelet activation and suggest MRP-8/14 as a potential biomarker and therapeutic target in patients with elevated Lp(a).

EFFECTS OF RUXOLITINIB TREATMENT ON GDF-15, ANOREXIA, AND BODY COMPOSITION IN MYELOFIBROSIS PATIENTS

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Rationale: Myelofibrosis (MF) is a BCR/ABL-negative myeloproliferative disorder characterized by clonal expansion of hematopoietic progenitors, fibrosis, and systemic inflammation. Cachexia is a multifactorial syndrome characterized by involuntary loss of skeletal muscle mass, systemic inflammation and increased protein catabolism. In myelofibrosis (MF), cachexia and reduced food intake are commonly observed and are primarily driven by chronic inflammation and splenomegaly. Aim of the present study was to evaluate the effects of Ruxolitinib, a JAK1/2 inhibitor used for disease treatment, on changes in body composition occurring in MF. Methods: We collected data from MF patients before (T0) (n=18) and after 6 months (T1) (n=22) of Ruxolitinib treatment. Nutritional risk and malnutrition were evaluated with the Malnutrition Universal Screening Tool (MUST) and Global Leadership Initiative for Malnutrition (GLIM) respectively. Anorexia was assessed with the Functional Assessment of Anorexia/Cachexia Therapy (FAACT) and body composition estimated with BIA. Sex-specific cut-off values for Fat Free Mass Index (FFMI, kg/m2) were made according to ESPEN criteria. Circulating GDF-15 was assessed with xMAP Intelliflex. Results: At T0, 50% of patients (n=9) were at risk of malnutrition (MUST), and 52% (N=11) were malnourished (GLIM). At T1, MUST decreased from 50% to 12%, and GLIM decreased from 52% to 8%. We observed a significant decrease of GDF-15 from T0 to T1 (p=0,010), as well as an increase of FAACT score (35(29;40) vs 41(37;44), p=0,01). Interestingly, changes in GDF-15 levels between T0 and T1 were inversely correlated with changes in FAACT (r=–0.531, p=0.023), FFMI (r=–0.488, p=0.047), muscle mass (r=–0.504, p=0.039), and lean body mass (r=–0.490, p=0.046). Conclusion: Ruxolitinib treatment resulted in improvements in body composition in patients with MF, which cannot be ascribed only to the improvement of splenomegaly and disease control, but also likely to the concomitant reduction in GDF-15 levels, suggesting that Ruxolinitib may play a role in the treatment of MF-induced anorexia and cachexia.

THE IMPACT OF CLIMATE CHANGE ON HEART FAILURE HOSPITALIZATION IN AN ITALIAN THIRD-LEVEL ACADEMIC MEDICAL CENTER

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Background: In recent years, climate change has garnered growing attention not only for its environmental consequences but also for its direct and indirect impact on human health. One area of particular concern is cardiovascular health. Climatic conditions, particularly extreme ambient temperatures, such as heatwaves and cold winter, are increasingly recognized as potential stressors that can trigger acute decompensation in patients with heart failure, contributing to a worsening of their condition often leading to hospitalization.
The aim of this retrospective monocentric observational study was to analyze the correlation between the minimum and maximum temperatures recorded in the years 2012, 2019, and 2022 and hospital admissions for heart failure among patients in an Italian third-level academic medical center in Rome (Fondazione Policlinico Gemelli, IRRCS).
Methods: Clinical data of 1060 patients (592 men and 468 women) hospitalized for heart failure who had hospital access in the years 2012, 2019, and 2022 were analyzed. Clinical variables were collected, included ejection fraction (FE), NT-pro BNP, age, sex, NYHA class. Daily minimum and maximum environmental temperatures were obtained from official meteorological sources. Statistical analysis was performed using one-way ANOVA, Bonferroni multiple comparisons, multivariate logistic regression, and linear regression, to evaluate potential associations.
Results: Statistical analyses of the data were performed to explore the relationship between clinical and environmental variables and hospital admissions for heart failure over multiple years. NYHA class, minimum temperature, and maximum temperature showed significant association according to one-way ANOVA analysis ($p < 0.001$, $p < 0.001$, and $p = 0.033$, respectively). Post-hoc analysis using the Bonferroni correction was used to assess whether there were significant differences between minimum and maximum temperatures in the years considered. The analysis revealed significant differences in minimum temperature between 2012 and 2019 ($p = 0.034$) and between 2012 and 2022 ($p < 0.001$), suggesting a progressive climate change over the observed period. In contrast, no significant year-to-year variation was observed in maximum temperature after adjustment. Multivariate logistic regression showed no statistically significant association between sex, or EF and the hospitalization over the considered years (p>0.05). Finally, the multivariate linear regression model showed that minimum temperature, as an independent variable, had a significant impact on the number of hospitalization for heart failure ($p = 0.001$), while maximum temperature, age, and sex showed no significant effects.
Conclusions: The results of our study show that lower ambient temperatures are significantly linked to a higher number of hospital admissions for heart failure, regardless of the patient's age and sex. Individuals with more advanced heart failure, particularly those in higher NYHA classes, appear to be especially at risk. These findings suggest that colder conditions may contribute to a worsening of symptoms and an increased likelihood of acute decompensation. This underlines the need to develop and adopt preventive measures to better protect vulnerable patients during periods of extreme or rapidly changing weather.

KHORANA RISK SCORE AND GENOMIC PROFILING FOR PREDICTION OF VENOUS THROMBOEMBOLISM IN WOMEN WITH OVARIAN CANCER

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Introduction: Ovarian cancer (OC) carries a high thromboembolic risk, with venous thromboembolism (VTE) incidence up to 13.3%. In this study, we tested the hypothesized that oncogenic mutations found in women with OC might influence the risk of VTE. We also assessed the ability of the Khorana Risk Score (KRS) to predict VTE among women with OC initiating systemic oncologic treatment.
Methods: We included women with OC consecutively enrolled in the Comprehensive Genomic Profiling (CGP) program (NCT 06020625) of the Fondazione Policlinico Universitario A. Gemelli IRCCS between March 2022 and December 2023. Informed consent was obtained prior to CGP. KRS was calculated at the

time of genomic profiling, before initiation of oncological treatment. KRS was dichotomized as low (1) or intermediate-high (≥2) risk. Regarding CGP, somatic mutations with a variant allele frequency ≥0.05, classified as oncogenic or likely oncogenic according to OncoKB, were included in the analysis. VTE events within 12 months from the beginning of chemotherapy were recorded.
Results: Of667profiled patients,413with at least12months follow-up were analyzed. Most had high-grade serous OC (84%) and advanced-stage disease (86%). VTE occurred in20% (n=84) of patients. Age, histology, and stage showed no significant differences between those with and without VTE. KRS showed a sensitivity of87% and a specificity of17% (72% accuracy), with no significant association with VTE (p=0.54). In patients with VTE, we observed a significantly higher proportion of mutations in *FGFR2*(OR11.7, p=0.03), *NFE2L2*(OR11.7, p=0.03), and *KEAP1*(OR5.3, p=0.03) (Fig.1a). Among patients with at least one of these mutations, VTE event rate was67% (Fig.1b). In these patients, significant enrichment was observed in pathways related to cellular response to oxidative stress and chemical stress, as well as fluid shear and atherosclerosis, driven by *NFE2L2* and *KEAP1*(Fig.1c).
Conclusion: Our study showed a limited predictive role of KRS in OC. Our mutational findings suggest a potential role for *KEAP1* and *NFE2L2* in VTE development, warranting further investigation through multiomic approach.

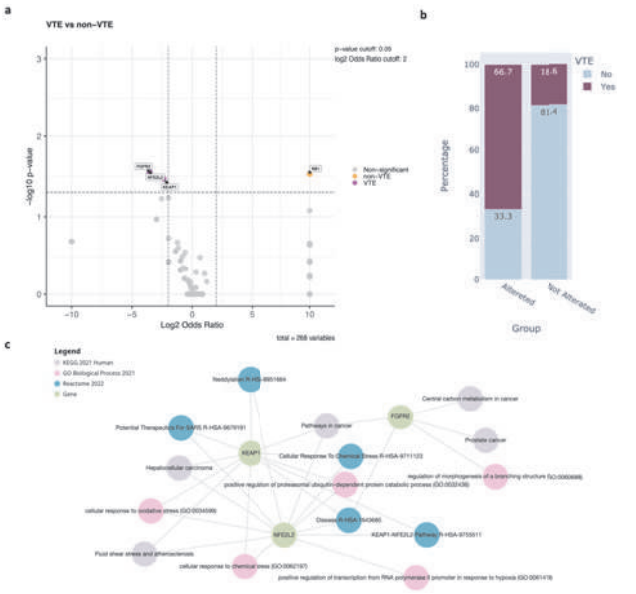

Figure 1. Evaluation of the predictive role of genomic mutations in patients with ovarian cancer. a. Volcano plot of gene mutations odds ratio. b. VTE distribution among patients with at least one of mutations in FGFR2, NFE2L2 or KEAP1. c. Enrich pathway analysis. VTE: Venous Thromboembolism.

WHEN RARITY MEETS COMPLEXITY: A JOURNEY BETWEEN TWO RARE DISEASES.

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Background: Acquired hemophilia is a rare autoimmune disorder characterized by hemorrhagic syndrome secondary to the production of antibodies with inhibitory activity against coagulation factors, most frequently Factor VIII. In about 50% of patients an underlying clinical condition can be identified; in the remaining 50% the cause remains unknown. Possible underlying conditions include autoimmune diseases, obstetric diseases, onco-hematological diseases and infectious diseases.
Clinical case: A 69-year-old man went to the emergency room for pain localized to the right lower limb. Few weeks before, he had gone to the general practitioner who prescribed therapy with subcutaneous enoxaparin in the suspicion of deep vein thrombosis (DVT). He also reported weight loss of about 8 kg in the previous month. His past medical history was significant for high blood pressure, type II diabetes mellitus treated with oral hypoglycemic agents and previous ischemic stroke without residual deficit, in treatment with cardioaspirin as secondary prevention. Upon admission to Internal Medicine Ward, palpable splenomegaly at about 2 cm from the costal arch, large hematoma of the abdominal wall and hematoma of the posterior surface of the right thigh were objected. Initial blood tests showed normochromic normocytic anemia (Hb 8.8 g/dL, MCV 89 fL, MCH 30 pg) and isolated aPTT elongation (69.5 sec, range 25-35). Venous echocolordoppler of the lower limbs excluded DVT but showed bilateral subcutaneous hematomas. During the hospitalization, the patient developed further spontaneous subcutaneous and muscular hematomas and macroscopic hematuria. In consideration of the blood tests and the hemorrhagic diathesis, the assay of the factors of the intrinsic coagulation pathway (VIII, IX, XI, XII) was then performed, showing marked reduction of Factor (F) VIII (3.5%, normal values 58-130). In the suspicion of acquired hemophilia A (AHA), the presence of anti-FVIII antibodies was investigated and measured at the level of 3.5 U Bethesda. Steroid therapy with prednisone 1 mg/Kg/day and therapy with activated prothrombin complex (FVIII inhibitor bypass activity-Feiba) at dosage of 4000 IU every 12 hours were then started, obtaining improvement in symptoms and slow and modest increase in FVIII values and reduction of the anti-FVIII antibody titer (Figure 1). In order to exclude paraneoplastic etiology, endoscopic examinations and Total Body Computed Tomography (CT) were performed, resulting negative for malignancies However, multiple hematomas (bilateral subdural, left adrenal gland, right thigh), splenomegaly (longitudinal diameter 16 cm) and multiple subcentrimetric lymphadenopathies were evidenced (Figure 2). The assay of tumor markers showed only an increase in chromogranin A (363 ng/mL, range <100). Serum protein electrophoresis showed the presence of two monoclonal components (IgG-kappa and IgG-lambda isotypes). Urinary immunofixation was negative. Autoantibodies (ANA and ENA) were absent. Due to the worsening of splenomegaly and the appearance of severe pancytopenia with the need for three-weekly transfusions of erythrocytes and platelets, cytomorphology of peripheral blood cells was investigated but was negative for immature cells. Subsequently, bone marrow biopsy showed non-specific maturation and architectural disorder of the hematopoietic cells. In order to exclude parainfectious etiology, microbiological screening was performed with the detection of Cytomegalovirus (CMV) infection (38644 copies/mL) and human herpesvirus type 8 (HHV8) infection (2501 copies/mL). Thus, intravenous antiviral therapy with Ganciclovir was initiated. In the doubt of primary hematological neoplasia, the patient was transferred to the Hematology department, where he underwent lymphadenectomy of two axillary lymph nodes (maximum diameter 1.4 cm) whose histological examination showed multicentric HHV8-related Castelman disease (MCD HHV8+), complicated by minute outbreaks of Kaposi's sarcoma. Subsequently, the patient began infusion therapy with Rituximab (monthly administration), which is currently ongoing.
Conclusions: . Castleman disease is a rare hematologic disorder characterized by lymph node hypertrophy in the presence of angiofollicular lymphatic hyperplasia; it can present as unicentric or multicentric form (MCD), associated with systemic inflammation, cytopenias, and life-threatening multi-organ dysfunction. Uncontrolled infection with HHV-8 is responsible for about 50% of MCD cases. This case demonstrates the importance of an accurate and thorough differential diagnosis in the context of multiple non-specific signs and symptoms. A multidisciplinary approach, combined with a careful integrated diagnostic evaluation, was fundamental for early identification of the rare underlying pathology, thus improving the patient's prognosis.

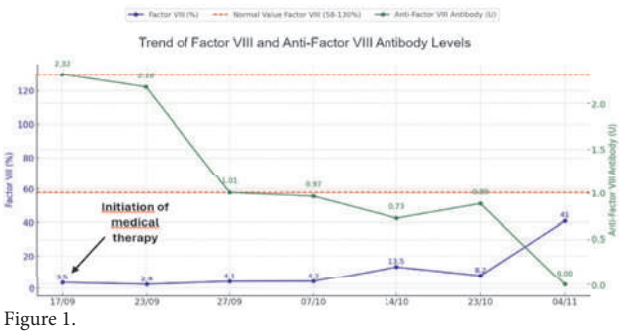

Figure 1.

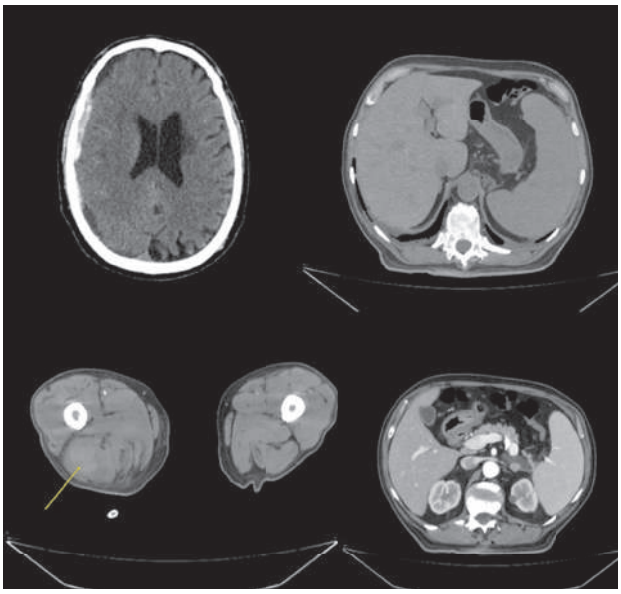

Figure 2.

THE ROLE OF BIOLOGICAL SEX IN THE MANAGEMENT OF SEVERE HYPERCHOLESTEROLEMIA: BEYOND GENETICS

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Background: Severe hypercholesterolemia, whether monogenic or polygenic, is a well-established risk factor for cardiovascular disease (CVD) (1). Sex-related disparities in the perception and management of CVD are documented, with women often receiving delayed diagnosis and suboptimal lipid-lowering therapy (LLT) (2, 3). These differences may contribute to an increased residual risk in females (4). This study aimed to evaluate sex-specific differences in lipid profiles and LLT use among patients with severe hypercholesterolemia.
Methods: We analyzed a cohort of 347 patients (51.6% female; mean age 46 ± 20 years) enrolled in the LIPIGEN project at the University Hospital of Ferrara (2016–2021). Severe hypercholesterolemia was defined by an elevated Dutch Lipid Clinic Network (DLCN) score. Patients underwent genotyping and lipid profile assessment (total cholesterol [TC], LDL-C, HDL-C, triglycerides [TG]) at baseline and follow-up. LLT data were collected at both time points. To estimate cumulative exposure, we calculated the average lipid profile across available visits. Continuous variables were expressed as median ± interquartile range and compared using the Mann-Whitney U test; categorical variables were analyzed using the Chi-squared test (SPSS v26).
Results: At enrollment, females were older than males (50 ± 21 vs 43 ± 18 years, p<0.001) and showed a more atherogenic profile: higher TC (320.5 ± 91.0 vs 298.0 ± 117.0 mg/dL, p=0.001), LDL-C (229.5 ± 93.1 vs 208.0 ± 102.6 mg/dL, p=0.018), and HDL-C (66.0 ± 23.0 vs 53.0 ± 16.0 mg/dL, p<0.001); lower TG (107.0 ± 62.0 vs 123.0 ± 80.0 mg/dL, p=0.002); and reduced statin use (43.6% vs 55.4%, p=0.028). The prevalence of genetically confirmed familial hypercholesterolemia did not differ by sex (41.3% vs 44.1%, p=0.610). At follow-up, differences in LDL-C (94.0 ± 52.0 vs 84.5 ± 70.0 mg/dL, p=0.082), TG (92.0 ± 51.0 vs 97.5 ± 55.0 mg/dL, p=0.332), and statin use (70.6% vs 77.1%, p=0.283) were no longer significant. However, TC (179.0 ± 69.0 vs 163.0 ± 78.0 mg/dL, p=0.017) and HDL-C (64.0 ± 21.0 vs 53.0 ± 18.0 mg/dL, p<0.001) remained higher in women. Overall, females had a greater cumulative burden of TC (253.0 ± 115.4 vs 230.8 ± 110.3 mg/dL, p<0.001) and LDL-C (170.7 ± 109.5 vs 148.0 ± 92.1 mg/dL, p=0.007).
Conclusions: Significant sex-based differences in lipid profile and LLT use were observed in patients with severe hypercholesterolemia at first referral. Although disparities diminished during follow-up, women experienced a higher cumulative lipid burden, potentially increasing long-term CVD risk. These findings underscore the need for sex-sensitive approaches in the diagnosis and treatment of severe hypercholesterolemia.

PLASMA CONCENTRATION OF DIRECT ORAL ANTICOAGULANTS IN PATIENTS WITH THROMBOEMBOLIC EVENTS: A CROSS-SECTIONAL STUDY

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Introduction: In the last decade the use of DOACs (Direct Oral Anticoagulants) for venous thromboembolic events (VTE) gradually replaced Vitamin K Antagonists, due to ease of use and lack of need for regular blood analysis monitoring. Recently the measure of plasma levels of DOACs have been validated for VTE and atrial fibrillation. Anyway, it remains an open issue their use in clinical practice, particularly regarding their predictive role in bleeding or thrombotic events during anticoagulant therapy. This study aims to assess whether DOACs plasma concentrations are associated with adverse outcomes in terms of bleeding events and of recurrence of VTE events and whether their monitoring could be useful in selected subgroups of patients (e.g. obese, underweight, chronic kidney disease, drug - interactions).
Materials and methods: This study is a no-profit, monocentric, observational cross-sectional study. Patients were consecutively enrolled from 1 January to 30 April 2025 in Department of Clinical Internal, Anesthesiologic and Cardiovascular Sciences of Sapienza University of Rome at the Atherothrombotic Center of Policlinico Umberto I. Inclusion criteria were: patients >18 years who were assuming DOACs for VTE treatment or secondary prophylaxis. Exclusion criteria included DOACs prescription for condition different from VTE or patients assuming DOACs for ≤7 days. During the first clinical examination a complete personal medical history was collected which included: type and dose of DOAC, comorbidities, cardiovascular risk factors, VTE risk factors, anthropometric factors and other drugs taken. All patients signed informed written consent at study entry. The study was approved by the local ethic committee of Sapienza University (No. 0073/2022) and was conducted according to the 1975 Declaration of Helsinki. Two blood samples were collected for DOACs plasma concentration: the trough sample, taken after the half-life of each DOAC, and the peak sample, collected 2 hours after DOAC administration. DOAC plasma levels were measured in the local laboratory, using the reference ranges provided in the 2019 Recommendations and Guidelines by Paoletti et al. Blood samples from patients were collected in tubes with anticoagulant (3.8% sodium citrate). Categorical variables were reported as numbers and percentages and were compared with Pearson's $\chi 2$ test. Mean and standard deviation (SD) or median and interquartile range (IQR) were used for continuous variables, which were compared using Student's t-test or Mann–Whitney U test, respectively. Normal distribution of variables was checked by the Kolmogorov–Smirnov test. We divided the cohort into two groups according to the trough plasma concentration: (1) in range, (2) out-of-range (comprehensive of below-range and above-range), according to each DOAC specific on-therapy range. Then, we performed the same procedure for peak dosage evaluation. All tests were two-tailed and only p-values < 0.05 were considered statistically significant. The analyses were performed using SPSS 25.0 software.
Results: A total of 45 patients receiving direct oral anticoagulants (DOACs) were enrolled. Of these, 44 underwent blood sampling for both peak and trough plasma concentrations, while 1 patient had only the trough measurement. The cohort included 31 males (68.9%) and 14 females (31.1%), with a mean age of 66.4 ± 14 years and a mean body mass index (BMI) of 26 ± 3.7 kg/m^2. About DOAC distribution, 28 patients were on Apixaban, 8 on Rivaroxaban, 6 on Edoxaban, and 3 on Dabigatran. As for trough plasma concentrations, 34 patients (75.6%) had values within the therapeutic range, while 11 patients (24.4%) had out-of-range levels. No statistically significant differences were found between the groups regarding age, BMI, DOAC type, comorbidities, or clinical history. Regarding peak plasma concentrations, among the 44 patients evaluated, 39 (88.6%) had in-range levels and 5 (11.4%) were out-of-range. Patients with out-of-range peak levels were significantly older (median age 84 vs. 65 years; p = 0.015). No other significant differences were observed between the groups. During follow-up, five clinical events were recorded. Specifically, two venous thromboembolism (VTE) recurrences occurred in patients who had both peak and trough plasma concentrations within the therapeutic range. Additionally, three bleeding events were observed—two minor and one clinically relevant non-major bleeding. All three had in-range trough concentrations, while only one case showed an out-of-range peak concentration.
Conclusions: Our preliminary results of ongoing recruitment confirm current clinical practice, which generally considers plasma DOAC measurement unnecessary in routine patient management. The lack of a significant correlation between out-of-range plasma levels and adverse events suggests that monitoring may not offer additional clinical benefit in VTE patients treated with DOACs.. However, ongoing enrollment with particular attention to BMI and patients' medication history may help identify subgroups in which DOAC level measurement could be useful, especially when there is a potential drug interactions.

IMPACT OF BODY COMPOSITION ON TREATMENT TOXICITY AND SURVIVAL IN PATIENTS RECEIVING TRASTUZUMAB DERUXTECAN FOR HER2-POSITIVE METASTATIC BREAST CANCER

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Introduction: Breast cancer continues to be a major global health issue, and HER2-positive metastatic cases remain particularly challenging to manage, even with recent progress in targeted treatments such as Trastuzumab Deruxtecan (T-DXd).
This study aimed to assess how changes in body composition affect treatment-related toxicities, dose adjustments, and clinical outcomes in patients undergoing T-DXd therapy.
Methods: A retrospective study was conducted on 35 patients with HER2-positive metastatic breast cancer to evaluate body composition parameters, including subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), skeletal muscle area (SMA), and skeletal muscle index (SMI). These parameters were assessed using CT scans performed at baseline (T0) and after a median follow-up of 4 months (T1). The percentage change between the two time points (ΔT0–T1%) was calculated for each parameter.
Results: Significant reductions over time were observed in SAT (mean ΔSAT% = -5.7%, p <0.05) and SMA (mean ΔSMA% = -4.9%, p < 0.01). Treatment-related adverse events (AEs) were common, with 31% of patients experiencing severe (Grade 3-4) toxicities. Patients with higher ΔSAT% (above the median value) experienced more frequently grade 3-4 toxicities compared to those with lower ΔSAT% (below the median) (p<0.05). Among patients without toxicities, a significant decrease in SAT was observed between T0 and T1 (p=0.003), while no significant change was detected in patients with grade 3-4 toxicities (p=0.929). Greater reductions in SMA were associated with increased rates of treatment discontinuation (75% vs. 29%, p = 0.009). Kaplan-Meier analysis confirmed that greater reductions in SMA significantly increased the risk of mortality (HR 5.1, 95% CI: 1.05–24.79; p=0.025) and showed a trend toward higher risk of disease progression (HR 2.58, 95% CI: 0.89–7.49; p=0.063).
Conclusions: Changes in body composition, especially reductions in SMA, were linked to higher rates of treatment discontinuation and mortality in patients with HER2-positive metastatic breast cancer receiving T-DXd. Conversely, an increase in SAT was associated with a greater incidence of severe toxicities, underscoring its potential role in predicting treatment-related complications and emphasizing the clinical significance of nutritional changes in this context

OUTCOMES OF PATIENTS WITH ALCOHOLIC CIRRHOSIS REFERRED TO A HEPATOLOGICAL OUTPATIENTS UNIT

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Background: and aims: Achieving abstinence is the most effective treatment of alcohol-related cirrhosis even if already decompensated. Patients with cirrhosis and alcohol use disorder (AUD) represents a special population and should be treated by a multidisciplinary team with a mandatory experience in addiction medicine (2020 AISF guidelines). This study aims to assess the outcome of patients with cirrhosis and alcohol-related cirrhosis referred to a hepatological service provided of an internal multidisciplinary alcohol unit.
Methods: Retrospective observational study assessing clinical trajectories and survival of patients with alcoholic cirrhosis referred to our hepatological service from 2016 to 2022 Prolonged abstinence was assessed by means of clinical and laboratory parameters.
Results: 175 patients (median age: 54 years; 77% male) were included. About 35% of patients had also a viral etiology and 26% MASLD. About 60% were decompensated, median MELD was 13 and MELD-Na 16. About 40% patients discontinued alcohol consumption at the hepatological evaluation without referral to the alcohol unit. About 45% accepted to be followed by the multidisciplinary alcohol team; of these patients, almost 35% achieved prolonged abstinence, while the remaining had several episodes of AUD recurrence alternating periods of abstinence in most cases. Interestingly, these latter patients showed an intermediate survival between abstinent individuals and active drinkers. Only 15% of patients refused any support and continued alcohol consumption. Clinical and socio-economic differences were observed among groups.
Conclusions: This study showed that, besides many patients able to stop drinking at the time of diagnosis of cirrhosis, combining a multidisciplinary alcohol unit embedded in a hepatological service is an effective approach for patients with cirrhosis and DUA even when prolonged abstinence is not fully achieved.

MANAGEMENT OF A SYSTEMIC LUPUS ERYTHEMATOSUS: A COMPLICATED CASE BY MACROPHAGE ACTIVATION SYNDROME

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Background: and aims: Macrophage activation syndrome (MAS) is a rare but severe complication of systemic lupus erythematosus (SLE), characterized by excessive immune activation leading to multiorgan failure. This case describes the diagnosis and treatment of a patient with SLE and MAS, highlighting the effectiveness of combined immunosuppressive therapy.
Methods: A 42-year-old patient presented with persistent fever, worsening asthenia, myalgias, and trilinear cytopenia. Investigations revealed a MAS-compatible profile, including hyperferritinemia and hypertriglyceridemia. Hematological and infectious causes were excluded, and positivity for ANA and anti-DNA antibodies suggested SLE with hematological, renal, and muscular involvement. High-dose steroid therapy and Mycophenolate Mofetil were initiated, later enhanced with Rituximab. Due to persistent nephrotic syndrome, Belimumab therapy was introduced.
Results: The patient exhibited progressive improvement in muscle strength, cytopenia, and renal function. Hemolysis indices, ferritin, and triglycerides significantly decreased with treatment. The subsequent introduction of Rituximab and Belimumab further stabilized the clinical picture, allowing gradual tapering of steroid therapy.
Conclusions: This case underscores the importance of timely and multidisciplinary management of MAS associated with SLE. Combined therapy with steroids and immunosuppressants resulted in effective control of the disease and its systemic complications.

5550. CIRCULATING MIRNAS AND STRESS CYTOKINES AS BIOMARKERS OF CARDIAC CACHEXIA IN CHRONIC HEART FAILURE

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Introduction: Cardiac cachexia (CC) affects approximately 10–15% of patients with chronic heart failure (CHF) and is strongly associated with poor prognosis and mortality. The prevalence of CC is higher among CHF patients with advanced myocardial dysfunction, particularly those with reduced left ventricular ejection fraction (HFrEF). Emerging evidence suggests dysregulation of both microRNAs (miRNAs) and stress-induced cytokines, including Growth Differentiation Factor-15 (GDF-15) and Fibroblast Growth Factor-21 (FGF-21), may contribute to the pathophysiology of CC.
The aims of the present study were i) to characterize circulating profile of muscle-specific miRNAs, GDF-15 and FGF-21 in CHF patients and ii) to explore their association with changes in body composition and heart failure severity.
Methods: CC was diagnosed according to Anker's definition. CHF patients were classified into HFrEF and HFpEF (heart failure with preserved ejection fraction) phenotypes based on the 2022 AHA/ACC/HFSA guidelines. Circulating miRNAs were quantified with RT-qPCR. GDF-15 and FGF-21 serum level were measured with enzyme-linked immunosorbent assay (ELISA). Associations with CC status and heart failure severity were analyzed.
Results: Compared to C (n = 10), CHF patients (n = 25) exhibited significant downregulation of miR-15b (p < 0.001), miR-29b (p < 0.001), miR-133a (p = 0.005), and miR-486 (p < 0.001), along with marked and significant higher levels of serum GDF-15 (p < 0.001). In CHF, GDF-15 positively correlated with miR-486 (p=0.046, r=0.403). When comparing CHF patients with CC (CC) (n=10) to those without CC (nCC) (n=15), there was a significant downregulation of miR-29b (p=0.019) and upregulation of FGF-21 (p=0.012) in CC group. FGF-21 levels were significantly elevated in HFrEF (n=12) vs HFpEF (n=13)

(p=0.046). Moreover, a significant downregulation of miR-29b was observed in HFrEF + CC (n=7) compared to HFpEF + nCC (n=5) (p=0.030).
Conclusion: Our data highlight a distinct circulating molecular signature involving muscle-related miRNAs, GDF-15 and FGF- in CHF patients with CC. These biomarkers may serve as potential indicators of disease progression and metabolic deterioration.Further studies are required to validate these molecular profiles and to investigate their diagnostic and pathogenic relevance in the onset and progression of CC.

PRURIGO NODULARIS: MORE THAN A DERMATOLOGICAL DISEASE

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Background: Prurigo nodularis is a rare chronic inflammatory skin disease characterized by multiple symmetrically distributed nodules that cause intense and persistent itching and skin lesions. Itching is often described as accompanied by pain, burning, and tingling of the skin. Signs and symptoms may negatively impact quality of life, including mental health, activities of daily living, and social interactions. It usually appears as firm, dome-shaped nodules that can range from a few millimeters to several centimeters in size, often symmetrically distributed on the extensor surfaces of the arms and legs, as well as on the trunk. Nodules may be flesh-colored, erythematous, or brown-black, and their number may vary from a few to hundreds. The extensor surfaces of the limbs are typically affected, but the upper back, abdomen, and sacrum may also be involved. The difficult-to-reach mid-upper back is usually spared ("butterfly" sign). The palms, soles, face, and flexor areas are rarely affected. Itching is always intense and bothersome; it may be paroxysmal, sporadic, or continuous and is worsened by heat, sweating, or irritation from clothing. In many cases, the cause of the itching is unknown. Approximately half of patients with prurigo nodularis have a history of atopic dermatitis. In these cases, it occurs at an earlier age than in non-atopic patients. The diagnosis is clinical, based on the history of severe itching and characteristic skin lesions, which do not make skin biopsy a routine examination. Biopsy is necessary in patients with no history of atopic dermatitis or in patients in whom other systemic diseases must be excluded. In fact, although rarely, prurigo nodularis may be the presenting symptom of a systemic disease (HIV or mycobacterial infection, parasitic, lymphoma, solid tumors). Clinical case: In December 2024, a 74-year-old patient came to our attention for persistent fever and suspected urinary tract sepsis. In remote pathological anamnesis, arterial hypertension well controlled with pharmacological therapy, nodule in the right breast in follow up, nodular prurigo diagnosed three years earlier for which she had already been subjected without benefit to topical therapies, phototherapy and immunosuppressive therapy with cyclosporine, interrupted due to intolerance by the patient. At the visit, the patient showed widespread and extensive scratching lesions, bleeding and with loss of substance, intensely itchy, such as to prevent her from sleeping at night and poorly responsive to topical therapy and to the antihistamine therapy undertaken. Blood tests showed neutrophilic leukocytosis, moderate normocytic normochromic anemia, slight increase in infectious indices. Culture tests performed found a positive urine culture for E. faecalis for which targeted antibiotic therapy was set, with resolution of the infectious state. The IgE dosage was normal. The QPE also showed a monoclonal gammopathy for which she was subjected to level II laboratory tests with detection of a light IgG kappa and lambda bandage. In light of the anamnesis, the severe skin condition and laboratory data, suspecting that this skin pathology could be a manifestation of a systemic pathology, the patient underwent breast ultrasound and mammography, total body CT with contrast and dermatological evaluation with indication for a new skin biopsy in the suspicion of a cutaneous lymphoproliferative disease. The instrumental tests performed highlighted the already known nodule in the right breast, as well as the presence of multiple nodular formations of repetitive appearance in the liver. For this reason, the patient underwent a biopsy of the breast nodule. The outcome of the skin biopsy confirmed the diagnosis of nodular prurigo with associated scratching lesions and excluded the suspicion of a cutaneous lymphoproliferative disease. The outcome of the breast biopsy concluded for low-grade infiltrating NST carcinoma. The patient was therefore subjected to a multidisciplinary evaluation, with indication for specialist oncological therapy and to undertake, for nodular prurigo, therapy with Dupilumab, an inhibitor of IL-4 and IL-13, a first-line drug in uncontrolled nodular prurigo. This medication is well tolerated, even among elderly and frail patients, due to its excellent safety profile. Conclusions: The exact causes of prurigo nodularis remain unknown. While it is commonly linked to an atopic phenotype, it can also be associated with systemic conditions such as cholestasis, thyroid disease, chronic renal failure, lymphoma, metastatic neoplasms, and psychiatric disorders. Therefore, clinicians treating prurigo nodularis should be vigilant in detecting signs and symptoms indicative of malignancy and ensure that patients undergo recommended, age-appropriate cancer screenings.

EVOLUTIONARY ASPECTS OF MULTI-DISTRICT ATHEROSCLEROSIS: CORRELATION WITH MAJOR ADVERSE CARDIOVASCULAR AND LOWER LIMB EVENTS

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Background: Atherosclerosis is the leading cause of mortality and one of the most significant causes of morbidity, disability, and hospitalization in industrialized countries. This is a progressive process that begins in childhood and typically becomes apparent in middle to older age. "Cardiovascular (CV) risk factors" are a set of conditions that trigger and sustain the disease process; some are modifiable (smoking, arterial hypertension, dyslipidemia, diabetes mellitus, obesity, and physical inactivity), while others are non-modifiable (such as age and sex). A characteristic aspect of atherosclerosis is the relation between lesion distribution and specific CV risk factors: some like age, cigarette smoking, dyslipidemia, arterial hypertension and inflammation appear to promote atherosclerotic manifestations in the large vessels of the extracranial region and the iliofemoral axis, while diabetes mellitus is associated with atheromatous damage in the distal arteries of the intracranial region and lower limbs. Smoking, male sex, advanced age, and diabetes are particularly associated with an increased risk of coronary artery disease. Another distinctive feature of atherosclerotic disease is its progressive nature, which typically unfolds over the course of several decades. After a typically long asymptomatic period, atherosclerosis presents clinically with chronic, predictable, and reproducible manifestations such as intermittent claudication and angina pectoris, or with more severe acute events, such as myocardial infarction or cerebral stroke. In the preclinical phase, the identification and management of modifiable risk factors remains the only intervention capable of significantly influencing the progression of atherosclerotic lesions.
Endpoint: The aim of this prospective longitudinal study is to evaluate the correlation between the evolutionary aspects of atherosclerotic disease and the risk of acute vascular events, collected in a ten-year follow-up population.
Materials and methods: This study was conducted on patients previously enrolled in the research study (protocol no. 14725/2014) carried out in our Angiology Department and evaluated ten years later; participants were interviewed regarding their CV family history, known CV diseases and risk factors, acute CV events that occurred over the past ten years, major comorbidities and current therapies. In this ten-years follow-up study, each participant underwent a comprehensive clinical and ultrasonographic evaluation, including Ankle-Brachial Index (ABI), carotid-vertebral and lower limb duplex ultrasound. The collected data were then compared with baseline data from ten years prior to evaluate the correlation between certain clinical and ultrasonographic conditions and the occurrence of any major adverse cardiovascular events (MACE: non-fatal myocardial infarction, non-fatal stroke, all-cause mortality) or major adverse lower limb event (MALE: critical limb ischemia requiring revascularization or amputation).
Results: Preliminary analysis demonstrated that both the presence and duration of exposure to established CV risk factors—such as male sex, type 2 diabetes mellitus, cigarette smoking and prior CV events—were significantly associated with an increased incidence of major adverse cardiovascular events (MACE). A higher incidence of MACE was observed in patients with greater baseline atherosclerotic burden, assessed via comprehensive duplex ultrasound. Furthermore, longitudinal ultrasound follow-up revealed a relation between the progression of atherosclerotic lesions, irrespective of vascular territory, and elevated risk of MACE and MALE, although this association did not reach statistical significance based on the data currently analyzed. Notably, the progression of non-stenotic, subclinical atherosclerotic plaques in the femoropopliteal segment—lesions not associated with alterations in the ABI—could be associated with adverse outcomes, underscoring the prognostic value of subclinical disease.
Conclusions: These preliminary findings reinforce the established association between traditional CV risk factors and the incidence of MACE, in a real-life

ten-year follow-up population. Importantly, total atherosclerotic burden emerged as a key predictor of adverse CV outcomes. Subclinical atherosclerosis, particularly in the femoro-popliteal district, may represent a significant prognostic marker. Given its detectability via non-invasive and widely accessible imaging modalities such as duplex ultrasound, this parameter may offer a cost-effective strategy to enhance individual CV risk stratification and guide preventive interventions.

CIRCULATING MICRORNAS SIGNATURE ASSOCIATED WITH CHANGES IN BODY COMPOSITION IN NEWLY DIAGNOSED BREAST CANCER PATIENTS

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Introduction: Women with newly diagnosed breast cancer (BC) may experience early and progressive alterations in body composition, including skeletal muscle (SM) mass and adipose tissue (AT) wasting. These changes are associated with increased risk of treatment-related toxicity and poorer outcomes overall prognosis. Emerging evidence suggests that microRNAs (miRNAs) expression, key regulators of gene expression, play important roles in the metabolism of SM and AT, suggesting their potential contribution to cancer-related changes in body composition.
The present study aimed i) to characterize the circulating miRNAs expression profile associated with SM and AT metabolism in women with newly diagnosed BC, and ii) to analyze associations between miRNA levels and body composition parameters.
Methods: We enrolled patients with newly diagnosed BC and age-matched healthy controls (C). Clinical data, medical history and anthropometric measurements, including height and weight, were recorded. Body composition was estimated using bioelectrical impedance analysis (BIA). The internal cut-off values for Fat-Free Mass Index (FFMI, kg/m²) and phase angle (PhA, °) were set at 16,9 kg/m2 and 4,5°, respectively. Fasting blood samples were obtained from all participants. Circulating levels of miRNAs involved in SM and AT metabolisms were quantified by RT-qPCR.
Results: Our results showed a significant downregulation of miR-15b, -26a, and -133a ($p<0.05$), along with a trend towards upregulation of miR-486 ($p=0.058$) in BC (n=51) compared to C (n=14). Levels of miR-133a were significantly lower in BC with low FFMI (n=26) vs high FFMI levels (n=25) ($p<0.05$). In addition, miR-15b, -29a, and -29b were significantly upregulated in BC with high PhA (n=24) compared to those with low PhA (n=27), while miR-486 was significantly downregulated in the high PhA group ($p<0.05$).
Conclusion: Our preliminary data indicate a distinct modulation of circulating miRNAs in patients with a new diagnosis of BC, that correlates with alterations in body composition. Further investigations are underway to elucidate the functional implications of these miRNAs in BC-associated SM and AT metabolic dysregulation.

EVALUATION OF MULTISENSORIAL ELECTRONIC TECHNOLOGIES AS NONINVASIVE TOOLS FOR THE DETECTION OF FIBROTIC MASH IN MASLD PATIENTS

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Background: and Aims: Fibrotic-MASH—the inflammatory form of MASLD characterized by significant necroinflammatory activity (necroinflammatory activity score -NAS- ≥4) and fibrosis (stage ≥2)—represents the most clinically relevant and treatment-eligible phenotype due to its progressive nature. Accordingly, current research efforts are increasingly focused on identifying noninvasive methods for its detection. In recent years, multisensorial technologies such as electronic nose (e-nose) and electronic tongue (e-tongue) have emerged as promising diagnostic and prognostic tools across a range of conditions, including liver diseases. This study aims to assess the performance of e-nose and e-tongue technologies as novel, noninvasive tools for identifying fibrotic-MASH.
Method: We prospectively enrolled consecutive patients with MASLD evaluated at the Hepatology Unit of the "Fondazione Policlinico Universitario Campus Bio-Medico" of Rome. MASLD diagnosis was based on the presence of cardiometabolic risk factors along with either histological or ultrasound-confirmed hepatic steatosis. Fibrotic MASH was defined noninvasively as a Fibroscan-AST (FAST) score ≥0.67 and histologically by the presence of NAS ≥4 and fibrosis stage ≥2. All patients underwent breath collection for analysis via BIONOTE e-nose, and urine and saliva sampling for BIONOTE e-tongue analysis. The discriminatory performance of these e-sensing technologies in detecting fibrotic MASH was assessed using Partial Least Squares Discriminant Analysis (PLS-DA) and evaluated through confusion matrices.
Results: We enrolled 121 MASLD patients (median age 57.4 years, male 60%, mean BMI 31.9 kg/m2), with 75 included in the non-invasive cohort and 46 in the histological cohort. Overall, FAST score was available for 107 patients. Fibrotic-MASH was identified in 15/107 by FAST score, and in 24/46 by histological criteria. Breath, urine, and saliva samples were suitable for analysis in 102, 118 and 116 patients, respectively. The accuracies of breath, saliva and urine in predicting fibrotic MASH according to FAST score were 77%, 79.8%, and 82%, respectively. In the histological subgroup, e-tongue saliva reached the best prediction capability (78.9%), while e-nose and e-tongue urine had lower accuracies (74% and 65%, respectively). Combining all the three sample analyses improved the predictive performance for histologically defined fibrotic-MASH to 79%. Overall, e-technologies outperformed FAST (68% accuracy) in predicting histologically confirmed fibrotic-MASH.
Conclusion: E-technologies demonstrated good accuracy in identifying fibrotic MASH, outperforming FAST, one of the widely used noninvasive score. These findings suggest a potential role for these tools in clinical risk assessment of MASLD/MASH, though confirmation in larger, prospective cohorts is needed.

UPPER EXTREMITY DEEP VEIN THROMBOSIS AS THE FIRST MANIFESTATION OF PRIMARY MEDIASTINAL LARGE B-CELL LYMPHOMA: A CASE REPORT

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Introduction: Upper extremity deep vein thrombosis (UEDVT) accounts for less than 10% of all deep vein thrombosis cases. It is typically classified as either primary or secondary, related to venous cannulation, trauma, or prothrombotic conditions including cancer. While the association between lower-extremity venous thrombosis and cancer is well established, the role of UEDVT as a marker of occult malignancy and its prognostic significance for all-cause mortality remains under investigation (1). We report a case of UEDVT that led to the diagnosis of a primary mediastinal large B-cell lymphoma.
Case report: A 38-year-old Caucasian female with no significant past medical history, except for endometriosis, presented to the emergency room with acute pain and swelling of the left upper extremity. Her family history was significant for colorectal cancer and deep venous thrombosis of the lower limb. Doppler ultrasound revealed complete thrombosis of the left humeral, axillary, and subclavian veins. Chest X-ray was unremarkable. Laboratory tests showed a hemoglobin level of 11.6 g/dL. The patient was started on subcutaneous enoxaparin at a dose of 1 mg/kg every 12 hours and was discharged with an appointment at the thrombosis clinic. At the follow-up visit seven days later, the pain and swelling had worsened, and the patient was admitted to the internal medicine department. A contrast-enhanced computed tomography (CT) scan of the chest and neck revealed a solitary anterior mediastinal mass measuring 45 × 35 mm, along with thrombosis of the left subclavian, innominate, and left jugular veins. A Positron Emission Tomography-CT scan showed increased uptake in the mediastinal mass and anterior mediastinal lymphadenopathy (SUV 24). A CT-guided biopsy of the mass was performed. Histological examination confirmed primary mediastinal large B-cell lymphoma. A bone marrow biopsy excluded bone marrow involvement. The patient began chemotherapy with the R-ECHOP regimen. Due to moderate hepatic cytolysis, enoxaparin was discontinued and replaced with fondaparinux 7.5 mg. After four cycles of chemotherapy, CT imaging showed a very good response. A three-month follow-up doppler ultrasound confirmed complete recanalization of the previously thrombosed veins. The patient was then switched to rivaroxaban 10 mg.
Discussion: The diagnostic work-up of patients presenting with UEDVT poses a clinical challenge in determining the need and extent of investigations to detect occult malignancy. UEDVT lacks a standardized approach due to its lower incidence and the heterogeneity of underlying causes. International Society on Thrombosis and Haemostatsis (ISHT) guidelines recommend limited cancer screening: a thorough medical history and physical examination, basic

laboratory tests and a chest X-ray; additionally, age- and gender-specific cancer screening should be performed according to national guidelines (2). Certain clinical features warrant further investigation: absence of typical risk factors (such as recent catheterization or trauma), bilateral or extensive thrombosis, constitutional symptoms, and lack of response to anticoagulant therapy. In such cases, a targeted approach using imaging studies like contrast-enhanced CT or PET-CT may be justified. In our case, the progressive swelling despite therapeutic anticoagulation, combined with the absence of mechanical risk factors, raised suspicion for an underlying neoplastic process. This highlights the importance of an individualized approach based on clinical context. UEDVT can be the first manifestation of an underlying malignancy, and early recognition may influence both prognosis and treatment strategy.

References:

1 Adelborg K, Horváth-Puhó E, Sundbøll J, Prandoni P, Ording A, Sørensen HT. Risk and prognosis of cancer after upper-extremity deep venous thrombosis: A population-based cohort study. Thromb Res. 2018 Jan;161:106-110. doi: 10.1016/j.thromres.2017.11.017. Epub 2017 Nov 22. PMID: 29245061

2 A. Delluc, D. Antic, R. Lecumberri, C. Ay, G. Meyer, M. Carrier, Occult cancer screening in patients with venous thromboembolism: guidance from the SSC of the ISTH, Journal of Thrombosis and Haemostasis, Volume 15, Issue 10, 2017

OVERLAP SYNDROME- CELIAC DISEASE AND AUTOIMMUNE HEPATITIS IN A YOUNG FEMALE: A TALE OF TWO AUTOIMMUNE TARGETS

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Background: Celiac disease (CD) is a common autoimmune disorder primarily affecting the small intestine and is often associated with various extraintestinal manifestations, including liver abnormalities. Liver damage related to CD, commonly referred to as celiac hepatitis, is typically asymptomatic and reversible with a gluten-free diet. However, in rare cases, progressive and symptomatic liver injury can occur, suggesting an overlap with autoimmune liver diseases (AILDs), such as autoimmune hepatitis (AIH). Genetic predisposition and the autoimmune nature of CD and AIH may explain this overlap, underscoring the importance of early diagnosis and management.

Case presentation: An 18-year-old female patient with a family history of psoriasis (sister), type 1 diabetes (cousin), and multiple sclerosis (maternal aunt) presented with a history of migraine with aura diagnosed in 2020, along with recurrent hospital visits for unexplained asthenia, initially attributed to reactive anxiety.In February 2023, during an emergency department visit, she was found to have monocytosis and elevated liver enzymes (AST ×5, ALT ×12). She was referred to our Unit for further evaluation of persistent transaminase elevation. A thorough diagnostic workup excluded relevant pharmacological history and lifestyle factors; the lipid profile, viral hepatitis serology, and stool microbiological tests were unremarkable. Abdominal ultrasound revealed mild hepatic steatosis and a slightly enlarged spleen. Additional investigations showed positive ANA (1:80, homogeneous pattern) and elevated IgG anti-deamidated gliadin peptides (IgG DGP). An esophagogastroduodenoscopy (EGDS) was performed, which showed histological findings consistent with CD, and the patient was advised to start a gluten-free diet.

In May 2024, the patient presented again with rising transaminase levels and abdominal discomfort. Despite strict adherence to a gluten-free diet, liver function tests revealed AST ×13 and ALT ×16. Consequently, the possibility of autoimmune hepatitis was considered, and a liver biopsy was conducted to substantiate this diagnosis (Scheuer stage 1, grade 3).The patient was started on Prednisone 25 mg/day after breakfast and 5 mg/day after lunch. By September 2024, steroid tapering was initiated, and Azathioprine 50 mg/day was added to the regimen. By January 2025, liver enzyme levels had normalized.

Discussion: In most cases, liver injury associated with CD is asymptomatic and resolves with dietary intervention. However, the persistence of elevated transaminases in patients adhering to a gluten-free diet should raise suspicion for underlying autoimmune liver disease, particularly autoimmune hepatitis. Genetic susceptibility, such as a family history of autoimmune diseases, including type 1 diabetes and multiple sclerosis, in this patient further increases the likelihood of developing AIH.The pathophysiological mechanism underlying the overlap between CD and AIH remains incompletely understood but may involve the "leaky gut" hypothesis, in which increased intestinal permeability allows antigenic stimuli to enter the circulation and trigger hepatic autoimmune responses. This concurrent immune-mediated injury to both the intestine and liver can lead to progressive hepatic damage, even in the context of a gluten-free diet.The presence of ANA positivity, persistent transaminase elevation, and a strong family history of autoimmune diseases strongly supports a diagnosis of CD-AIH overlap syndrome. Early recognition and timely initiation of immunosuppressive therapy are essential to prevent further hepatic injury and reduce the long-term risk of cirrhosis or hepatocellular carcinoma.

Conclusion: This case highlights the importance of considering autoimmune hepatitis in patients with celiac disease who exhibit persistent liver enzyme abnormalities despite dietary compliance. Genetic predisposition and a positive family history of autoimmune disorders may increase the risk of overlap syndromes. Prompt diagnosis and immunosuppressive treatment of AIH can rapidly normalize liver function and prevent long-term hepatic complications, particularly in young patients with a favourable life expectancy.

USE OF ANTIBIOTIC THERAPY IN HOSPITALIZED ELDERLY PATIENTS: 'LESS IS MORE'?

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The appropriate use of antibiotic therapy in elderly patients remains challenging for clinicians. Infections are particularly prevalent in end-of-life phases, often necessitating antimicrobial treatment. We present data from an internal medicine department with a median follow-up observation of approximately one year.

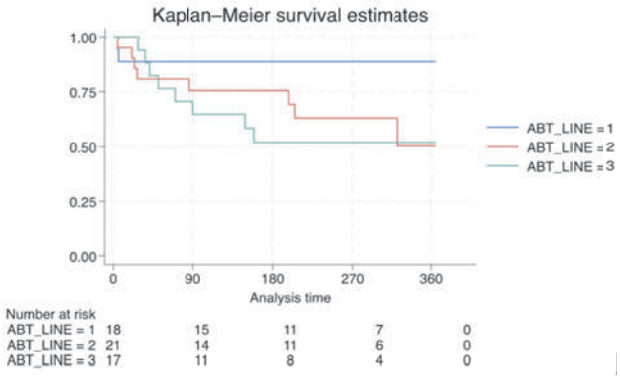
Materials and Methods: Data were extracted from a prospective observational registry (Med-Cli protocol) including patients hospitalized from January 2024 to February 2025 in a large academic hospital. The inclusion criteria were age over 80 years, hospitalization for infection, and antimicrobial therapy. Patients were stratified into three groups according to the use of first, second, or third-line antimicrobial therapy (Tab.1). Collected data included demographics, comorbidities (quantitated through the Cumulative Illness Rating Scale, CIRS, and the Charlson Comorbidity Index, CCI), and disability grade (Barthel Index). Hospital admissions in the 6 and 12 months preceding the enrollment were also quantitated. Expected benefit from intensive care (IC benefit) was categorized in three levels (low, medium, and high) and evaluated by clinicians on admission and discharge. Clinician's impression about patient severity and likelihood to die was summarized on a 0-10 analog scale (0 = not at all surprised; 10 = much surprised by patient death during hospitalization). In-hospital survival, discharge modality (at home vs to palliative care) and post-discharge survival were defined as outcomes of interest. Data are expressed as percentages and median (interquartile range, IQR) unless otherwise stated.

Results: We enrolled 86 patients (60% males), who had a median age of 85 years (83-88) and a median hospitalization length of 21 (15-31) days. Of them, 22 (26%) received first-line antimicrobials, 29 (34%) second-line therapy, and 35 (41%) third-line therapy. The median Barthel's score was 90 (55-100) before admission and 40 (20-80) after discharge, with almost 2/3 of subjects showing partial or total dependence. Among the 13 (15%) subjects deemed fit to benefit from highly intensive care at baseline one died, one was referred to palliative care and 11 were discharged back to primary care. Globally, 10 patients (12%) died during hospitalization, 36 after 281 (204–365) days post-discharge. Of notice, among these patients only 47% were discharged to palliative care. The three groups had comparable demographics, expected IC benefit and total CIRS scores. However, compared to patients receiving first-line treatments, second/third-line antimicrobial users had significantly higher CCI scores [8(6-11) and 9 (6-10) vs7 (5-8); p=0.049], longer hospitalizations [27 (15-41) and 22 (17-31) vs 17 (15-19) days, p=0.008), and a higher prevalence of dependence [41% and 40% vs 18% ; p=0.047]. The third-line treatment group showed a significantly lower Barthel index at discharge [35(0-62)] compared both to second- [50(30-80)p=0.023] and first-line antimicrobial users [55(30-90), p=0.039]. Hospitalization rates within the previous 6 and 12 months were also higher in patients with second/third-line treatments compared to first-line antimicrobial users (p<0.009 and p=0.034 respectively). In-hospital deaths were observed only in the group with the highest intensity of antimicrobial treatment. The same group also showed higher post-discharge mortality rates among non-palliative care patients (Fig.1).

Conclusions: Complicated infections prompting advanced lines of antimicrobial treatments are frequent in hospitalized elderly people and are associated with recurrent access to healthcare, higher comorbidity and functional disability burden along with high in-hospital and post-discharge mortality. Inadequate evaluation of baseline patient fitness might cause highly effective third-line antimicrobial treatments to just temporarily prolong the lifespan of patients with exhausted functional reserves, possibly only leading to disproportionately long

hospitalizations and uncertain benefits in terms of overall short-/medium-term survival and quality of life. Further research is warranted to define predictive tools to profile elderly patients accessing acute care, facilitate early referral to palliative care and promote optimal adjustment of antimicrobial treatments and intensity of care to individual clinical needs.

Figure 1



SILENT SHIFT: UNVEILING AIH FEATURES IN A PATIENT WITH STABLE PBC

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Background: Primary Biliary Cholangitis (PBC) is a chronic autoimmune cholestatic liver disease with a progressive course that can lead to cirrhosis. Previously known as primary biliary cirrhosis, it is an autoimmune condition, and its diagnosis—after ruling out biliary obstruction—is based on the presence of anti-mitochondrial antibodies (AMAs) or elevated levels of PBC-specific anti-nuclear antibodies (ANAs) in the context of chronic cholestasis, with or without typical bile duct lesions on histology. PBC is typically well controlled with Ursodeoxycholic acid (UDCA).
However, a subset of patients may develop an overlap with autoimmune hepatitis (AIH), potentially leading to disease progression if not promptly identified and treated.
Case presentation: We report the case of a 52-year-old female patient with a 20-year history of PBC, maintained on stable UDCA therapy.
She was referred to our Unit due to newly detected mild hypertransaminasemia, elevated cholestatic markers, hypoalbuminemia, hypergammaglobulinemia, and a reduced albumin-to-gamma-globulin ratio.Serologic testing revealed ANA positivity (cytoplasmic mitochondrial pattern, titer 1:1280), AMA positivity, and the presence of anti-M2 (BCOAD-E2, PDC-E2, nPDC) and anti-GP210 antibodies. Hepatotropic viral serologies were negative. Abdominal ultrasound showed a liver with mildly heterogeneous echotexture, while liver elastography demonstrated clinically significant fibrosis.Due to clinical suspicion of PBC-AIH overlap syndrome, a liver biopsy was performed, confirming the diagnosis (Scheuer grade 2, stage 2). Corticosteroid therapy with Prednisone was initiated in March 2024 at a dose of 25 mg/day, followed by gradual tapering. Azathioprine 50 mg/day was introduced after initial biochemical improvement. By May 2024, transaminase and cholestasis markers had normalized, allowing for steroid discontinuation. Follow-up in September 2024 and February 2025 confirmed sustained biochemical remission.
Discussion: This case illustrates a diagnosis of autoimmune hepatitis (AIH) arising in the context of previously well-controlled primary biliary cholangitis (PBC) under long-term Ursodeoxycholic acid (UDCA) therapy. Despite treatment adherence, the patient experienced hepatic function deterioration, as evidenced by rising transaminases and hypoalbuminemia suggestive of an overlap syndrome between PBC and AIH.
A comprehensive diagnostic work-up was performed to investigate the aetiology of the persistent liver enzyme elevation, excluding viral, metabolic, and drug-induced causes. Identification of disease-specific autoantibodies and histological confirmation were essential for an accurate diagnosis.
This diagnosis justified the addition of immunosuppressive therapy to ongoing UDCA, starting with Corticosteroids followed by Azathioprine. Liver enzymes normalized within six months of initiating immunosuppression.
This clinical case underscores the importance of timely therapeutic intervention in autoimmune liver diseases to prevent fibrotic progression. Despite the relatively young age of the patient, early-stage liver fibrosis had already developed, emphasizing the need for vigilance and a personalized treatment strategy in the management of complex autoimmune hepatopathies.
Conclusion: PBC-AIH overlap syndrome should be considered in patients with established PBC who develop unexplained biochemical abnormalities. Early diagnosis and initiation of immunosuppressive therapy are critical to improving outcomes and preventing irreversible liver damage, even in patients with initially favorable prognostic indicators.

IMPACT OF COMORBIDITIES IN SEPSIS AND SEPTIC SHOCK: A RETROSPECTIVE COHORT STUDY

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Background: and purpose of the study: Comorbidities represent significant determinants of prognosis in cases of sepsis and septic shock; however, a preliminary analysis conducted on our data, focusing on a geriatric patient population, revealed that these factors were not significantly associated with adverse outcomes. Our objective was to evaluate the role of the Charlson Comorbidity Index (CCI) in the prognosis of elderly subjects with sepsis or septic shock within an extended cohort of elderly patients admitted for this condition in an Internal Medicine department.
Materials and methods: Retrospective single-center cohort study conducted in a geriatric internal medicine (INRCA Internal Medicine Department, Osimo). Age, sex, CCI items, length of hospital stay, and the main outcome, defined as either death or transfer to the ICU, were collected. Continous variables were compared with t-test if normally distributed; dichotomous variables were compared with chi-squared test. We assessed the relationships between variables with Pearson's bivariate analysis; the accuracy of CCI in predicting the outcome was assessed with ROC curve analysis; the best cutoff for CCI was assessed with ROC curve analysis adopting Youden's index; last, we assessed the hazard ratio (HR) for the main outcome adopting both a Kaplan Meier curve and Cox regression model considering: days of hospitalization as the time variable, the main outcome as the independent variable, and the dichotomous CCI, adopting the cutoff derived from the ROC curve, as the main predictor.
Results: We obtained a cohort of 593 consecutive patients, mean age 81.04±7.22 years, 300 (50.6%) men, mean hospital stay 12.3±9.6 days, 243 (41%) death or ICU transfer. The CCI was associated with the main outcome (Pearson's:0.25; p<0.0001) and significantly higher if the outcome was unfavorable (6.74±2.08 versus 7.92±2.41; p<0.0001). The CCI was had a low accuracy (AUC:0.64; 95%CI:0.61-0.66; p<0.0001). At survival analysis, CCI≥7 was associated with a higher risk of events (HR:1.78; 95%CI:1.3-2.3; p<0.0001): 58.8% of the considered subjects with CCI<7 and 22.5% of those with CCI≥7 had not developed outcomes at 36 days (p<0.0001; log-rank test).
Conclusions: CCI is associated with worse outcomes in sepsis and septic shock. Howver, the significance of this finding emerged only by expanding our case series, suggesting that other factors, e.g., those contained in the SOFA score, may have a greater influence on survival in the acute phase of disease.

CASE REPORT OF CVID WITH A PHENOTYPE DOMINATED BY IMMUNE DISORDERS RATHER THAN INFECTIOUS ONES

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Common variable immunodeficiency (CVID) is the most common symptomatic primary immunodeficiency disorder in adults, characterized by defects in B-cell differentiation and low levels of circulating immunoglobulins (Ig). It has been increasingly appreciated that these patients exhibit not only increased susceptibility to infections but also paradoxical manifestations of autoimmunity that became the leading cause of death after the introduction of immunoglobulin therapy.
We present the case of a patient diagnosed with CVID associated with GLILD followed since2012(36years old). Since childhood, she had recurrent upper respiratory tract infections for which at the age of8years she had undergone adenoidectomy and tonsillectomy. At the age of18years, she had autoimmune hemolytic anemia that was treated with steroid therapy. The following year, she had worsened respiratory symptoms and the appearance of pulmonary infiltrates on chest X-rays, interpreted as sarcoidosis and treated with steroid cycles,

resulting in a transient clinical improvement followed by multiple relapses. At26years of age, due to the onset of epigastric pain, a duodenal biopsy was performed with evidence of lymphoid nodular hyperplasia. At34years old, she underwent bronchoscopy and lung biopsy, finally demonstrating the presence of lymphocytic interstitial pneumonia and granulomatous lesions (GLILD), evidence of marked hypogammaglobulinemia. A diagnosis of CVID was made with the start of Ig replacement therapy, with benefit on infections. After a year, an autoimmune thrombocytopenia was diagnosed, for which she underwent therapy with Rituximab (RTX) and i.v. steroids with clinical remission and continuation of RTX for18months.Splenomegaly (diameter long132cm) was found, in association with alterations in cytolysis and cholestasis indices. After about a year the patient presented ascitic decompensation and hemorrhoidal bleeding. The liver biopsy showed nodular regenerative hyperplasia (NRH). No other factors responsible for liver disease were present (alcohol, viruses, metals, drugs, etc.). Due to frequent episodes of rectal bleeding with severe anemia, she underwent hemorrhoidectomy. A clinical exome was also performed subsequently, which showed the heterozygous mutation c.55A>G, p. (Lys19Glu) in NFAT5and c.1228G>A, p. (Val410Ile) in CASP10. Given initial experiences and reports in the treatment of dysimmune complications of CVID by B-cell depletion, in2021she repeated a single administration of RTX; the planned infusion schedule was not completed due to the onset of C. Jejuni sepsis and protracted Norovirus gastrointestinal infection. Considered some trials demonstrating the efficacy and safety of Abatacept in CVID to treat autoimmune or dysregulation manifestations, she started Abatacept for about six months without evidence of efficacy. She was then hospitalized for meningoencephalitis from HHV6and Enterovirus, with the patient's death after some severe infectious episodes in the following months.

In the case of our patient, among the various manifestations of immune dysregulation, liver disease was especially relevant, negatively impacting both prognosis and her quality of life. The histological hepatic pattern of NRH associated with the presence of esophageal varices and bleeding from the hemorrhoidal plexuses, allows us to frame the liver disease as a non-cirrhotic portal hypertension in the context of a porto-sinusoidal vascular disorder. The most relevant complication from portal hypertension was chronic bleeding from varices. With respect to splenomegaly (long diam. reached 20 cm), the hypothesis of performing the splenectomy was considered; however, this procedure was not performed due to the excessively high risks associated with the procedure itself and possible repercussions on portal hemodynamics. Several immunosuppressive therapeutic strategies such as RTX and Abatacept have been attempted; however, their use in this case was not beneficial and, in this case, overlapped with infectious complications. Another relevant manifestation was enteropathy. Liver damage in patients with CVID is strongly associated with lymphocytic enteropathy, suggesting a pathogenetic role of the gut-liver axis. From a genetic point of view, both mutations found have already been associated with immune dysregulation diseases. In particular, NFAT5 is a transcription factor that regulates immune cell function and cellular adaptation to hyperosmotic stress and has been associated with enterocolopathy in the context of CVID. In conclusion, the prognosis of CVID depends on various factors, including age of onset and diagnosis, diagnostic delay, malignancies, immunoglobulin levels, and lymphocyte count (e.g., CD21 low B cells) in peripheral blood. Non-infectious complications, such as granulomas, gastrointestinal and hepatic involvement, and pulmonary disease may indicate a poor prognosis. A deeper understanding of the etiology and pathophysiology will help in early diagnosis and appropriate treatments to improve the prognosis.

A RARE CASE OF ENOXAPARIN-INDUCED LIVER INJURY IN THE SETTING OF RECENT OBSTRUCTIVE CHOLANGITIS

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Drug-induced liver injury (DILI) accounts for ten of all cases of hepatitis and can be triggered by a wide range of medications, herbal and dietary supplements. While enoxaparin is widely used for anticoagulation, its potential hepatotoxicity is underrecognized. Here we present a case of hepatocellular DILI occurring in the setting of recent enoxaparin administration in a patient with a recent episode of obstructive cholangitis.

A 58-year-old man, with a history of hypertension, glucose-6-phosphate dehydrogenase deficiency and antiphospholipid antibody syndrome (on long-term anticoagulation with warfarin), was admitted with abdominal pain, fever and obstructive jaundice due to gallstones. Imaging (CT and MRCP) revealed gallbladder hydrops, dense biliary sludge, and multiple small stones within the gallbladder and cystic duct. On January 4, 2025, intravenous ceftriaxone (2 g/day) was started. On January 9, warfarin was switched to enoxaparin (6000 IU BID) due to the ongoing need for anticoagulation. Initial labs showed elevated bilirubin (total 7.54 mg/dL, direct 6.29 mg/dL), ALT 110 U/L, AST 43 U/L, GGT 241 U/L, and ALP 199 U/L. From January 10 onward, liver enzymes began to increase progressively. By January 21, labs showed AST 775 U/L, ALT 1293 U/L, GGT 88 U/L, total bilirubin 2.99 mg/dL, direct bilirubin 2.0 mg/dL, and ALP 147 U/L. Workup for viral hepatitis (HBsAg, anti-HBc, anti-HBs, anti-HCV), autoimmune hepatitis (ANA, AMA, LKM, SMA), and celiac disease was negative. The patient did not consume alcohol and had no features of metabolic syndrome. Enoxaparin was discontinued on January 20 due to suspicion of DILI. On January 22, liver enzymes further increased (AST 871 U/L, ALT 1648 U/L, total bilirubin 3.25 mg/Dl, direct bilirubin 2.55 mg/dL), prompting discontinuation of ceftriaxone as well. A liver biopsy performed on January 22 revealed centrilobular hepatocellular collapse with acinar macrophages containing PAS-positive diastase-resistant material. There was no significant inflammatory infiltrate or plasma cell component, findings favoring toxic liver injury. Following the withdrawal of both medications, liver enzymes gradually normalized over the next month. The patient was followed up for three months, with complete biochemical recovery. (Figure 1).

Causality assessment was performed using the updated RUCAM for both enoxaparin and ceftriaxone. Enoxaparin yielded a total score of 10, and ceftriaxone a score of 9, both falling within the "highly probable" range. However, the latency period was significantly shorter for enoxaparin (2 days) compared to ceftriaxone (6 days), and the peak transaminase levels occurred while enoxaparin was still being administered. Furthermore, liver histology favored a pattern consistent with toxic hepatocellular damage, which is more commonly reported with heparin derivatives. The course of recovery also suggests a closer temporal association with enoxaparin withdrawal. These findings support enoxaparin as the most likely causative agent in this case of DILI.

This case reinforces the need for heightened clinical awareness regarding drug-induced liver injury (DILI) associated with low molecular weight heparins (LMWHs), particularly enoxaparin. Although typically well-tolerated, enoxaparin has been implicated in rare but potentially severe hepatocellular injury, as described in several case reports and pharmacovigilance analyses. The hepatotoxic potential appears idiosyncratic and non-immunoallergic, with a rapid onset and resolution upon drug withdrawal, as observed in our patients. In this case, a structured causality assessment using the RUCAM score, in conjunction with histological findings and exclusion of alternative etiologies, supported a "highly probable" diagnosis of enoxaparin-induced DILI. Importantly, while ceftriaxone was also considered a possible contributor, the timing, clinical evolution, and liver biopsy findings favored enoxaparin as the most likely culprit.

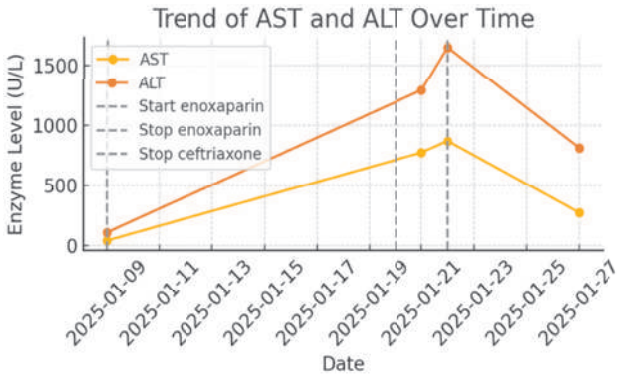

Figure 1. Trend of AST and ALT serum levels showing temporal relationship with drug administration and withdrawal.

A MOSAIC OF VASCULITIC AND AUTOIMMUNE MANIFESTATIONS: DIAGNOSTIC AND THERAPEUTIC CHALLENGES BETWEEN INFLAMMATION AND ORGAN INVOLVEMENT

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Clinical Case: A 61-year-old woman was admitted to the Emergency Department for progressive dysphagia, dysphonia, severe weight loss (>20% of habitual body weight), reduced appetite, progressive physical impairment, and diffuse

arthro-myalgias. Upon admission, physical examination revealed digital ulcers, purpura, and a necrotic lesion on the right tibial area.Baseline laboratory tests showed normochromic normocytic anemia (hemoglobin 9.5 g/dL), neutrophilic leukocytosis (WBC 14.150/mm³, with 12.500/mm³ neutrophils), thrombocytosis (platelets 620.000/mm³), elevated inflammatory markers (CRP 9.15 mg/dL; ESR 96 mm/h), and hyponatremia (128 mEq/L).The patient was admitted to our Internal Medicine Unit with the following differential diagnoses were hypothesized: acute/subacute infection(s), cancer disease, and/or autoimmune disorder.Microbiological cultures revealed urinary tract infection and digital ulcers colonized by methicillin-resistant Staphylococcus aureus(MRSA), and targeted antibiotic therapy was initiated.Both transthoracic and transesophageal echocardiograms ruled out valvular vegetations. Blood cultures were also negative. Serum immunofixation revealed a monoclonal IgM-Kappa component, and urinary immunofixation tested positive for Bence-Jones proteinuria. Due to the ulcerative pattern and localization, serum cryoglobulins were assessed and found to be positive (cryocrit: 9%). Since hepatitis C virus (HCV) infection accounts for more than half of all mixed cryoglobulinemia cases, serological tests for major hepatotropic viruses were performed and were found negative. To rule out a paraneoplastic origin, endoscopy and total-body CT scan were performed, resulting negative for neoplastic lesions but showing bilateral interstitial lung thickening, bilateral pleural and pericardial effusion. These findings, in association with the clinical manifestations, raised suspicion of an autoimmune disease. An autoimmune panel showed high-titer rheumatoid factor (107 IU/mL), positive ANA (1:1280, homogeneous pattern), SSA (Ro52 and Ro60) positivity, and reduced complement levels (C3 88.9 mg/dL; C4 <6.67 mg/dL). Taking into consideration the presence of dysphagia, endoscopic swallowing evaluation by fiber optic laryngoscopy was performed, revealing delayed oropharyngeal swallowing with minimal vallecular residues and a diminished cough reflex.These findings supported a diagnosis of Sjögren's Syndrome, not only due to xerostomia but also due to the presence of oropharyngeal dysphagia, in the context of the patient's poor nutritional status.

Discussion: Mixed cryoglobulinemia, classified as type II or III, is characterized by the presence in serum of immune complexes formed by IgM (monoclonal or polyclonal) with rheumatoid activity against IgG, which precipitate at temperatures below 37°C.Cryoglobulinemic vasculitis is a multisystem disorder marked by "gravitational" purpura, skin ulcers, sensorimotor neuropathy, membranoproliferative glomerulonephritis, and more rarely, arthralgia/arthritis and Raynaud's phenomenon.Mixed cryoglobulinemia and hypocomplementemia are poor prognostic factors in autoimmune diseases such as Sjögren's Syndrome. Sjögren's Syndrome is characterized by specific autoantibodies (anti-Ro/SS-A), with a prevalence estimated at 0.5–1% and a female-to-male ratio of 9:1. The clinical features include sicca symptoms (xerostomia and xerophthalmia), arthralgia/arthritis, and fatigue.

Conclusion: The complexity of this clinical case highlighted the need for a multidisciplinary approach to reach a definitive diagnosis. The presence of mixed cryoglobulinemia, autoimmune serologic positivity (anti-Ro/SS-A), hypocomplementemia, monoclonal IgM-Kappa component, and systemic symptoms including arthralgia, myalgia, and oropharyngeal dysphagia led to the diagnosis of Sjögren's Syndrome with vasculitic complications. Following evaluation by a multidisciplinary team including internist, rheumatologist, immunologist, and hematologist, therapeutic apheresis was recommended.The association between systemic autoimmune manifestations and mixed cryoglobulinemia represents a significant negative prognostic factor, underlining the need for close clinical monitoring to prevent further complications, including lymphoproliferative manifestations.

SERONEGATIVE PRIMARY BILIARY CHOLANGITIS IN A PATIENT WITH A HISTORY OF SARCOIDOSIS: A CASE REPORT AND PATHOGENETIC CONSIDERATIONS

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Background: Primary biliary cholangitis (PBC) and sarcoidosis represent two distinct, chronic immune-mediated diseases, despite exhibiting disparities in their respective etiological processes and the organ systems they target. PBC is a chronic autoimmune cholangitis targeting intrahepatic small bile ducts, while sarcoidosis is a systemic granulomatous disease of unknown etiology. Their co-occurrence, though rare, has been reported and may reflect shared immunogenetic and environmental triggers.

Case presentation: In May 2024, a 62-year-old male patient was referred to our Unit for evaluation of newly detected liver enzyme abnormalities (AST ×7, ALT ×3, GGT ×18 U/L), accompanied by a 12-kilogram weight loss over the past year, preserved appetite, and light-colored, malodorous diarrhea. He had no history of allergies or substance use and a family history of thyroid disease. His medical history included sarcoidosis, type 2 diabetes, dyslipidemia, and benign prostatic hyperplasia.Laboratory tests revealed persistent elevated cytolysis (AST ×6, ALT ×6) and cholestasis (GGT ×24, ALP ×5), elevated ESR (110 mm/h), serum IgG4 12,7 g/L, and negative autoantibodies. Abdominal ultrasound showed mild hepatic steatosis, slight intrahepatic bile duct dilation, and gallbladder wall thickening without lithiasis. The common bile duct appeared thickened and mildly dilated at the hepatic hilum. The pancreas had preserved morphology; however, a poorly defined 20 mm lesion was noted in the pancreatic head.Magnetic resonance cholangiopancreatography (MRCP) revealed concentric wall thickening involving the right and left hepatic ducts and the common bile duct, without significant ductal dilatation. The patient was hospitalized in our Unit in August 2024, and liver biopsy confirmed stage 2 PBC according to the Scheuer classification. Ursodeoxycholic acid (UDCA) 300 mg twice daily was initiated.At follow-up in December 2024, the patient achieved complete biochemical remission, normalizing liver enzymes and cholestasis indices, confirming a diagnosis of UDCA-responsive PBC.

Discussion: Hepatic involvement in sarcoidosis may mimic or overlap with PBC due to cholestatic features and granulomatous inflammation. Such overlap presents a diagnostic challenge requiring a multidisciplinary approach incorporating serology, imaging, and histopathology.

From a pathogenic point of view, the rare coexistence of sarcoidosis and PBC may share overlapping immunopathogenic mechanisms, including:
Cutibacterium acnes
E. coli
Novosphingobium aromaticivorans

Conclusion: Although rare, the coexistence of sarcoidosis and PBC reflects shared immunopathogenic pathways. Clinicians should consider PBC in sarcoidosis patients presenting with cholestatic liver enzyme abnormalities. Comprehensive diagnostic evaluation, including liver biopsy, is essential for accurate diagnosis and appropriate therapeutic management. Early identification of PBC allows the timely initiation of UDCA therapy and may lead to excellent clinical outcomes.

GLOBAL PREVALENCE OF HEREDITARY HEMORRHAGIC TELANGIECTASIA ESTIMATED BY GENETIC ANALYSIS

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Introduction: Hereditary Hemorrhagic Telangiectasia (HHT) is an autosomal dominant disease characterized by recurrent spontaneous epistaxis, visceral arteriovenous malformations (AVMs), and mucocutaneous telangiectases. Up to90% of disease-causal variants are observed in the ENG and ACVRL1genes. HHT is considered a rare disease, with a prevalence of approximately1/5,000. However, HHT is often not detected until it reaches an advanced stage, or the full clinical picture becomes evident, which usually occurs in adulthood. Indeed, it has been reported that usually an average of18years elapses between the first signs of disease and the diagnosis of HHT. In addition, HHT is extremely heterogeneous in terms of clinical presentation, even within members of the same family that carry the same mutations. For this reason, the disease is often underdiagnosed, or diagnosed late. Finally, issues related to reduced access to care and health services might impact prompt identification of patients with HHT in rural and underdeveloped areas. Therefore, it is likely that there is substantial underestimation of the actual prevalence of HHT at the global level. In this study, we analyzed large-scale genomic databases to estimate the global prevalence of HHT.

Methods: We extracted and analyzed genetic data from the following three publicly accessible databases: gnomAD4.1(807,162individuals), All of Us (414,840individuals), and Regeneron Genetics Center - Million Exome (RGC-ME) (821,979individuals). We focused on pathogenic and likely pathogenic variants in the ENG and ACVRL1genes. We collected5,100variants from gnomAD4.1,35,762variants from All of Us, and6,297variants from RGC-ME. To identify pathogenic and likely pathogenic variants linked to HHT, we gathered data from three distinct sources: the electronic repository curated by the ClinGen Hereditary Hemorrhagic Telangiectasia Expert Panel (consulted in February2025), the Human Gene Mutation Database (HGMD), a manually curated collection of published germline mutations (accessed in December2024), and ClinVar, a publicly accessible archive of human variations associated with diseases (accessed in February2025). All the collected variants were aligned with the human genome assembly GRCh38/hg38and were annotated using Ensembl Variant Effect Predictor tool (VEP). Variants were categorized through three distinct strategies with decreasing levels of stringency. This led to the identification of: a)17pathogenic variants according to the ClinGen HHT Panel Experts; b)1,239single nucleotide variants labeled as pathogenic or likely pathogenic according to ClinGen, HGMD and ClinVar; c)1,553variants identified

as potentially pathogenic collected from clinical databases and following the specification of the ACMG/AMP Variant Curation Guidelines for HHT. Prevalence of HHT was estimate using Hardy-Weinberg equilibrium and statistical analyses were performed using a two-sided binomial test.
Results: Considering the 17 variants classified as pathogenic and likely pathogenic by the HHT Curation Panel (the most stringent filter), the observed prevalence of HHT was found to be significantly lower than the known HHT prevalence rate of 1/5,000 cases (0.050/5000 with gnomAD, 0.217/5000 with All of Us and 0.091/5000 with RGC-ME). This means that the filter was too stringent and was not utilized further in the analysis. Considering the 1,239 variants identified in the HGMD and ClinVar databases, we observed a prevalence higher than previously known (from 1.753 to 2.555/5,000). Considering the 1,553 Single Nucleotide Variants and small insertions and deletions collected from clinical databases and following the specification of the ACMG/AMP Variant Curation Guidelines for HHT, the HHT prevalence was significantly higher than previously known (from 2,773 to 5,290 times greater, p-value < 0.05).
Conclusion: Our findings support the hypothesis that the global prevalence of HHT is higher than currently reported. The application of genomic epidemiology might represent a novel way to reassess the burden of HHT and other rare genetic diseases in the general population. These results highlight the importance of updated diagnostic approaches that incorporate molecular data, especially in underrepresented populations, so that affected individuals may benefit from earlier diagnosis and management.

DIAGNOSIS AND MANAGEMENT OF DAPTOMYCIN-INDUCED ACUTE EOSINOPHILIC PNEUMONIA: A CASE REPORT

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Daptomycin is nowadays a first-line therapeutic choice for serious MRSA infections of skin and soft tissue. Daptomycin-induced eosinophilic pneumonia (DIEP) is a rare but potentially fatal adverse reaction of daptomycin therapy. The precise pathophysiology remains partially unknown; however, it is believed that daptomycin, acting as an antigen, irreversibly binds to surfactant in the lungs triggering a TH2 lymphocytes-mediated inflammatory cascade and through the recruitment of eosinophil cells leading to tissue damage. The main treatment of DIEP is prompt discontinuation of drug and, if symptoms are severe, supplemental oxygen and corticosteroid treatment may be needed.
We report the case of a 72-year-old man who was admitted to our department for acute onset of pain and edema in the right limb associated with fever. In his medical history hypertension and Obstructive Sleep Apnoea Syndrome (OSAS) were reported. A venous echocolordoppler of limbs immediately ruled out acute thrombotic events. On clinical suspicion of dermohypodermitis, blood cultures and wound swabs were taken and empirical antibiotic therapy with piperacillin/tazobactam and daptomycin was started. This treatment, confirmed by the isolation on wound swab of Staphylococcus simulans totiS, gradually lead to improvement of the lesion and inflammation indicators and normalization of the thermal curve. Nevertheless, hospitalization was complicated by concomitant worsening of respiratory exchanges requiring high flow oxygen therapy support. An angio-CT ruled out pulmonary embolism and detected bilateral confluent parenchymalconsolidations (upper and lower lobes) mainly located dorsally. Given the fast and significant progression on serial CT scans performed, in absence of microbiologic isolations on blood samples, therapy was further extended with empirical addition of trimethoprim/sulfamethoxazole in order to treat possible infection by opportunistic germ without any clinical improvement. Considering the rapid evolution of the imaging findings and the lack of clinical improvement under such broad-spectrum antibiotic therapy, the patient underwent bronchoscopy with broncho-alveolar lavage (BAL). Microbiological tests of BAL fluid ruled out the main bacterial, fungal and opportunistic germs infections; immunological test revealed WBC 375/microL with 40% of T lymphocytes (mainly CD4) and 48.2% of eosinophilic cells although the absence of peripheral eosinophilia in the leukocyte formula. On suspicion of ANCA associated-vasculitis PET-FDG and autoimmune screening were also taken, all tested negative. DIEP was then suspected and antibiotic treatment was suspended. Given the severity of the case, also high steroidal therapy (1mg/kg/die) was performed. After that, inflammatory indicators decreased and respiratory exchanges rapidly improved allowing progressive decrement of oxygen support. Patient was then discharged. CT scan after one month detected disappearance of parenchymal consolidations.
The diagnosis of DIEP involves a comprehensive assessment of patient's medical history, laboratory tests and imaging findings. In literature DIEP is frequently associated with peripheral eosinophilia which may represent a red flag. However, while peripheral eosinophilia is very common in DIEP, its absence does not exclude the diagnosis highlighting the importance of bronchoalveolar lavage (BAL). Specifically our patient did not exhibit peripheral eosinophilia in leukocyte count, while BAL fluid showed high title of eosinophils (>25%). Other conditions associated to eosinophilia were considered in differential diagnosis. In our case, negativity of microbiological tests on blood and BAL could exclude infections, moreover, lack of history of asthma of sinusitis, in addition to negativity of ANCA antibodies, allowed exclusion of eosinophilic granulomatosis with polyangioitis (EGPA). Radiological findings raised suspicion of cryptogenic organizing pneumonia (COP) andidiopathic pulmonary fibrosis (IPF), but absence of typical patterns, such as the atoll sign or honeycombing, in addition to acute onset of symptoms, made this hypothesis unlikely. Moreover the significant improvement reported after discontinuation of daptomycin therapy left no further doubts. In conclusion, DIEP should be considered in the diagnosis of patients with respiratory failureand bilateral pulmonary opacities who are using or have recently used daptomycin.

DIFFERENT CLINICAL OUTCOMES OF ISCHEMIC STROKE RELATED TO ONSET-TO-GROIN TIME: A REAL-LIFE STUDY

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Background: and aims: International trial results suggest the efficacy of extending the therapeutic window for acute ischaemic stroke (AIS). However, robust data regarding efficacy and safety are still lacking in real-life settings. This study aimed to compare patients who underwent mechanical thrombectomy (MT) with or without intravenous thrombolysis (IT) within 6 hours from the onset of symptoms to those treated at >6 and >12 hours.
Methods: All AIS patients attending the Emergency Department of our hospital who underwent MT were enrolled. Epidemiological, clinical, and radiological variables were collected. We used the National Institutes of Health Stroke Scale (NIHSS) to evaluate our patients and calculated the delta(NIHSS) as the difference between NIHSS at admission and NIHSS at discharge.
Results: delta(NIHSS) was statistically different between patients who underwent MT before or after 6 hours from the onset of symptoms, with a significant improvement in the former group. A significantly better delta(NIHSS) was also observed for patients treated <12 hours compared to those treated >12 hours. The overall prevalence of post-procedural intracranial bleeding was not significantly different between patients with a time-to-groin <=6 hours (32.3%) and those >6 hours (38.2%; p=0.266), nor between patients with a time-to-groin <=12 hours (34.7%) and those >12 hours (37.9%). In-hospital deaths significantly increased for patients treated >6 hours and >12 hours.
Conclusions: Our results confirm favourable outcomes for AIS even when treated several hours after the onset of symptoms. However, better results were achieved when IT and MT were performed early, supporting the "golden hour" concept.

BEYOND THE SKIN: A MULTISYSTEM AUTOIMMUNE MOSAIC OF SWEET'S SYNDROME, UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE, AND PRIMARY BILIARY CHOLANGITIS

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Background: Autoimmune diseases can present with overlapping features, particularly in genetically predisposed individuals.
The coexistence of dermatological, hepatic, and systemic autoimmune manifestations, such as Sweet's syndrome, undifferentiated connective tissue disease (UCTD), and primary biliary cholangitis (PBC), although rare, illustrates the complex interplay between immune-mediated diseases. These overlaps need to be recognised to facilitate accurate diagnosis and individualised treatment.
Sweet's syndrome (SS) is a rare inflammatory disorder characterized by the sudden onset of edematous, erythematous, and painful cutaneous papules, plaques, and nodules, often accompanied by fever and neutrophilia, with a dense infiltration of mature neutrophils, typically localized in the upper dermis. It is commonly associated with inflammatory diseases, pregnancy, or infections (primarily of the upper respiratory tract). Still, it may also be idiopathic, related to hematologic or visceral malignancies, or drug-induced.

Undifferentiated connective tissue diseases (UCTDs) are clinical conditions characterized by signs and symptoms suggestive of an autoimmune connective tissue disorder that, however, do not fulfill the classification criteria for a specific disease such as systemic lupus erythematosus, systemic sclerosis, or Sjögren's syndrome. These conditions may evolve into more defined autoimmune diseases, usually within the first 3 to 5 years after onset, but in most cases, they remain stable as UCTDs.
Primary Biliary Cholangitis (PBC) is a chronic autoimmune cholestatic liver disease with a progressive course that can lead to cirrhosis. Previously known as primary biliary cirrhosis, it is an autoimmune condition, and its diagnosis—after ruling out biliary obstruction—is based on the presence of anti-mitochondrial antibodies (AMAs) or elevated levels of PBC-specific anti-nuclear antibodies (ANAs) in the context of chronic cholestasis, with or without typical bile duct lesions on histology.
Case presentation: We report the case of a 58-year-old female patient with a complex history of autoimmune disorders. Her medical history includes SS diagnosed in 2001, cystic renal dysplasia (medullary sponge kidney), and positive antinuclear antibodies (ANA 1:320).A liver biopsy performed in 2008 had revealed fibrotic and dysmorphic bile ducts consistent with biliary ductal plate malformation and congenital hepatic fibrosis. Subsequent investigations confirmed the presence of antiphospholipid antibodies and lupus anticoagulant (LAC). In 2020, cholangio-MRI findings suggested evolving PBC. In 2023, the patient was diagnosed with UCTD, characterized by positive ANA (1:1280 homogeneous pattern), Anti-ENA, Anti-dsDNA, anti-beta2 glycoprotein lgG, and LAC study, negative associated myositis and myositis-specific antibodies, mild hypocomplementemia, mild thrombocytopenia, mild elevation of muscle enzymes, and previous left coxarthritis. Treatment with Hydroxychloroquine was initiated. In late 2024, she performed a Gastroenterological examination following the onset of diffuse serotonin pruritus, asthenia, and elevated GGT, leading to the initiation of Ursodeoxycholic acid (UDCA). In 2025, she was referred to our Unit. Despite subsequent normalization of GGT, follow-up imaging revealed biliary duct dilation and hepatic fibrosis with signs of portal hypertension. A diagnosis of UDCA-responsive PBC, with underlying congenital hepatic fibrosis and UCTD, was established.
Discussion: This case illustrates the convergence of multiple autoimmune and dysgenetic conditions, underscoring the diagnostic intricacy that ensues when systemic inflammation affects multiple organ systems.
Although primarily dermatologic, SS can serve as an early indicator of systemic immune dysregulation. UCTD and PBC may coexist and contribute to multiorgan involvement through persistent immune activation and autoantibody-mediated injury. The patient's family history (diabetes, lupus, hypothyroidism) supports a genetic predisposition to autoimmunity. The chronicity and overlap of these conditions necessitated coordinated multidisciplinary care and targeted therapeutic strategies.
Conclusion: The co-occurrence of SS, UCTD, and PBC in this patient underscores the need for a comprehensive diagnostic approach in individuals presenting with systemic symptoms and immune seropositivity. Multidisciplinary management is essential in addressing overlapping autoimmune syndromes and preventing organ damage. Recognizing potential associations among rare autoimmune conditions may allow for earlier diagnosis and improved long-term outcomes.

DIAGNOSTIC CHALLENGES IN POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDERS: A CASE OF DIFFUSE LARGE B-CELL LYMPHOMA AFTER SIMULTANEOUS KIDNEY-PANCREAS TRANSPLANTATION

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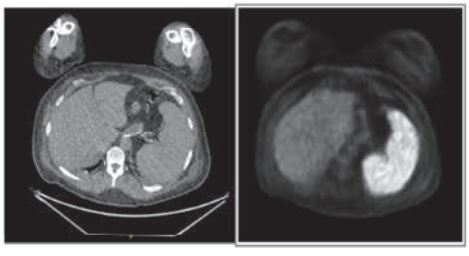
Introduction: Post-transplant lymphoproliferative diseases (PTLD) represent a wide group of lymphoproliferative disorders that develop after solid organ transplantation. PTLD can show clinically in a variety of ways, from accidental asymptomatic signs to a fulminant presentation that includes spontaneous tumor lysis and ultimately organ failure. We report the case of a 62-year-old male who presented with fever of unknown origin, in the absence of specific organ involvement, and was ultimately diagnosed with post-transplant diffuse large B-cell lymphoma.
Case Report: A62-year-old male with a history of renal and pancreatic transplantation presented on January16th to the Department of Transplantation at San Raffaele Hospital with fever, dyspnea and infiltrative lesions of the lower limbs. His past medical history included pluri-complicated type1diabetes for which he underwent combined kidney and pancreas transplantation in2008, arterial hypertension and a past sleeve gastrectomy for severe obesity. Upon admission, laboratory exams evidenced significant thrombocytopenia (27,000/mm^3), schistocytosis (1–2%) and elevated C-reactive protein (CRP) and lactate dehydrogenase levels (LDH) (1111U/L [125-220U/L]). Blood and urine cultures were negative, as well as chest radiography and abdominal ultrasonography. Empiric antibiotic therapy with piperacillin-tazobactam was initiated. For diagnostic completion, a whole-body CT scan was performed revealing splenomegaly without other evident signs of infection. At this stage, thrombocytopenia was initially correlated to an infectious process. Despite initial improvement, after a few days the patient presented again with recurrent fever and hyperemic lower limb lesions. The clinical scenario resembled the one upon admission: laboratory tests demonstrated a decline in platelet count (22,000/mm^3), persistent schistocytosis (2%) and rising levels of CRP and LDH. Another infectious event was considered to be the main thrive of the clinical scenario. A wide infectious screening was perfomed (including hepatitis viruses, Leishmania, Treponema pallidum, varicella-zoster virus, HIV, parvovirus B19, CMV and EBV DNA). All resulted negative. A positron emission tomography (PET) scan was performed which evidenced the presence of marked splenomegaly (Figure1). Despite the atypical PET findings, a lymphoproliferative disease was suspected and a bone marrow biopsy was performed. Histological examination revealed a minimal and occasional presence of medium-to-large B lymphocytes associated with erythro-/hemophagocytosis. Cytofluorimetry did not demonstrate any findings consistent with a lymphoproliferative process. Given the presence of hemophagocytosis at bone marrow biopsy and elevated markers of systemic inflammation at laboratory tests; including triglycerides (496mg/dL [<150mg/dL]), ferritin (1,246ng/mL [30-400ng/mL]), and soluble IL-2receptor (43,673U/mL [1900-13100U/mL]); we suspected a macrophage activation syndrome. High-dose corticosteroid therapy (prednisone1mg/kg) was initiated, resulting in improvement in laboratory parameters: decreased LDH, triglycerides, and ferritin levels and rising platelet count. However, with the initial tapering of the corticosteroid therapy, the whole clinical scenario began to reappear: recurrence of thrombocytopenia, increased inflammatory markers and hyperferritinemia. Given the poor response to corticosteroid therapy, intravenous immunoglobulin therapy (IVIG) was considered. However, right before the beginning of IVIG, the patient developed high fever with blood cultures resulting positive for Klebsiella pneumoniae OXA-48and respiratory swabs being positive for SARS-CoV-2infection. Antimicrobial and antiviral therapies were initiated, and IVIG was temporarily withheld. After resolution of the infectious event, IVIG therapy was resumed (1g/kg/day for5days), with no clinical improvement. Given the poor response to corticosteroid therapy and IGIV therapy and the presence of cytopenias, hyperinflammation and hemophagocytosis, primary hemophagocytic lymphohistiocytosis was suspected. Splenectomy was planned for potentially diagnostic and therapeutic purposes. However, the patient presented hemodynamic instable, with altered consciousness and oliguria. He was transferred to the intensive care unit for close monitoring. On March17th, the patient underwent splenectomy. The postoperative course was complicated by a severe infectious event for which the patient died on the24th of March. Histological examination of the spleen revealed the diagnosis of post-transplant-associated non-germinal center diffuse large B-cell lymphoma associated with hemophagocytosis.
Discussion: This case highlights the significant challenges encountered in diagnosing PTLD. Clinical suspicion may sometimes outweigh the sensitivity of standard laboratory tests and imaging, especially in immunocompromised patients. This case report emphasizes the need of a multidisciplinary approach when dealing with immunocompromised post-transplanted patients, where prompt identification can significantly change the patient's outcome.

Figure 1. The examination was performed using a low-dose PET technique, following intravenous administration of [18F]FDG. The PET scan shows increased tracer uptake at the level of the spleen.



INCIDENCE OF THROMBOEMBOLIC AND BLEEDING EVENTS IN A COHORT OF PATIENTS WITH UNRESECTABLE HCC ON SYSTEMIC THERAPY

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Background: HCC is among the top five leading causes of cancer-related deaths worldwide [1]. Atezolizumab/Bevacizumab is a first-line systemic therapy for HCC [2], but concerns remain regarding bleedings and thrombosis risks, particularly with VEGF inhibitors, such as Bevacizumab [3, 4]. Real-life data on safety of this regimen in patients with advanced liver disease and CSPH are needed.
Aims: To evaluate the incidence of thrombosis and MB in HCC patients undergoing systemic therapy in a real-life setting. The secondary aim was to identify potential risk factors predicting thrombosis and MB in this patient cohort.
Results: 138 patients were included with a median follow up of 15 months.
In the Cox regression analyses, no risk factors for bleeding were identified. BMI and hemoglobin levels emerged as predictive factors in the univariate analysis for thrombotic risk; but were not significant in multivariate analysis.
Conclusion: No significant differences in thrombotic or bleeding risks were observed among systemic therapies for HCC, including Atezolizumab/Bevacizumab. These findings align with prior studies.Despite the modest sample size and the retrospective design, the results suggest that systemic therapies, including VEGF inhibitors, are not predictive of thrombosis or bleeding in real-life settings.
Abbreviations: HCC: Hepatocellular carcinoma, MB: major bleeding, VTE: Venous thromboembolism, VEGF: vascular endothelial growth factor, CSPH: clinically significant portal hypertension; HR: Hazard ratio; CI: confidence interval.
References:
[1] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN stimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
[2] Finn RS, Qin S, Ikeda M, et al. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. N Engl J Med 2020;382:1894-1905.
[3] Ollivier-Hourmand I, Allaire M, Cervoni JP, et al. Management of portal hypertension in patients treated with atezolizumab and bevacizumab for hepatocellular carcinoma. J Hepatol 2022; 77:566-567;
[4] Chen HX, Cleck JN. Adverse effects of anticancer agents that target the VEGF pathway. Nat Rev Clin Oncol 2009;6:465-77;

ACUTE HEPATITIS WITH CHOLESTASIS: CAMPYLOBACTER OUTSIDE THE GUT

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A 48-year-old man presented to the emergency department with abdominal pain associated with nausea, vomiting, jaundice and hyperchromic urine. His past medical history included chronic alcohol abuse (about 1 liter of wine per day), severe alcoholic hepatic steatosis, hypertension andhypercholesterolemia, with a high-fat diet. He was not taking any therapy. He denied any risk factors for viral hepatitis. He also reported that one month before he drunk well water, and shortly after watery diarrhea for about a week which resolved spontaneously. On examination his temperature was 38°C, pulse rate 90/min, and blood pressure 130/85 mmHg. The remainder of the examination was normal; in particular, there were no signs of cardiac failure and no abdominal tenderness or abnormal palpable masses. Initial investigations revealed haemoglobin 12 g/dl, total leucocytes 9,27x10 9 microL and platelets 203 1000/microL. C-reactive protein was 4.90 mg/L (reference range, < 5 mg/L). Clotting tests were within the reference ranges. Creatinine 1.35 mg/dl (r.r, 0.67-1.17) Liver function tests were markedly abnormal: bilirubin was 5.2 mg/dL (r.r. 0.2-1 mg/dL), direct conjugated bilirubin 4.20 mg/dL (r.r. 0-0.20mg/dL), alanine transaminase (ALT) 537 U/L (r.r, 16-63 U/L), aspartate transaminase (AST) 1026 U/L (r.r, 15-37 U/L), gamma-glutamyl transpeptidase ('γ-GT) 2018 U/L (r.r 15-85 U/L), and alkaline phosphatase (ALP) 974 U/L (r.r. 0-220 U/L), LDH 532 U/L (r.r. 85-227 U/L), serum albumin 2.3 g/dL (r.r. 3.4-5 g/dL). Abdominal ultrasound and computed tomography scans demonstrated severe hepatic steatosis, with no focal lesions and mild dilatation of intra and extra-hepatic bile ducts associated with moderate pericholecystic fluid. Doppler ultrasound showed normal flow in the hepatic and portal venous system and in the inferior vena cava and in the the abdominal aorta. Serological tests for viral
hepatitis A, B, C, and Toxoplasma were all negative. Cytomegalovirus immunoglobulin G (IgG) and Epstein-Barr virus viral capsid antigen IgG were consistent with past infection. No rheumatoid or antinuclear factors or antimitochondrial, antismooth muscle, or antineutrophil cytoplasmic antibodies were detected. Treatment was started empirically for gram-negative sepsis with Piperacillin Tazobactam 4,5 g i. v three times a day., and the patient improved rapidly, becoming afebrile within hours; later IV Ciprofloxacin was added. No blood cultures resulted positive. The magnetic resonance cholangiograhy which demonstrates mild signs of hepatic steatosis, distended gallbladder with dysmorphic morphology due to the presence of an area of narrowing of the lumen in the body, thickening of the fundus walls with post-contrast enhancement as in cholecystitis.
Campylobacter jejuni was isolated from culture of feces. Seven days after presentation, the liver function values had improved: bilirubin was 0.5 mg/dL, conjugated bilirubin 0.30 mg/dL, ALT 17 U/L, AST 14U/L, y-GT 56 U/L, and ALP 76 U/L. Due to the improvement in liver function abnormalities, a liver biopsy was not performed.

Discussion: This case demonstrates that acute hepatitis can be associated with human Campylobacter jejuni infection. The patient presented with symptoms of cholestatic hepatitis and transaminase levels were increased over 30-fold. Campylobacter jejuni was isolated from fecal culture. Most known infective and noninfective etiologies of acute hepatitis were excluded, although a liver biopsy was not performed. Alcohol-related hepatitis was considered; however the patient reported that he had not consumed alcohol for more than a month. Cholangitis wa s also considered; however, imaging studies including magnetic resonance cholangiography did not reveal biliary gallstones. In this patient, whose history included hypertension and hypercholesterolemia, ischemia was another possible cause of hepatitis. However, there was no identified cause for an acute fall in cardiac output (apart from possible volume depletion due to diarrhoea), no documented hypotension or evidence of cardiac failure, and lactate dehydrogenase was normal. The most common clinical manifestation of Campylobacter jejuni infection is diarrhoea, which may be bloody, accompanied by fever. Most complications of Campylobacter jejuni infection (e. g., gastrointestinal haemorrhage, proctitis) result from local invasion. Blaser et al. demonstrated that Campylobacterjejuni can multiply and survive for long periods in bile, and there are a few reports of cholecystitis and pancreatitis associated with Campylobacter jejuni infections. Campylobacter jejuni bacteremia appears to be uncommon; however, blood cultures are obtained infrequently in patients with enteritis, and Campylobacter jejuni was difficult to isolate prior to the introduction of
modern blood culture systems. Other systemic manifestations reported include meningitis and purulent arthritis. In addition, postinfectious complications such as reactive arthritis, Guillain-Barrè syndrome, and acute motor axonal neuropathy are being increasingly recognized. Acute hepatitis should be included in the expanding spectrum of extraintestinal manifestations of Campylobacter jejuni infections.

BONE FRAGILITY AND FRACTURE RISK ASSESSMENT IN METABOLIC DISFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

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Background: and Aims: Metabolic dysfunction-associated steatotic liver disease (MASLD) and type 2 diabetes mellitus (T2D) share several risk factors for bone fragility. However, the mechanisms underlying fracture development in these patients remain poorly defined. This study aims to assess fracture risk in individuals with MASLD and T2D using the trabecular bone score (TBS) as a marker of bone quality.
Patients and methods: All patients with MASLD, who consecutively attended the Medicine and Hepatology Unit of the University Hospital of Messina from

February 1st to October 31st 2024, were considered potentially eligible for this cross-sectional study. Inclusion criteria were: diagnosis of MASLD according to the update criteria, with at least T2D as the required cardiometabolic criterion; post-menopausal status for women; age >50 years for men. Exclusion criteria included the presence of decompensated cirrhosis, indirect signs of portal hypertension, chronic viral hepatitis or human immunodeficiency virus infection, other causes of liver disease, excessive alcohol consumption, thyroid or parathyroid disorders, chronic kidney disease, heart failure, active malignancy, or previous treatments affecting bone metabolism lasting more than three months. All patients underwent liver stiffness measurements (LSM) and controlled attenuation parameter (CAP) evaluation using Fibroscan, as well as Dual-Energy X-Ray Absorptiometry (DXA) with TBS and vertebral fracture assessment (VFA). Statistical analyses were performed using R software.
Results: One-hundred and five patients [median age 62 years (range 57 - 69), 53.3% male, 21% cirrhotic] were enrolled and included in the final analysis. Obesity (BMI ≥ 30 kg/m2) was observed in 50 patients (48.5%), and 29 individuals (27.9%) had glycaemic impairment at the time of the enrolment. The study population showed median LSM and CAP values of 7.6 kPa (5.8 – 13.9) and 299 dB/m (262 – 325), respectively. Based on the T-scores at the lumbar spine and femur, 52 patients (49.5%) had normal bone density, 43 (41%) had osteopenia, and 10 (9.5%) had osteoporosis. The median TBS was 1.326 (1.218 – 1.396), with 60 patients (57.1%) classified as having a pathological TBS (cut-off < 1.350). Morphometric vertebral fragility fractures (Vfx), assessed by vertebral fracture assessment (VFA), were present in 54 patients (51.4%). Compared to those without fractures, patients with VFx had significantly higher BMI ($p = 0.001$), LSM ($p = 0.015$), CAP values ($p = 0.005$), and waist circumference (WC) ($p = 0.004$). TBS values were significantly lower in patients with Vfx than those without (1.227 vs. 1.382, $p < 0.001$). Among patients with Vfx, 45 out of 54 (83.3%) had TBS < 1.350, compared to 15 out of 51 (29.4%) in the non-Vfx group ($p < 0.001$). The risk of Vfx was significantly higher in patients with TBS < 1.350 (38.9% vs. 3.9%, $p < 0.001$). Patients with pathological TBS (< 1.350) were more frequently female ($p = 0.003$) and had significantly higher BMI ($p < 0.001$), WC ($p = 0.002$), visceral adiposity index (VAI) ($p = 0.014$), CAP values ($p = 0.008$), and LDL-c levels ($p = 0.025$) compared to those with normal TBS (≥ 1.350). Vfx were significantly more common in patients with pathological TBS (75% vs. 20%, $p < 0.001$). TBS showed a significant inverse correlation with BMI ($r = -0.436$, $p < 0.0001$), LSM ($r = -0.191$, $p = 0.05$), CAP ($r = -0.311$, $p = 0.001$), total cholesterol ($r = -0.242$, $p = 0.013$), LDL-c ($r = -0.247$, $p = 0.012$), WC ($r = -0.376$, $p < 0.0001$), and VAI ($r = -0.291$, $p = 0.003$). Conversely, TBS positively correlated with serum albumin ($r = 0.216$, $p = 0.031$), creatinine ($r = 0.227$, $p = 0.02$), lumbar spine T-score ($r = 0.201$, $p = 0.04$) and BMD ($r = 0.341$, $p < 0.0001$), femur T-score ($r = 0.201$, $p = 0.04$) and BMD ($r = 0.296$, $p = 0.002$). In univariate analysis, BMI ≥ 30 kg/m2 ($p = 0.005$), CAP ≥ 248 dB/m ($p = 0.043$), and TBS < 1.350 ($p < 0.001$) were significantly associated with increased Vfx risk. In multivariate analysis, only TBS <1.350 remained an independent and strong predictor of Vfx (OR: 9.276, 95% CI: 3.439–27.584, $p < 0.001$). Regarding factors associated with pathological TBS, univariate analysis identified male sex ($p = 0.002$), BMI ≥ 30 Kg/m2 ($p < 0.001$), and CAP ≥ 248 dB/m ($p = 0.009$) as significant. These associations remained statistically significant in multivariate analysis: male sex (OR: 0.202, 95% CI: 0.070–0.531, $p = 0.002$), BMI ≥ 30 kg/m² (OR: 8.614, 95% CI: 3.285–25.246, $p < 0.001$), and CAP ≥ 248 dB/m (OR: 3.725, 95% CI: 1.144–13.432, $p = 0.034$). When CAP was evaluated by discrete categories, higher grades of steatosis (CAP ≥ 280 dB/m, S3) were significantly associated with pathological TBS.
Conclusions: Patients with MASLD and T2D are at increased risk of Vfx, even with normal BMD. TBS emerged as a strong and independent predictor of bone fragility, closely associated with obesity, VAI, liver steatosis severity, and elevated LDL-c levels. Evaluation of TBS in MASLD and T2D patients could be useful for assessing bone fragility and prevent fractures onset.

WHO COMES FIRST: GRAFT-VERSUS-HOST DISEASE OR MACROPHAGE ACTIVATION SYNDROME?

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Graft-versus-Host Disease (GVHD) is the immune reaction exerted by the transplanted cells from the donor against the tissues of the recipient. It is a complication more commonly associated with allogeneic stem cell transplants, with only a few cases described following solid organ transplants.Macrophage activation syndrome (MAS) is a rare immune system disorder, caused by the uncontrolled proliferation of activated lymphocytes and macrophages that secrete high amounts of inflammatory cytokines.Primary MAS is caused by genetic mutations that alter the immunoregulatory capabilities of CD8+ lymphocytes and NK cells. The secondary form is caused by malignant diseases, generally hematological ones, by autoimmune disorders or infections but also by iatrogenic causes such as bone marrow transplantation or solid transplants, chemo or immunosuppressive therapy.
A 61-year-old woman was admitted to our Internal Medicine ward on August 27 2024, for urosepsis sustained by Klebsiella Pneumoniae and a diffuse punctate skin rash.The patient had been discharged a few days earlier from the Transplant Surgery department after a liver transplant in July 2024 for alcohol-related decompensated cirrhosis and for which she was on immunosuppressive therapy with Tacrolimus . Upon admission antibiotic therapy with piperacillin-tazobactam was started, with initial clinical and laboratory improvement. However, a couple of days after admission, the patient developed pharyngodynia with palpable submandibular lymphadenopathy, diarrhea and abdominal pain. Thus, the following investigations were performed: ORL evaluation, rectal and nasal swabs for MDR pathogens, nasal swabs for respiratory virus including SARS-Cov2, determination of CMV DNA and EBV DNA, beta-D-glucan and serial blood and stool cultures, all of which turned out negative. A contrast-enhance abdominal CT showed no hepatosplenomegaly nor lymphadenopathy. In addition, due to the persistence of the skin rash, a punch biopsy was performed on August 29.During hospitalization, the patient further developed progressive anemia and thrombocytopenia, accompanied by spontaneous gingival bleeding, for which platelet pool and concentrated red blood cell transfusions were administered, with modest clinical answer. A parvovirus DNA test was requested and turned out negative.A diagnosis of thrombotic thrombocytopenic purpura was excluded due to normal ADAMST13 values. In the next days a severe worsening of the pancytopenia was observed (WBC 200/mmc, PLT 10,000/mmc, Hb 7g/dL), poorly responsive to transfusion support and leukocytes growth factor, leading to the suspension of the immunosuppressive therapy.The patient also developed hyperpyrexia (40°C) associated with hyperferritinemia (15,000 µg/L), hypertriglyceridemia (505 mg/dL), increased D-dimer (12,000 µg/L) and fibrinogen (587 mg/dL). In the suspicion of MAS, a hematologic evaluation was requested and concluded for a multifactorial bone marrow hypofunction possibly linked to the infectious process so that a bone marrow biopsy was declined. The antibiotic therapy was then intensified with IV administration of amikacin.In the following days, the clinical conditions of the patient deteriorated, with the development of respiratory failure, attributed to small circle congestion, and acute kidney injury, for which albumin and furosemide were administered. Meanwhile, the gastrointestinal symptoms (diarrhea, vomiting and abdominal pain) worsened and a new abdominal CT scan revealed thickening of the duodenal and jejunal walls due to widespread severe inflammation. On September 3 HHV6 DNA testing turned out positive and therapy with Ganciclovir iv was started. Therefore, given the clear evidence of multi-organ failure (MOF) (bone marrow, respiratory and kidney failure), the patient was transferred to the Intensive Care Unit (ICU), with the diagnosis of suspected MAS activated by HHV6 versus GVHD after the recent liver transplant.Once in the ICU molecular chimerism testing, diagnostic for GVHD, turned out positive for circulating donor-derived cells but not reliable due to the very severe leukopenia (WBC 4/µL). The very same day the previously performed skin punch biopsy turned out suggestive of MAS, and a bone marrow biopsy (BOM) was performed, suggesting total marrow aplasia with occasional hemophagocytes and lymphocytes. Dexamethasone therapy was started at 10 mg IV, then switched to methylprednisolone 1 g/day and IV immunoglobulins but it was too late: the patient passed away after 4 days in ICU.
This clinical case seems to suggest a rare case of GVHD post-liver transplant, associated with MAS, in a septic patient. It is difficult to determine the primary cause: whether an infectious state (HHV6 reactivation) activated the donor liver tissue, which then triggered a MAS-like syndrome, or if GVHD itself caused MOF, complicated by MAS. Treatment in these cases is not standardized and may involve either intensifying immunosuppressive therapy to limit donor activation or reducing it to allow the recipient's immune system to take control. However, despite the therapy, mortality is extremely high.

DEVELOPMENT OF NEW CRITERIA FOR EARLY RESPONSE TO TERLIPRESSIN AND ALBUMIN IN PATIENT WITH HEPATORENAL SYNDROME - ACUTE KIDNEY INJURY

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Background: Hepatorenal syndrome (HRS-AKI) is a life-threatening type of Acute Kidney Injury that occurs in patients with advanced cirrhosis and

ascites. The use of terlipressin and albumin represents the first line pharmacological treatment of HRS-AKI. The response to terlipressin is traditionally evaluated after 48 hours and the dose is escalated in patients in whom serum creatinine (SCr) has not decreased by 25% from baseline. In 2024, the Acute Disease Quality Initiative/International Club of Ascites (ADQI/ICA) consensus, recommended to anticipate the assessment of response to terlipressin at 24 hours and to increase the dose in case SCr has not decreased by 25% from baseline. However, no study explored the use of this timeframe.
Aim: The aim of the study was to evaluate the applicability of the ADQI/ICA recommendations on early response to terlipressin for HRS-AKI and to develop new criteria for response to HRS-AKI at 24 hours.
Methods: We conducted a retrospective study in patients with cirrhosis and HRS-AKI treated with terlipressin and albumin. Clinical and biochemical data were collected at baseline (when terlipressin/albumin was started), and after 24 hours, 48 hours and at the end of treatment. We followed patients until death, LT or the end of follow-up (90 days). The primary endpoint was the response at 48 hours (defined as a reduction of SCr > 25% vs baseline). The secondary endpoints were the resolution of HRS-AKI, (defined as SCr < 133 umol/l at the end of treatment) and survival at 90 days. Death and LT were considered competing events for the resolution of HRS-AKI.
Results: We enrolled 108 patients (mean age=59 ± 9 years; male=70%; MELD=29 ±7). The most prevalent cirrhosis etiology was alcohol (58%). The median creatinine at the start of treatment was 242 µmol/L (IQR 203.5 – 306.8 µmol/L). Overall, 16 patients had a reduction of SCr >25% at 24 hours (14.8%) and 40 patients had a reduction of SCR >25% at 48 hours (37%). Among the patients who achieved an early response 94% had confirmed response at 48 hours. However, 25 out of 40 responders at 48 hours, were erroneously classified as non-responders at 24-hours (62.5%). Therefore, we analyzed the discrimination ability for early response at 48 hours of the delta creatinine (ΔSCr) at 24 hours to identify a new threshold for non-response at 24 hours. The area under the ROC was 0.87 (0.80 - 0.94) and the best threshold for non-response was a ΔSCr >0% (i.e. an increase in SCr vs baseline). Among patients with a ΔSCr >0% (n=36; 33%), only 2 (5%) had a response at 48 hours. Reversal of HRS-AKI was found in 56 patients (52%). Early non-responders (patient who had an increase of SCr levels at 24 hours and a reduction <25% at 48 hours) were less likely to achieve a resolution of HRS-AKI (24 hourd: 25% vs 65%, p<0.001; 48 hours: 40% vs 73%, p<0.001). Early non-responders had a significantly lower probability of 90-day survival than those without (24 hours: 20% vs 52%; p<0.001; 48 hours: 34% vs 54%; p=0.044).
Discussion: and conclusion: The current recommendation of ADQI/ICA misclassified 62% of responders at 48 hours as non-responder, with the risk of unnecessary escalation of treatment with terlipressin. We developed a new definition of non-response at 24 hours that can reduce the misclassification and allow early escalation of therapy in about one third of patients with HRS-AKI. The new definition of non-response is associated with a lack of HRS-AKI resolution and lower probability of survival.

SERUM BONE PROTEIN MODIFICATIONS IN UNTREATED AND TREATED COELIAC DISEASE PATIENTS: TOWARD NON-INVASIVE BIOMARKERS PREDICTING GLUTEN-FREE DIET-INDUCED BONE MASS GAIN

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Background: Alterations in bone mass and mineral metabolism are common in coeliac disease (CD) patients and tend to be more severe in patients with overt malabsorption compared to those with subclinical presentations. Elevated levels of the propeptide of type I procollagen, a marker of bone formation, predicts bone mass gain after two years on a gluten-free diet (GFD). Conversely, low levels of osteoprotegerin, a decoy receptor that inhibits osteoclast activation via RANKL signalling, predict persistently low bone mass in long-term GFD patients. This study aimed to evaluate serum bone proteins involved in different phases of bone metabolism in CD patients, with the goal of improving the management of bone-related complications in this population.
Methods: Sixty-seven CD patients were consecutively enrolled at our tertiary referral centre. Twenty newly diagnosed untreated patients (UCD; median age 42 yrs, IQR 27-56), and 47 treated patients (TCD; median age 45 yrs, IQR 29-54; median GFD duration 7 years, IQR 3-12) were enrolled. Canonical serum markers measured included 25-hydrixyvitaminD, 1,25-dihydrixyvitaminD, collagen I telopeptide, parathyroid hormone, and osteoprotegerin. In addition, serum levels of novel bone proteins, i.e. irisin, osteocalcin, bone sialoprotein, and osteonectin, were evaluated. At the time of serum collection, all patients underwent dual-energy X-ray absorptiometry (DEXA) to assess bone mineral density (BMD) at the lumbar spine and femur, recording T-scores and Z-scores – expressed as SD- and BMD in g/cm2. We compared serum markers values between UCD and TCD groups and analysed correlations among the biomarkers and between biomarkers and GFD or DEXA measurements.
Results: As expected, lumbar spine T-scores were significantly higher in TCD (-0.4 SD, range -1.8-0.8) compared to UCD (-1.4 SD, range -2.4- 0.3). Bone sialoprotein levels were higher in TCD (median 525 pg/ml, IQR 418-622) versus UCD (median 357 pg/ml, IQR 189-563), suggesting the GFD-induced improvement of bone remodelling. Conversely, osteocalcin was higher in UCD (median 9.7 ng/ml, IQR 3.9-12.7) than TCD (median 6.1 ng/ml, IQR 3.3-11.5), reflecting the increased but ineffective bone turnover. Serum osteocalcin positively correlated with collagen I telopeptide (r=0.45, p<0.01), and negatively with lumbar spine T-scores (r=-0.25, p<0.03). Bone sialoprotein and irisin positively correlated with GFD duration and femoral DEXA parameters, suggesting an effective role in the prediction of bone mass improvement after GFD.
Conclusions: The non invasive identification of patients showing BMD improvement after the beginning of GFD is an important clinical issue, as DEXA low short-term sensitivity and the use of X-ray limit a frequent re-evaluation of patients. Our results support further studies on GFD-induced bone protein modifications as the availability of predictive markers of GFD-induced bone mass and mineral metabolism modification might be enriched through the use of bone sialoprotein and irisin.

PROGNOSTIC ROLE OF FOUR CLINICAL AND RADIOLOGICAL SCORES IN ACUTE PANCREATITIS: A MULTICENTER RETROSPECTIVE STUDY IN THE EMERGENCY DEPARTMENT

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Introduction: Acute pancreatitis (AP) is a disease with a significant clinical and prognostic impact. The clinical presentation is extremely variable, ranging from mild-moderate inflammation without local or systemic involvement to life-threatening multiorgan involvement. Early identification and management of conditions requiring intensive treatment are essential to improve prognosis. The aim of this study is to compare and evaluate the prognostic accuracy of clinical and radiological scores such as Balthazar, BISAP, HAPS and SOFA in predicting in-hospital mortality (IHM) in patients with first diagnosis of acute pancreatitis presenting to the Emergency Department.
Methods: This is a retrospective, multicenter cohort study conducted in the Emergency Departments of three hospitals in Emilia Romagna (Ferrara, Ravenna and Faenza). The patients included in the study were adults (> 18 years) and with a first episode of acute pancreatitis. Vital parameters, laboratory and instrumental tests were recorded and comorbidities were assessed by calculating the Charlson Comorbidity Index (CCI).
Results: A total of 1306 patients were admitted to the Emergency Department (ED) during the study period. A total of 979 patients were selected (median age 70 years and in-hospital mortality 2.6%). The total results of the analyzed scores were higher in patients experiencing IHM, with a median Balthazar score of 4.0 (IQR 3.0-6.0) vs. 0 (IQR 0.0-2.0), p<0.001, BISAP of 3 (IQR 2.0-3.0) vs. 1.0 (IQR 1.0-2.0), p<0.001, and a median SOFA score of 3.0 (IQR 1.8-5.2) vs. 1.0 (IQR 1.0-2.0), p<0.001. Sixty-eight percent of patients who underwent IHM showed a HAPS > 0 (p = 0.012) while 8% showed a HAPS = 0. In multivariate analysis, independent predictors of IHM in the individual scores were the percentage of pancreatic necrosis 0-30% in the Balthazar score OR 6.31 [95% CI 2.07-19.38] (p = 0.001) and the presence of acute abdomen in the HAPS score OR 7.04 [95% CI 2.18-22.79] (p = 0.001). BISAP and SOFA score each showed three independent predictors of IHM: elevation of blood urea nitrogen OR 3.38 [95% CI 1.43-8.04] (p=0.006), altered mental status OR 12.32 [95% CI 4.05-37.46] (p<0.001) and presence of pleural effusion OR 5.43 [95% CI 2.24-13.15] (p<0.001) for BISAP, altered P/F OR 3.02 [95% CI 1.24-7.39] (p=0.015, MAP < 70 mmHg OR 8.81 [95% CI 1.19-65.20] (p=0.033) and elevated creatinine OR 1.64 [95% CI 1.03-2.62] (p=0.035) for the SOFA score. Balthazar and BISAP score showed good accuracy in the AUROC curve analysis equal to AUROC 0.806, (95% CI 0.777-0.832), 0.863 (95% CI 0.838-0.886), respectively, with no significant differences between the two scores.
Conclusions: Acute pancreatitis (AP) is a potentially serious disease with high clinical variability. Although heterogeneous, clinical risk scores evaluate different clinical aspects of AP: the Balthazar score requires an abdominal CT with intravenous contrast medium, however confirms its high sensitivity for the identification of IHM; the SOFA score evaluates the degree of multiorgan failure with high specificity in identifying patients at higher risk of IHM and the

BISAP score, specifically designed to measure the clinical severity of AP and predict IHM, showed good diagnostic accuracy without significant differences compared to the Balthazar. The HAPS score, although designed to perform a safe rule out of the patient not candidate for intensification, in our population, its negativity, did not show a negative predictive value of 100%, losing its prognostic efficacy.

TERAPIA DELLO SCOMPENSO ALLA DIMISSIONE (TESCODI): HOW FAR ARE WE STILL FROM THE OPTIMUM IN TREATING HEART FAILURE?

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HEALTHCARE-ASSOCIATED INFECTIONS AFTER SOLID ORGAN TRANSPLANTATION: SINGLE-CENTRE EXPERIENCE

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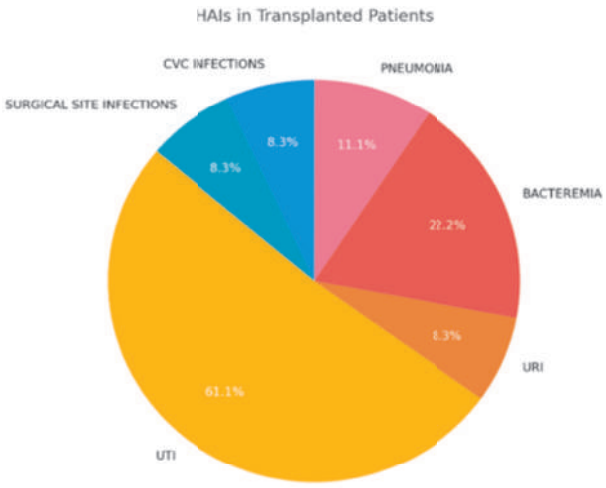
Introduction: Health care-associated infections (HAI) are a global health concern leading to increased hospital admissions, mortality and healthcare costs. One group at risk are patients who underwent solid organ transplantation. Immunosuppressive therapy, which is necessary to prevent organ rejection, greatly increases vulnerability to opportunistic infections. Postoperative infections are further exacerbated by prolonged hospital stays and frequent use of post-operative devices and exposure to multidrug-resistant organisms. Furthermore, infections in transplanted patients may impair graft function, further complicating post-operative recovery. It is therefore essential to identify high-risk patients and implement tailored infection protocols to maintain an adequate graft function and reduce hospital stay.
Aim of the study: To describe the occurrence of HAIs after single, dual kidney transplantation and simultaneous kidney-pancreas transplantation and to compare patients with HAIs and patients without HAIs in order to compare selected clinical parameters in both study populations.
Methods: Data from 99 patients who underwent single kidney, dual kidney or simultaneous kidney-pancreas transplantation were collected at the Regenerative Medicine and Transplantation Unit at San Raffaele Hospital (Milan), from January to December 2024. For each individual the following variables were analysed: baseline characteristics, hospital-acquired infections, post-operative management of medical devices and serum creatinine levels on postoperative day 5 and day 10.
Results: 99 patients were included with a mean age of 54.9 years (±12.7) and a predominant male distribution (68.7%). 74 patients underwent single kidney transplantation (75.5%), 14 underwent dual kidney transplantation (14.3%) and 10 underwent simultaneous kidney-pancreas transplantation (10.2%). Regarding donor classification, 74 patients (75.5%) received grafts from donation after brain death (DBD), 18 (18.4%) from donation after circulatory death (DCD), and 6 (6.1%) from DBD with extracorporeal membrane oxygenation support. The baseline patient characteristics are shown in Table 1.
36 out of 99 (36.3%) patients developed HAIs. Urinary tract infection (UTI) was the most common infection (61%), followed by bacteremia, defined as positive blood cultures, (22%), pneumonia (11%), upper respiratory tract infections (URI) (8.3%), central venous catheter (CVC)-related infections (8.3%), and surgical site related-infections (8.3%). The median length of hospital stay for HAI patients was 20 days (IQR 14.50-33.75) compared to days 11 (IQR 9-15) in patients without HAIs. The ureteral DJ stent was maintained for a median duration of 20.50 days (IQR 15.25-30) in HAI patients, compared to 26 days (IQR 21-32) in non-HAI patients. HAI patients presented a significantly longer length of hospital stay with respect to non-HAI patients (p-value=0.000). Moreover, HAI patients presented a lower duration of the maintenance of ureteral DJ stent with respect to non-HAI patients (p-value=0.034). Regarding the subpopulation with UTI, the median length of hospital stay was 20 days (IQR 14-33) compared to 12 days (IQR 9-19.50) in patients without UTI. Ureteral DJ stent removal was maintained for a median length of 19 days (IQR 15.2-28.5) in patients without UTI compared to 25.50 (IQR 20.25-32) in patients without UTI. Patients with UTI presented a significantly longer length of hospital stay with respect to non-UTI patients (p-value=0.001). No significance was observed with regards to the maintenance of the ureteral DJ stent (p-value=0.072). Patients with UTI had a median serum creatinine level of 3.79 mg/dL (IQR 2.52-5.73) on postoperative day 5 and 2.41 mg/dL (IQR 1.44-3.33) on day 10, compared to 1.86 mg/dL (IQR 1.335-4.9156) and 1.61 mg/dL (IQR 1.19-3.045), respectively, in patients without UTI. Patients with UTI presented a significant higher median creatinine level on postoperative day 5 with respect to patients without UTI (p-value=0.019). No significance was observed regarding creatinine level on postoperative day 10 (p-value=0.092).
Conclusions: Our single centre retrospective study compares two different populations who underwent solid organ transplantation, especially taking into consideration patients who developed UTI. Hospital stays for patients with HAIs were noticeably longer, which may indicate a higher burden of postoperative complications and the need for prolonged medical care. Interestingly, ureteral DJ stent maintenance was shorter in the HAI group, which may reflect early removal due to ongoing infections. The subgroup analysis of patients with UTI revealed higher serum creatinine levels on postoperative day 5, suggesting an early negative impact on graft function due to an ongoing infection. These results demonstrate how infections, particularly UTIs, affect transplant patients' clinical outcomes and prolong hospital stays. Overall, our findings highlight the importance of strict infection monitoring in order to lower hospital stays, maintain an adequate graft function and a post-transplant recovery.

Variable	Value(n)
Number of patients	99
Male sex distribution	68 (68.7%)
Mean age (±SD)	54.9(±12.7)
BMI Group	
Underweight (< 18.5)	1(1.1%)
Normal (18.5-24.9)	56(56.6%)
Overweight (25-29.9)	33(33.3%)
Obese I (30-34.4)	9(9.1%)
CKD Type	
Glomerulonephritis	6(6.1%)
Nephroangiosclrosis	14(14.1%)
ADPKD	24(24.2%)
DM Nephropathy	20(20.2%)
Focal segmental glomerulosclerosis	8(8.1%)
Obstructive Nephropathy	5(5.1%)
IgA Nephropathy	8(8.1%)
Alport Syndrome	3(3.1%)
LES Nephropathy	3(3.1%)
Others	8(8.1%)
Comorbidities	
Diabetes Mellitus	27(27.3%)
Coronaropathy	9(9.1%)
Hypertension	81(81.8%)
Dialysis	83(83.8%)
Diuresis (mL)	
0	28(28.3%)
<999	19(19.2%)
1000-1999	40(40.9%)
2000>	12(12.1%)

Table 1: Baseline patient characteristics



WHEN CROHN'S DISEASE HIDES BEYOND THE INTESTINE

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A 69-year-old man was admitted to the Internal Medicine department with various symptoms such as anorexia, significant weight loss, and severe hypoalbuminemia, along with a clinical history of prolonged diarrhea and recurrent H. pylori-associated gastropathy. At the physical examination, the patient presented with cachexia and generalized anasarca, previously unsuccessfully treated at home with intravenous albumin. Laboratory tests showed a leukocyte differential inversion, with normal absolute neutrophil and lymphocyte counts. Inflammatory markers and tumor markers relevant to the clinical context were within normal ranges, as was an extensive infectious disease work-up on various biological samples. Endoscopic investigations, including EGD and colonoscopy, were non-diagnostic for neoplastic or inflammatory bowel diseases. Due to the persistence of the clinical condition, further imaging was performed. A total-body CT revealed multiple subcapsular hepatic cystic lesions, with the largest one further characterized by hepatospecific MRI and PET-CT, showing a hypodense lesion in liver segment VI (26x21 mm, SUV max 7), likely representing an abscess. An entero-MRI also showed a nonspecific pattern of diffuse enteritis/colitis. A CEUS-guided liver biopsy of the lesion revealed chronic inflammatory infiltration with mixed lymphoplasmacytic cells (CD20+, CD3+, MUM1+), fibrosis, dysmorphic bile ducts, and focal regenerative atypia, suggestive of an hepatic involvement in a systemic inflammatory disease. Due to PET-CT uptake (SUV max 6) in the mesenteric jejunal loops in the left lower quadrant, video capsule endoscopy was performed and showed diffuse inflammatory changes in the jejunum and distal ileum, raising suspicion for Crohn's disease or lymphoma. Final confirmation came from enteroscopy, which revealed chronic enteritis with foveolar metaplasia and low-grade glandular dysplasia. This exam was decisive in diagnosing late-onset Crohn's disease with predominant jejunal involvement, associated with an aseptic hepatic abscess as a systemic manifestation.
Crohn's disease (CD) is a chronic inflammatory bowel disease that may present with extraintestinal manifestations, either as the initial presentation or following gastrointestinal symptoms. Aseptic hepatic abscess is a rare and poorly described systemic presentation. As such, differential diagnosis with infectious or neoplastic lesions can delay early recognition. This clinical case describes a late-onset Crohn's disease diagnosis with atypical hepatic involvement in an elderly patient. The presence of a hepatic abscess in a patient with no prior diagnosis of CD, combined with nonspecific symptoms and negative inflammatory markers, complicated the diagnostic process. The patient's cachectic and edematous state, recurrent severe hypoalbuminemia, and biopsy-proven H. pylori-associated chronic gastritis created further diagnostic confusion. Celiac disease was also excluded as a potential cause of protein-losing enteropathy and persistent hypoalbuminemia. Crohn's disease can present at an advanced age and with uncommon extraintestinal manifestations such as an aseptic hepatic abscess, even in the absence of typical gastrointestinal symptoms. Therefore, a nonspecific clinical picture involving weight loss, persistent hypoalbuminemia, and unexplained hepatic lesions should raise suspicion for CD, even in elderly patients, to facilitate early diagnosis.

MICHELANGELO: MANAGEMENT OF SPLANCHNIC AND OTHER UNUSUAL SITE VEIN THROMBOSIS WITH DIRECT ORAL ANTICOAGULANTS: A TRIAL EVALUATING EFFICACY AND SAFETY OF APIXABAN PRELIMINARY FINDING

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Venous thrombosis at unusual sites (VTUS) accounts for approximately 10% of all venous thromboembolic events and is defined as thrombosis occurring in venous territories outside of the deep or superficial veins of the lower extremities and the pulmonary vasculature. These atypical thrombotic events include cerebral venous sinus thrombosis (CVST), upper extremity deep vein thrombosis (UEDVT), renal vein thrombosis (RVT), ovarian vein thrombosis (OVT), and splanchnic vein thrombosis (SVT). SVT encompasses thromboses within the splanchnic venous system, which drains blood from the digestive tract. This category includes portal vein thrombosis (PVT), mesenteric vein thrombosis (MVT), splenic vein thrombosis, and Budd-Chiari syndrome (BCS)—a rare condition involving hepatic venous outflow obstruction. PVT is the most common SVT and has a prevalence of approximately 1% in the general population but increases significantly among patients with cirrhosis, reaching up to 40% in advanced disease. The pathophysiology in cirrhotic patients involves both reduced portal flow and a hypercoagulable state due to altered synthesis of coagulation and anticoagulation proteins such as protein C, protein S, and von Willebrand factor.
SVTs can present acutely or chronically and exhibit nonspecific clinical features. Compared to conventional VTE, patients with SVT exhibit a significantly higher early and late mortality, with 30-day mortality rates around 20.6% and 2-year mortality approaching 10.3%. The cornerstone of treatment for VTUS, particularly SVT, traditionally consists of low molecular weight heparin (LMWH) or unfractionated heparin (UFH), followed by oral anticoagulation with vitamin K antagonists (VKAs). The general treatment strategy involves an initial phase with parenteral anticoagulation, transitioning to VKAs once a therapeutic INR (2.0–3.0) is achieved. These recommendations align with current guidelines, such as those issued by the European Association for the Study of the Liver (EASL) in 2022.
While there is robust randomized controlled trial (RCT) data guiding the treatment of CVST and to a lesser extent OVT and RVT, no RCTs are currently available for most other forms of VTUS, especially SVT. The paucity of high-level evidence, compounded by the rarity and heterogeneity of these thrombotic conditions, results in varying levels of recommendation and guideline consensus. Moreover, real-world patients frequently present with complexities not fully addressed by existing studies or guidelines, necessitating an individualized approach that carefully weighs the risks and benefits of anticoagulation. Diagnostic challenges and the clinical heterogeneity of SVT further complicate standardized treatment algorithms.
Direct oral anticoagulants (DOACs) have transformed the management of common site VTE. However, their use in atypical thromboses such as SVT remains off-label and is supported mainly by observational studies. Nonetheless, emerging data suggest promising efficacy and safety profiles. For instance, a 2022 prospective study by Ageno et al. showed that rivaroxaban resulted in complete vessel recanalization in 47% of patients with non-cirrhotic SVT. Furthermore, these outcomes were not significantly different from those seen with LMWH, suggesting that DOACs may provide a viable alternative, especially for patients in whom parenteral therapy is impractical.
Building on the MICHELANGELO framework for unusual-site venous thrombosis, we conducted a pilot cohort to inform the definitive sample-size calculation. The primary objective is to demonstrate the superiority of direct oral anticoagulants (DOACs) over low-molecular-weight heparin (LMWH) for radiological resolution of venous thrombosis at unusual sites (VTUS), analysed with a one-sided Fisher exact test at $\alpha = 0.05$. From January to April 2025, 18 cirrhotic patients with splanchnic vein thrombosis (SVT) were enrolled (DOAC n = 9, LMWH n = 9). As of this writing, three-month follow-up imaging is available for 5 and 7 patients, respectively. Among DOAC recipients, 1 achieved complete recanalisation, 3 partial recanalisation, and 1 showed no response, yielding an overall 80% response rate. Among LMWH recipients, none achieved complete recanalisation, 1 achieved partial recanalisation, and 6 showed no response, for an overall 14.3% response rate. The absolute difference is 65.7 % (risk ratio 5.6); the one-sided Fisher test gives $p = 0.045$. No major or clinically relevant non-major bleeding has occurred in either group. Assuming the definitive trial attains at least half this effect, a clinically important 35 % absolute difference can be detected with 80 % power using 25 patients per arm.

These interim data support feasibility and justify continuation to the full MICHELANGELO cohort.
Interpretation the interim results show a pronounced early efficacy signal without safety concerns. Completion of enrolment and longer follow-up will determine whether apixaban can be adopted as first-line therapy for VTUS. Until such data become available, therapeutic decisions should be individualized, considering patient comorbidities, bleeding risk, and logistical factors.

LOOKING BEYOND THE OBVIOUS: INVESTIGATING LAMBL'S EXCRESCENCES IN CRYPTOGENIC STROKE.

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Ischemic stroke remains a frequent and disabling event, with well-established etiologies including cardioembolism, atherothrombosis and small vessel disease. However, in 20-30% of cases, the underlying cause remains undetermined even after comprehensive evaluation, resulting in the diagnosis of cryptogenic stroke.
In these instances, rare conditions such as Lambl's excrescences (LE) should be considered, particularly when conventional diagnostic approaches fail to identify a definitive cause.
We present the case of an 87-year-old man admitted to our Internal Medicine Ward with sudden-onset left hemiparesis. His medical history included heart failure with preserved ejection fraction, arterial hypertension, type 2 diabetes, COPD, and benign prostatic hyperplasia. He was independent in daily activities and chronically treated with ramipril, furosemide, potassium canrenoate, dapagliflozin, metformin, atorvastatin, and dutasteride.
On presentation, the patient was apyretic with stable vital signs. Neurological exam confirmed a left-sided motor deficit. Routine blood tests were unremarkable. ECG showed sinus rhythm at 80 bpm; continuous ECG monitoring and 24-hour Holter ECG excluded paroxysmal atrial fibrillation or other arrhythmias. Initial and subsequent cranial CT scans were negative for acute ischemia or hemorrhage. A carotid Doppler ultrasound revealed mild bilateral carotid stenosis (30%), without hemodynamic significance.
Transthoracic echocardiography (TTE) showed no intracardiac thrombi or valvular vegetations, but identified subtle filiform, hypermobile structures on the aortic valve. This prompted further investigation with a transesophageal echocardiogram (TEE), which confirmed the presence of thin, elongated strands arising from valve closure lines – the so-called Lambl's excrescens (figure 1). Given the exclusion of all more common causes of stroke, this finding was considered the most likely source of embolism.
Meanwhile, the neurological deficit improved spontaneously, and no additional emboli were detected in the chest or abdominal organs.The patient was discharged in stable condition and referred for outpatient follow-up.
LE are filiform, avascular endocardial projections, thought to originate from wear and tear along valve closure lines. They are histologically benign structures, typically asymptomatic and found incidentally. However, in rare cases, they have been associated with arterial embolism, including stroke [1,2]. Because they are often missed on standard transthoracic imaging, TEE becomes essential, particularly when routine work-up yields no clear etiology.
In this case, LE as cause of the minor stroke were considered a diagnosis of exclusion, only after extensive investigations ruled out more common causes of embolic stroke.
The literature lacks definitive guidelines for management. In our case, given the absence of prior events and the patient's bleeding risk profile, single antiplatelet therapy with aspirin was initiated [3]. Oral anticoagulation or surgical intervention may be considered in recurrent cases, though evidence on outcomes remains limited [4].
This case highlights the importance of considering LE in the differential diagnosis of cryptogenic stroke, especially when routine work-up yields no clear cause. While TTE is often inconclusive, TEE can reveal valvular microstructures otherwise undetected. Given the lack of consensus on management, clinical decisions should be individualized, balancing embolic and hemorrhagic risk. As Internists, our role remains crucial in navigating complex diagnostic pathways and identifying overlooked causes of common presentations.
References:
1. Freedberg RS et al. Lambl's excrescences: echocardiographic observations and clinical implications. Am Heart J. 1995;130(2):367–70.
2. Roldan CA, et al. Cardiac sources of embolism: diagnosis and management. Am J Med Sci. 2013;346(6):493–8.
3. Elgendy AY, et al. Lambl's excrescences and ischemic stroke: case report and review of literature. Cardiol Res. 2016;7(5):174–176.
4. Chiari E, et al. Stroke caused by Lambl's excrescences: treatment dilemma. Eur J Neurol. 2012;19(8):e84–e85.

Figure 1

ANEMIA AND INFECTIONS: A CASE OF PURE RED CELL APLASIA CAUSED BY PARVOVIRUS B19

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Anemia is a problem that we internists face every day. In the diagnostic process we decide to undertake, it is necessary to consider, as a differential diagnosis, "Pure red cell aplasia" (PRCA), a rare cause of acquired anemia.
"Pure red cell aplasia" (PRCA) is a syndrome defined by normochromic normocytic anemia with severe reticulocytopenia and marked reduction or absence of erythroid precursors in the bone marrow (1). It can be congenital (Diamond-Blackfan anemia, frequently associated with morphological and physical abnormalities and resulting from mutations in genes encoding various ribosomal proteins) (2); acquired primary (represented by an autoimmune disorder, often mediated by autoantibodies, that disrupt erythroid differentiation) (3); acquired secondary, associated with autoimmune disorders such as systemic lupus erythematosus, lymphoproliferative disorders such as chronic lymphocytic leukemia or large granular lymphocytic leukemia, solid tumors (particularly thymoma), drugs or toxic agents, and finally, infections - particularly Parvovirus B19 in immunocompromised subjects (4).
Parvovirus B19 (or Erythrovirus B19), responsible for Erythema infectiosum (fifth disease) in children, is completely asymptomatic in the vast majority of cases in adults. However, it can cause the aplastic crises observed in patients with chronic hemolytic disorders such as sickle cell anemia; a chronic form of PRCA in immunocompromised patients, or an acute self-limiting form of PRCA. (7)
The virus infects erythroid progenitor cells in the bone marrow, initially interacting with globosides (P antigen; individuals whose erythroid precursors do not exhibit this antigen are resistant to infection) (5). It then reaches the nucleus and replicates, causing apoptosis of the infected cells. The distinctive signs of Parvovirus B19-induced PRCA are the decrease or absence of reticulocytes and erythroid hypoplasia on osteomedullary biopsy (BOM) (6).
We report the clinical case of a 46-year-old female patient with systemic lupus erythematosus (SLE), treated with hydroxychloroquine and sulfasalazine, and chronic macrocytic anemia, who presented to the emergency room of our hospital for a syncopal episode, high fever, asthenia, arthralgia, and a skin rash on her arms, legs, torso, and cheeks. Drug switching with steroids for SLE was performed - for the possible iatrogenic cause of anemia, especially from sulfasalazine - and after performing first-level tests, it was necessary to perform a BOM which showed: "Hypoplasia of erythro- and megakaryopoiesis. CD34+ blasts <5%. Numerous interstitial histiocytes without erythrophagocytic activity were recognizable." The real-time PCR test for the detection and quantification of Parvovirus B19 DNA was positive. After an initial phase where blood transfusions were used for support, the patient entered a phase of remission with progressive improvement in hemoglobin values and reticulocyte count. Steroid tapering was then started. As it was an acute transient form, it was not

necessary to use Immunoglobulins. (7)

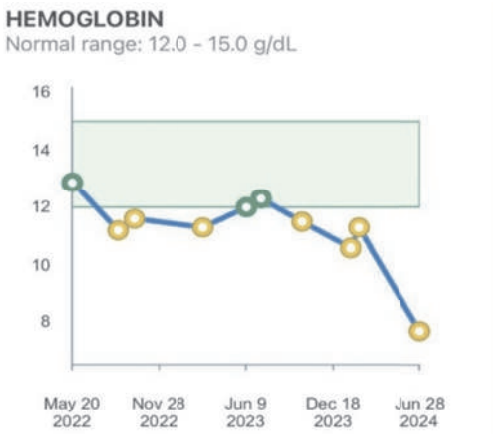

Figure1. The graph represents the variation in the patient's hemoglobin v alues over time

We wish to present this clinical case because the management of anemic patients is of particular importance for the internist and because we believe that in patients with isolated anemia associated with marked reticulocytopenia, PRCA should be suspected.
The evaluation of acquired PRCA should focus on identifying patients with myelodysplastic syndrome presenting with erythroid hypoplasia or patients with PRCA associated with drugs, thymoma, or lymphoproliferative disorders, for whom specific syndrome management is necessary. For other patients with acquired PRCA, the treatment of choice is immunosuppression. (8) While for acute non-transient/chronic forms or in severely immunocompromised patients, it is important to promptly initiate immunoglobulin therapy at a dosage of 2 g/kg, usually divided over 5 days for each therapeutic cycle (400 mg/kg/day). (7) A recent literature review demonstrated remission of Parvovirus B19-induced PRCA after a first therapeutic cycle in 93% of patients treated with intravenous immunoglobulins. (9)

FROM PERIPHERAL NEUROPATHY TO MULTIORGAN DYSFUNCTION: ACUTE HEPATIC PORPHYRIA IN A INTERNAL MEDICINE SETTING

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Introduction: Acute hepatic porphyrias are rare metabolic disorders of heme biosynthesis that present with acute or subacute systemic manifestations. Their clinical presentation may mimic neurological, gastrointestinal, or psychiatric conditions, making diagnosis particularly challenging. We report the case of a man with severe motor and visceral polyneuropathy, whose diagnostic workup included the hypothesis of hepatic porphyria.
Case presentation: Mr. R.A.A., 66 years old, was admitted to the Internal Medicine department after a prolonged clinical course that began in November 2024 in the Emergency Department for recurrent vomiting and progressive lower limb weakness. His symptoms included worsening motor deficits, hypoesthesia, and visceral dysfunction, in the absence of central neurological signs. He was admitted to the Neurology Unit. A lumbar puncture was performed to exclude paraneoplastic, auto-inflammatory and infectious conditions. An EMG was performed, which revealed a severe axonal sensorimotor polyneuropathy, with absent deep tendon reflexes, profound hypoesthesia, and marked weakness in the lower limbs.
Spinal and brain MRI ruled out compressive or central inflammatory processes. The patient did not respond to plasma exchange or IVIG therapy but showed partial improvement with thiamine supplementation. During hospitalization, he developed dysphagia, fecal-smelling vomiting, diarrhea, and respiratory desaturation, leading to a diagnosis of aspiration pneumonia and bilateral subsegmental pulmonary embolism. Blood cultures grew S. epidermidis, and urine cultures revealed P. aeruginosa, leading to removal of the central venous catheter and urinary catheter. The clinical condition evolved into sepsis.
Gastrointestinal investigations showed dolichocolon with fecal stasis, saccular dilatation of the celiac trunk with thrombotic apposition on the left gastric artery, and upper endoscopy revealed a prepyloric ulcer and esophageal mass with intense FDG uptake on PET-CT, suggestive of malignancy. Paraneoplastic syndrome was suspected but not confirmed.
Muscle MRI showed signs of myositis with early fatty degeneration of pelvic and leg muscles. Muscle lysis markers (e.g., myoglobin 139 ng/mL) were mildly elevated. A muscle biopsy was planned for further evaluation.
Given the subacute onset, prolonged vomiting, severe motor neuropathy, hyponatremia, and visceral dysfunction, acute hepatic porphyria was suspected. The first urinary porphyrin analysis showed elevated total porphyrins with predominant coproporphyrin (86% of total). Therapy with 20% glucose solution and hemin was initiated.
The respiratory status improved with targeted antibiotics, bronchodilators, and corticosteroids. The patient continued daily physical and speech therapy, nutritional support via parenteral and oral feeding.
Conclusions: Acute hepatic porphyria presents a significant diagnostic challenge for internal medicine physicians, particularly when overlapping with other complex medical conditions. In this case, the combination of severe motor neuropathy, recurrent gastrointestinal symptoms, hyponatremia, and visceral dysfunction necessitated a broad differential diagnosis.
This case highlights the importance, in Internal Medicine, of maintaining a high index of suspicion for acute porphyrias in patients with progressive polyneuropathy, unexplained gastrointestinal symptoms, and electrolyte disturbances. Early recognition may be hindered by symptom fragmentation and the low prevalence of the disease, but it is essential for initiating specific therapy and preventing irreversible neurological damage. Multidisciplinary collaboration is crucial in managing such clinically complex and high-risk scenarios.

A MONOCENTRIC STUDY ON INFLIXIMAB DISCONTINUATION IN SEVERE MULTISISTEMIC SARCOIDOSIS: OUR EXPERIENCE IN TREVISO

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Background: Infliximab (IFX) is a chimeric monoclonal antibody that binds and neutralizes circulating tumor necrosis factor-alpha, a key inflammatory cytokine in the formation of granulomas in sarcoidosis. Many studies demonstrated its efficacy and safety for systemic and severe refractory sarcoidosis, usually as third line therapy (1). Nevertheless, in 21% of cases IFX may be suspended due to severe infectious complications, loss of efficacy (2) or the production of neutralising IFX- autoantibodies (AA) (3). For the latter, the use of a combination treatment with an immunomodulator to prevent the IFX-AA formation is suggested by many authors. In a single-centre cohort we aimed at analysing the clinical characteristics of patients affected by multisystemic sarcoidosis treated with IFX and the reasons of its discontinuation.
Methods: We retrospectively enrolled all patients with multisystemic sarcoidosis treated with IFX at our Institution from November 2017 to May 2025. We analysed the organ involvement using the WASOG criteria (4), the delay in IFX initiation from sarcoidosis' diagnosis, IFX treatment duration as well as the causes for its interruption. Mean and standard deviation (SD) and median and IQR were calculated for quantitative variables.
Results: In our cohort, 47 out of 450 patients (10.4%) were treated with IFX. All patients were treated with IFX 5 mg/kg during the induction phase at 0, 2, 4 weeks, followed by a maintenance phase with 5 mg/kg every 8 weeks and always associated with a disease modifying anti-rheumatic drug (DMARD), mainly methotrexate. The mean age was 54 years (± 10.5). The organ involvement showed the following distribution: 85% intra- and extra-thoracic lymph nodes, 70% lung, 60% central and peripheral nervous system, 32% skin, 26% heart, 15% kidney, 11% spleen, 11% bones, 11% eyes, 6% liver. The mean interval from the diagnosis to IFX administration was 62.6 (±58,5) months for the whole cohort. 19 out of 47 (40%) stopped IFX; in these, time to IFX administration was 52.6 months (±50.2) and treatment was suspended after a median time of 20.8 months (IQR:8). 4 out of 19 (21.1%) were able to successfully discontinue IFX after achieving a median of 50.5 (IQR:46.4) months of disease remission. None of these patients showed relapse after the suspension among a mean period of 52.4 (IQR: 46.4) months. On the other hand, in 15 out of 19 (78.9%) the suspension was determined by different reasons: 3/19 (15.8%) for severe infections (one died for Nocardial brain abscess and one for COVID pneumonia), 4/19 (21.1%) for the production of IFX-AA, two for hypersensitivity reactions (skin rash and arthralgia), 1/19 (5.3%) for ineffectiveness, three for development of neoplasms (namely lung cancer, melanoma and hepatic lymphoma), one died for a myocardial infarction, one patients refused to continue the IFX treatment. 3 of 4 patients who developed IFX-AA had autonomously interrupted the IFX-associated DMARD, experiencing disease progression. Antibodies were developed in a median of 11.6 months (IQR: 12.6). In the whole cohort of patients that have IFX suspension, 9 patients (47.3%) needed a subsequent drug to control sarcoidosis following IFX interruption, and those drugs were: in 2 cases glucocorticoids, in 2 cases adalimumab and in 2 cases mycophenolate mofetil, while tofacitinib,

tocilizumab and methotrexate were used in 1 case respectively. Patients that have IFX dismission were treated also with Methotrexate with a median of 0,17 mg/Kg (IQR: 0,05), azatioprine with a median of 1,31 mg/Kg (IQR: 0,55) and micophenolate Mofetil with a median of 12,50 mg/Kg (IQR: 5,55).
Conclusion: Infliximab is an effective drug for multisystem sarcoidosis, although a risk of infections and immunogenicity have to be evaluated. Our results showed remission without relapses in all patients who suspended IFX therapy following a prolonged disease control. Our observations also suggest a careful monitoring of infections risk before IFX initiation and to constantly verify the adherence to the concomitant immunomodulating treatment, especially in the first years of administration.
Key word: Sarcoidosis, Infliximab, Anti-TNF-Alpha, Infection, anti-IFX antibodies.

POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER FOLLOWING SOLID ORGAN TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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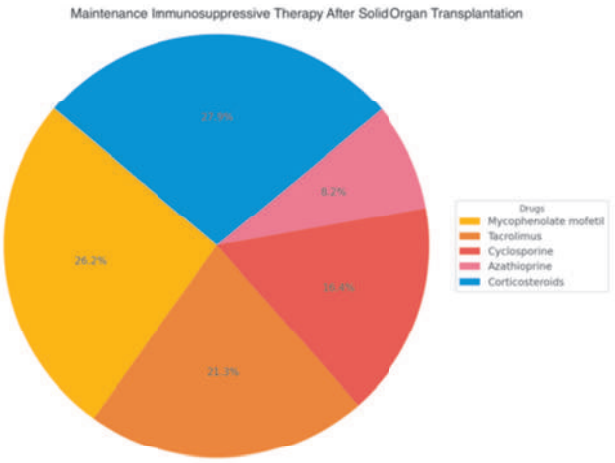
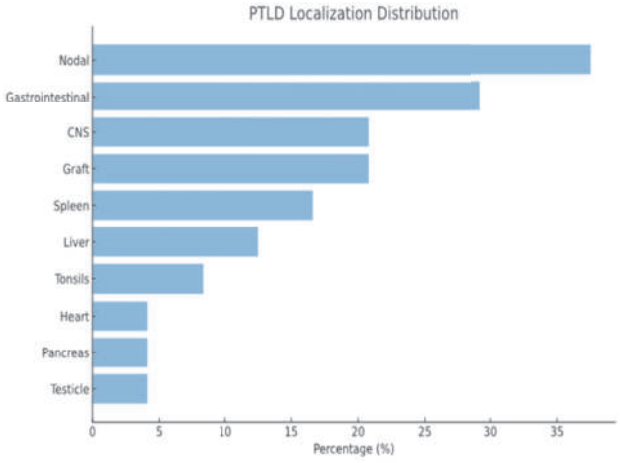
Introduction: Post-transplant lymphoproliferative disorder (PTLD) includes a heterogenous group of lymphoid malignant neoplasms that develop after solid organ or hematopoietic stem cell transplantation. The main risk factors for PTLD development include a diminished T-cell immune surveillance due to immunosuppressive therapy and, most notably, primary Epstein–Barr virus (EBV) infection. It has been shown that PTLD is associated with reduced patient and graft survival, with five-year post-diagnosis survival rates ranging between 37% and 65%. Therapeutic strategies for PTLD focus mainly on a reduction of immunosuppression therapy and the additional use of different regimens of chemotherapy depending on disease subtype and progression.
Aim of the study: To describe the baseline characteristics of patients with a confirmed diagnosis of PTLD who underwent solid organ transplantation and to evaluate potential correlations between selected clinical parameters and overall survival rate.
Methods: Data from 24 patients diagnosed with PLTD who underwent single kidney, dual kidney or simultaneous kidney-pancreas transplantation were collected at the Regenerative Medicine and Transplantation Unit at San Raffaele Hospital (Milan), from January 1986 to May 2025. For each individual the following variables were analysed: baseline patient characteristics, time to diagnosis of PTLD, histopathological diagnosis of PTLD, type of immunosuppressive therapy, PTLD treatment and mortality rate.
Results: 24 patients were included in the study, with a mean age of 40.5 years (±13.1) at the time of their first transplant; 12 (50%) were female. At baseline, 17 patients (70.8%) had diabetes mellitus, 16 (66.7%) were on dialysis, and 1 patient (4.2%) had a prior history of Kaposi sarcoma. The median time from diabetes diagnosis to transplantation was 28 years, while the median duration of dialysis prior to transplant was 3 years. Most patients (n=16; 66.7%) underwent simultaneous kidney-pancreas transplantation, 6 (25%) received a single kidney transplant, and 2 (8.3%) received a double kidney transplant. Seven patients (29.2%) underwent a second transplant—six of them received a second kidney transplant, and one received a second simultaneous kidney-pancreas transplant. The most common indication for transplantation was diabetic nephropathy (70.8%), followed by isolated cases of IgA nephropathy, renal vein thrombosis, vesicoureteral reflux, and ADPKD (each 4.1%). The cause of kidney disease was unknown in two patients (8.3%). Maintenance immunosuppressive therapy after solid organ transplantation included mycophenolate mofetil (66.7%), tacrolimus (54.2%), cyclosporine (41.7%), azathioprine (20.8%), and corticosteroids (70.8%). PTLD was diagnosed after a median of 3301 days (IQR 59–10,227) from transplant with mean age of 50.6 years (±11.7). The median ECOG performance status at diagnosis was 1 (IQR 0–2). PTLD localization was most frequently nodal (37.5%), followed by gastrointestinal (29.2%), central nervous system (20.8%), graft involvement (20.8%), spleen (16.6%), liver (12.5%), tonsils (8.3%), and isolated cases involving the heart, pancreas, and testicle (each 4.1%). Histologically, diffuse large B-cell lymphoma (DLBCL) was the predominant subtype (79.2%), followed by Burkitt lymphoma (12.5%) and Hodgkin lymphoma (8.3%). EBV positivity in tumor tissue was found in 66.6% of cases and CD20 was expressed in 66.7%. The median lactate dehydrogenase (LDH) level was 212 U/L (IQR 154–17,000), and the median International Prognostic Index (IPI) score was 1 (IQR 0–3). Half of the patients (50%) received chemotherapy after PTLD diagnosis. Immunosuppressive therapy was suspended in 19 patients (79.2%). Of these, 14 (58.3%) switched to a new immunosuppressive regimen: 6 patients (42.8%) to everolimus plus corticosteroids, 5 (35.7%) to sirolimus plus corticosteroids and 3 (21.4%) to corticosteroids alone. Graft rejection occurred in 6 patients (25%), and PTLD relapse was observed in one case (4.2%). The overall mortality rate was 50%, with a mean age at death of 54.6 years (±18.4). Among these, 4 deaths (44.4%) were attributed to PTLD progression. No significant correlation was found between mortality and EBV status, PTLD localization or type of immunosuppressive therapy. However, suspension of immunosuppressive therapy showed a nearly significant association with improved survival (p = 0.090).
Conclusions: Although the sample size in our study is small, the findings highlight the importance of early recognition and timely intervention. A relevant finding in our study population was the potential benefit of reducing immunosuppressive therapy, which was associated with a nearly significant improvement in patient survival. Immunosuppressive therapy remains a double-edged sword: while necessary to prevent graft rejection, it also predisposes patients to an increased risk of developing lymphoproliferative disorders. Therefore, optimizing immunosuppressive therapy and considering targeted therapeutic approaches are essential in improving long-term outcomes in PTLD patients.





FROM DRUG ABUSE TO ACUTE DECOMPENSATION: MULTIDISCIPLINARY MANAGEMENT OF SEVERE AORTIC REGURGITATION IN A HYPERTENSIVE PATIENT

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Introduction: Acute valvular insufficiencies are rare but potentially fatal events.

Their presentation can be insidious in patients with chronic hypertension, especially when associated with a history of drug abuse. This case illustrates how an unrecognized condition can rapidly progress into acute decompensated heart failure, requiring urgent multidisciplinary management.
Clinical Case: A 48-year-old man with a history of poorly controlled longstanding hypertension and past heroin abuse presented to the Emergency Department with oppressive, non-radiating retrosternal chest pain lasting approximately three days, associated with dyspnea - initially on moderate exertion, then at rest - associated with orthopnea and paroxysmal nocturnal dyspnea. On admission, he had (TC 38.5°C), he was markedly dyspnoic at rest, agitated, pale, and diaphoretic. He required an orthopnoic position and
showed clear use of accessory respiratory muscles. Vital signs showed a blood pressure of 155/75 mmHg, heart rate of 120 bpm, and SpO_2 of 80% on room air; oxygen therapy was initiated with a simple face mask at 4L/min, which improved SpO_2 to 90-91%. Cardiac auscultation revealed rhythmic, tachycardic, and muffled heart sounds with a 3/6 diastolic murmur at the aortic focus radiating along the right sternal border. An Austin Flint murmur was also present. . Pulmonary examination detected bilateral mid-to-basal crackles and diffuse wheezing, consistent with acute pulmonary edema and cardiac asthma. Signs of systemic congestion were also present, including jugular venous distention and bilateral pitting edema of the lower limbs. The overall clinical picture was suggestive of severe acute heart failure requiring immediate diagnostic evaluation and hemodynamic stabilization.
Diagnostic Workup: On admission, the ECG showed sinus tachycardia (HR 120 bpm), signs of left ventricular hypertrophy, and repolarization abnormalities indicative of strain. Chest X-ray confirmed heart failure with marked bilateral pulmonary vascular congestion, central alveolar infiltrates in a "bat wing" distribution, and cardiomegaly (cardiothoracic ratio >0.5).
Laboratory tests showed an extremely elevated NT-proBNP (20,000 pg/mL), indicating advanced acute decompensation. Troponin was negative, ruling out ongoing myocardial injury. Blood cultures (two sets) were negative. An urgent echocardiogram revealed: a normal-sized left ventricle (LVEDD 52 mm), concentric hypertrophy (IVS 13 mm, PW 12 mm), hyperkinetic function with EF 70%, no segmental wall motion abnormalities; a dilated
left atrium (42 ml/m²); a right ventricle at the upper limit of normal size (RVEDD 41 mm) with mildly reduced systolic function (TAPSE 16 mm); a normal right atrium. Mildly dilated aortic root (38 mm) with a normal ascending aorta. The aortic valve was tricuspid with severe regurgitation type Id from El Khoury classification, with vena contracta 7 mm, jet width/LVOT 67%, PHT 187 ms, EROA 0.35 cm², and RVol 68 mL/beat; moderate tricuspid regurgitation; estimated PAPs 50 mmHg; dilated IVC with <50% collapsible. Intensive medical treatment was immediately started with a 40 mg bolus of IV furosemide followed by continuous infusion (250 mg/24h), and ventilatory support with CPAP. Empiric antibiotic therapy with IV ceftriaxone and vancomycin was initiated due to suspected infective endocarditis. The patient was first transferred to the ICU and then referred to a
second-level Emergency Center for urgent cardiac surgery evaluation. Surgical assessment indicated the need for urgent aortic valve replacement, preceded by coronary angiography and aortic CT.
Discussion and Conclusions: Aortic regurgitation (AR) is a defect of the aortic valve that prevents proper closure, causing blood to flow back from the aorta into the left ventricle during diastole. It can be acute (a hemodynamic emergency) or chronic. Common causes include infective endocarditis, aortic dissection, degenerative diseases (e.g., senile calcification), aortic root dilation (e.g., Marfan syndrome, aneurysm), rheumatic disease (less common today), chronic hypertension (valve degeneration), and connective tissue diseases (e.g., SLE, RA, ankylosing spondylitis). Our case is illustrative of acute AR likely secondary to infective endocarditis. In acute AR, the left ventricle cannot adapt quickly, leading to a sudden increase in LV diastolic pressure, which is transmitted to the left atrium, pulmonary veins, and capillaries, resulting first in interstitial and then alveolar edema and cardiogenic shock. Despite negative blood cultures, the history of heroin use, fever peaking at 38°C, rapid hemodynamic deterioration, and echocardiographic evidence of severe AR due to valvular leaflet perforation strongly support a diagnosis of infective endocarditis-related AR. Although tricuspid involvement is more common among IV drug users, cases of aortic valve involvement are well described and associated with worse outcomes. Early recognition and integrated management are crucial to prevent fatal outcomes. Prompt multidisciplinary evaluation is essential for determining optimal surgical timing.

EXTRACARDIAC MANIFESTATIONS IN A LARGE FAMILY WITH FABRY DISEASE DUE TO N215S VARIANT

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Background: La malattia di Fabry è una malattia genetica ereditaria X-linked causata da varianti patogenetiche del gene GLA. È caratterizzata da un difetto dell'attività dell'enzima lisosomiale alfa galattosidasi A, che determina l'accumulo in diverse cellule dell'organismo di glicosfingolipidi, in particolare di globotriaosilceramide (Gb3) e di globotriaosilsfingosina (lisoGb3). L'accumulo di questi metaboliti è responsabile delle manifestazioni cliniche della malattia, che possono coinvolgere cuore, reni, sistema nervoso e altri organi. Sono tipicamente descritti due fenotipi clinici della malattia, la forma classica e la forma a esordio tardivo, quest'ultima comunemente considerata come attenuata. I pazienti di sesso maschile presentano solitamente manifestazioni più severe e precoci di malattia, mentre nelle pazienti di sesso femminile si riconosce un'ampia eterogeneità delle manifestazioni cliniche, da forme asintomatiche a forme altrettanto severe quanto quelle del sesso maschile. Sono state identificate oltre mille varianti del gene GLA. È documentata in letteratura una relazione, seppur non lineare, tra la percentuale dell'attività enzimatica residua dell'enzima alfa galattosidasi A e le manifestazioni cliniche della malattia. La variante N215S (p.Asn215Ser) è la più comune variante patogenetica dei paesi occidentali associata a forme di malattia a esordio tardivo ed è stata descritta finora in letteratura come tipicamente associata a manifestazioni cardiache della malattia di Fabry.
Pazienti e metodi: In questo lavoro analizziamo le manifestazioni cliniche di una grande famiglia portatrice della variante N215S. L'albero genealogico è composto da 4 generazioni, in cui sono stati identificati 13 portatori della variante N215S, di cui 5 di sesso maschile (età media 24 anni, range 9-64 anni) e 8 di sesso femminile (età media 42,1 anni, range 19-82 anni). In 4 dei 5 soggetti di sesso maschile sono state rilevate manifestazioni cliniche della malattia, in particolare diarrea e dolore addominale (3/4 pazienti), iposudorazione e xerosi cutanea (2/4 pazienti), alterazione della funzionalità renale con proteinuria (2/4 pazienti) ed insufficienza renale cronica (1/4 pazienti). Sono state inoltre riscontrate alterazioni del T1 mapping alla cardio-RMN e parestesie a livello delle estremità degli arti superiori (1/4 pazienti). L'età media di esordio dei sintomi nei pazienti di sesso maschile è stata 27 anni, età minima 9 anni. In 3 degli 8 soggetti di sesso femminile sono state rilevate manifestazioni cliniche della malattia, in particolare dolore addominale e alterazioni dell'alvo (2/3 pazienti), alterazioni della sudorazione (2/3 pazienti), parestesie a livello delle estremità degli arti (2/3 pazienti), secchezza oculare (1/3 pazienti) e alterazioni del T1 mapping alla cardio-RMN (1/3 pazienti). L'età media di esordio dei sintomi nelle pazienti di sesso femminile è stata 53 anni. In tutti i pazienti sintomatici è stata avviata terapia specifica.
Discussione: Negli ultimi anni si è assistito a un significativo aumento della diagnosi di malattia di Fabry, legato soprattutto ad un sempre maggiore utilizzo dello screening genetico nei pazienti ad alto rischio. Nella grande famiglia oggetto dello studio 13 pazienti presentavano la mutazione N215S del gene GLA, associata in letteratura a forme a esordio tardivo, e in particolare a coinvolgimento cardiaco. Dei 13 pazienti presi in esame in questo lavoro, solo in 2 di essi sono stati segnalati segni di cardiopatia alla RMN cardiaca, mentre sono state più frequentemente riscontrate manifestazioni extracardiache della malattia, in particolare sintomi gastrointestinali (dolore addominale e alterazioni dell'alvo), alterazione della sudorazione, parestesie e riduzione della funzione renale con proteinuria. Mentre nei soggetti di sesso femminile presi in esame l'esordio dei sintomi è stato tardivo (età media di esordio 53 anni), nei soggetti di sesso maschile le prime manifestazioni della malattia sono state riscontrate precocemente, in un caso già a partire dall'infanzia.
Conclusioni: Abbiamo descritto una grande famiglia portatrice della variante N215S del gene GLA, evidenziando quanto possano essere numerose e polimorfe le manifestazioni extracardiache della malattia associata a questa mutazione. Ai fini di un'adeguata gestione di questi pazienti, risulta pertanto indispensabile un inquadramento globale e un approccio multidisciplinare per l'identificazione anche delle diverse possibili complicanze extracardiache della malattia. E' interessante notare inoltre che, nonostante questa variante sia associata in letteratura a forme di malattia ad esordio tardivo, nei pazienti presi in esame in questo lavoro si siano riscontrate anche forme ad esordio precoce, soprattutto nel sesso maschile. È pertanto opportuno un attento monitoraggio di tutte le complicanze d'organo, già a partire dal momento dalla diagnosi.

THE EMERGING ROLE OF LEFT ATRIAL STRAIN IN CARDIOVASCULAR RISK STRATIFICATION FOR MULTIPLE MYELOMA PATIENTS UNDERGOING CARFILZOMIB THERAPY

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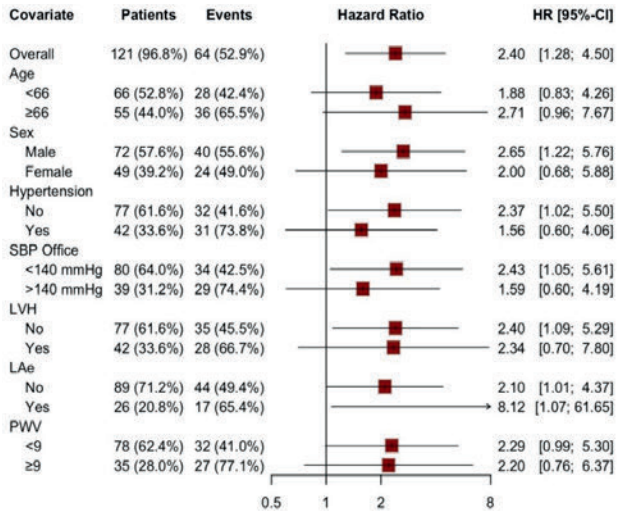
Introduction: Carfilzomib (CFZ) is a proteasome inhibitor used in the treatment of multiple myeloma (MM) known for its cardiotoxic adverse events. Cardio-Oncology guidelines emphasize cardiovascular risk assessment during cardiotoxic therapy, with echocardiography as the first-line imaging technique. Evaluations typically include left ventricular ejection fraction (EF) and global longitudinal strain (GLS); left atrial strain (LAS), not currently included in the definition of cardiotoxicity, is emerging as a potential marker of cardiac dysfunction. Recent studies highlight LAS in early myocardial damage detection and as a mortality predictor in cancer patients, but its role in CFZ-induced hypertensive events in MM remains unclear.
Aim: This study explores LAS as a predictor of CFZ-related hypertensive adverse events in MM patients, with or without pre-existing hypertension.
Methods: 125 MM patients undergoing CFZ treatment were recruited at the Hypertension Centre, "Città della Salute e della Scienza" in Turin. Baseline assessments included medical history, clinical examination, office blood pressure measurement, 24-hour ambulatory blood pressure monitoring (ABPM), Pulse Wave Velocity (PWV), electrocardiography, and transthoracic echocardiography (TTE). LAS values were analysed using Philips QLAB software. Patients were monitored for hypertensive events during CFZ therapy.
Results: 52% of the study population developed CVAEs, predominantly as a worsening of pre-existing arterial hypertension. LAS conduit values were significantly impaired in hypertensive patients compared to normotensive individuals (-15.1 [8.32] % vs. -21.0 ± 7.59 %, p=0.002), as well as in the subgroup experiencing hypertensive events compared to those without CVAEs (-16.2 [-20.75; -12.65] % vs. -20.8 [-26.3; -15.4] %, p=0.006). LAS was a significant predictor of hypertensive adverse events in normotensive patients (OR 2.37 [1.02; 5.50]) and in the subgroup without evidence of cardiac organ damage (OR 2.4 [1.09; 5.29]).
Conclusion: LAS conduit alteration is associated with increased risk of adverse hypertensive events during CFZ therapy. Its integration in current cardiovascular evaluation protocols dedicated to normotensive MM patients could be useful to identify early myocardial damage and allow better risk stratification in candidates for cardiotoxic therapies.



ONE CUP TOO MANY: GREEN TEA–ASSOCIATED LIVER INJURY IN A PATIENT WITH METABOLIC STEATOHEPATITIS. A CASE REPORT

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A 34-year-old female with no significant past liver history was referred to our Hepatology Clinic following routine blood tests revealing markedly elevated liver enzymes: AST 88 U/L, ALT 194 U/L, and GGT 85 U/L. Abdominal ultrasound demonstrated a 12 mm focal hepatic lesion in segment 4 in the context of a moderately steatotic liver.
Her medical history included insulin resistance with impaired fasting glucose, androgenetic alopecia, and a subcentimetric colloid-cystic euthyroid thyroid nodule. She denied alcohol use, smoking, or known risk factors for viral hepatitis. Diet was reported as generally balanced, although she disclosed consuming 1–1.5 liters per day of green tea prepared by infusion of whole leaves. There was no family history of liver disease or malignancy. Screening tests for viral hepatitis (HAV, HBV, HCV,) autoimmune liver disease (ANA, AMA, ENA, ANCA, ASMA, LKM antibodies), iron and copper metabolism (ferritin, transferrin saturation, ceruloplasmin), alpha-1 antitrypsin, thyroid function, and celiac serology were all within normal limits.
Magnetic resonance imaging (MRI) of the abdomen with contrast revealed a steatotic liver and four nodular lesions (14 mm in S8, 9.5 mm in S2, 10 mm and 8 mm in S7), radiologically consistent with cavernous hemangiomas. No biliary dilation or portal vein abnormalities were seen.
Given persistent enzyme abnormalities with no clear etiology, a liver biopsy was performed. Histology revealed preserved lobular architecture, extensive macrovesicular and microvesicular steatosis, mild pericellular fibrosis, and minimal intralobular lymphogranulocytic inflammation. These findings supported a diagnosis of steatohepatitis, likely metabolic in origin, though a potential contribution from green tea–related hepatotoxicity could not be excluded.
The patient was advised to discontinue green tea, maintain a hypocaloric diet, and begin physical activity. At two months, liver enzymes had significantly improved (AST 43, ALT 82, GGT 88, ALP 94 U/L), despite no significant changes in exercise or dietetic habits. At six months, values had nearly normalized (AST 32, ALT 47, GGT 51 U/L), strongly suggesting a reversible liver injury potentially related to green tea intake.
Green tea (Camellia sinensis) is widely used for its expected health benefits, including weight loss and cardiovascular protection, largely attributed to its high catechin content, particularly epigallocatechin-3-gallate (EGCG). However, idiosyncratic liver injury associated with green tea has been documented, typically presenting as an acute hepatocellular injury. Although most cases involve concentrated green tea extracts, there are reports of liver injury from traditional infusions, likely related to EGCG content and individual susceptibility. The presence of the HLA B*35:01 allele has been associated with increased risk.
This case illustrates a possible synergistic liver injury in a patient with underlying metabolic dysfunction. While MAFLD was evident histologically, the significant biochemical improvement after green tea cessation implicates an additional hepatotoxic component. The pathogenesis is likely idiosyncratic, with no clear dose-response relationship, and may involve mitochondrial dysfunction or immune-mediated mechanisms.Clinicians should be aware of the potential hepatotoxicity of green tea, even in infusion form, particularly in patients with underlying metabolic liver disease. A thorough history of herbal supplement use is essential in the diagnostic evaluation of elevated liver enzymes.

BILATERAL RENAL ARTERY STENOSIS IN A FEMALE WITH RESISTANT HYPERTENSION AND RENAL FAILURE: A CASE REPORT

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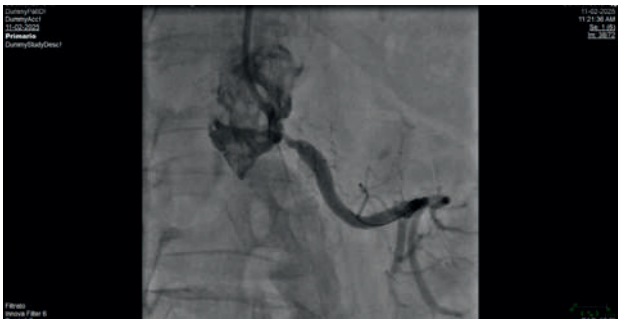
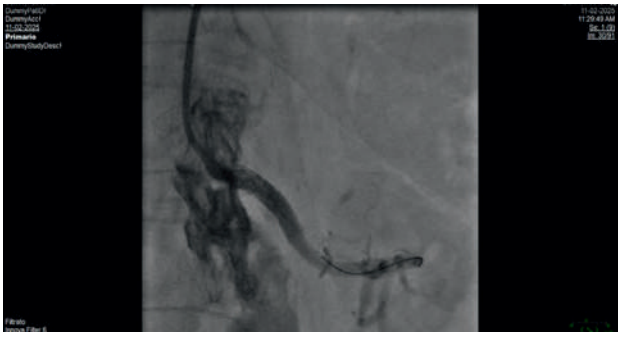
We describe the clinical case of Q.A., a 72-year-old woman affected by chronic ischemic heart disease, carotid atherosclerosis treated with PTCA and stent on the right internal carotid artery, arterial hypertension, dyslipidemia and chronic renal failure at stage IV.
Due to the finding of arterial hypertension resistant to pharmacological treatment and for the worsening of renal function, the patient was referred to the Hypertension Center of the A.O.U. Federico II of Naples where admission to the Day Hospital regime was indicated for further investigation of the case.
During the interview, the patient reported uncontrolled arterial hypertension despite therapy with the following drugs: Olmesartan/amlodipine 40/10 mg, bisoprolol 2.5 mg, doxazosin 4 mg, chlortalidone 25 mg and clonidine 2.5 mg patches. At the visit the patient presented blood pressure (BP): 200/100 mmHg, weight 52 kg, dyspnea on mild-moderate exertion (NYHA II). ECG, echocardiography and blood tests were performed which showed:
K= 4.7 mmol/L (VN 3.5-5 mmol/L)
Creatinine= 1.80 mg/dl with eGFR 29 ml/min/1.73 m2 (VN 0.51-0.95 mg/dl)
Renin= 29.8 pg/ml (VN 2.52-35.82 pg/ml)
Aldosterone= 107.1 pg/ml (VN 40-310 pg/ml)
In the suspicion of hypertension secondary to renal artery stenosis an echocolordoppler of the renal arteries was performed, which found "acceleration of the flow at the origin of the celiac tripod, the superior mesenteric artery and the right renal artery, as from stenosis higher than 70% and absence of significant stenosis at the origin of the left renal artery."
An abdominal CT angio with and without contrast medium was performed, it

showed "focal stenosis of the right renal artery immediately downstream from the origin, with regular opacification and caliber of the vessel downstream and post-ostial stenosis of the left renal artery extending for approximately 5 mm with regular opacification and caliber of the vessel downstream." The instrumental examination confirmed the suspected diagnosis of bilateral renal artery stenosis. To reduce the risk of acute renal failure, before and after the examination, 500cc of NaCl 0.9% and 2 vials of N-acetylcysteine were infused. A few hours after the infusion, the patient complained of general malaise and dyspnea. Vital parameters were recorded with SpO2 86% and BP: 160/80 mmHg; the following were performed: arterial EGA (pH 7.46, pCO2 29.1 mmHG, pO2 48.6 mmHg, sO2 87%, HCO3- 20.4 mmol/L), ECG, echocardiography showing moderately increased PAPs and dilated and hypocollapsing inferior vena cava, and chest ultrasound with the presence of B lines in the right basal field, configuring a picture of flash pulmonary edema, a condition that can affect patients with renal artery stenosis in response to water loading. After adequate therapy and stabilization of the clinical conditions, the patient was discharged home and placed on the waiting list for ordinary hospitalization with an indication to perform angiography of the renal arteries.
Angiographic examination, subsequently performed, showed critical stenosis of the right renal artery treated with angioplasty with a drug-eluting stent and critical stenosis of the left renal artery treated with angioplasty with two drug-eluting stents.
The patient was discharged from the cardiology department without therapeutic changes and with a BP of 160/80 mmHg. She went for a check-up at the Hypertension Center approximately 15 days after the procedure. BP was found to be: 140/70 mmHg, so the antihypertensive therapy was reduced; she showed blood tests with creatinine 1.2 mg/dl (eGFR 48 ml/min/1.73m2), with concomitant improvement in renal function.
At the time of the visit, the patient complained of pain in the fingers of the lower limbs. On physical examination, erythematous and edematous fingers were observed, therefore arterial color Doppler of the lower limbs was performed which showed atheromasia at the level of the femoro-popliteal district bilaterally with reduced flow at the level of the posterior tibial arteries, in particular on the left, with the configuration of blue toe syndrome due to probable post-procedural aorto-iliac embolization, for which anticoagulant therapy with enoxaparin sodium was added.





A CASE OF RESISTANT ARTERIAL HYPERTENSION COMPLICATED DURING FOLLOW-UP

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A 36-year-old male patient presented to our Internal Medicine outpatient clinic for grade II arterial hypertension resistant to pharmacological therapy (BP 160/105 mmHg), glucose intolerance, tachycardia (108 bpm), and oxygen saturation of 95% in room air. His personal medical history revealed mixed dyslipidemia, recently diagnosed stage II chronic kidney disease, and heavy tobacco use. His family history was negative for cardiovascular diseases.
A resting ECG showed a leftward deviation of the cardiac electrical axis. Resting echocardiography revealed left ventricular hypertrophy due to systolic overload with preserved ejection fraction and mild mitral and tricuspid regurgitation. A tricuspid aortic valve was also noted.
To investigate the possibility of secondary hypertension, the patient was hospitalized. Antihypertensive therapy was modified to allow for testing of plasma metanephrines, vanillylmandelic acid, urinary catecholamines, renin, and aldosterone levels—all of which were within normal ranges. Blood tests showed erythrocytosis (Hb 18.4 g/dl, HCT 55.6%), leukocytosis, HbA1c of 7.6%, low-normal serum calcium, elevated PTH in the setting of marked vitamin D deficiency, and normal thyroid function with negative anti-thyroglobulin and anti-thyroid peroxidase antibodies.
Attention was then drawn to elevated serum cortisol levels (34.5 mcg/dl) and 24-hour urinary free cortisol (935 mcg/24h), with ACTH levels at 8 pg/ml. These laboratory findings were supported by clinical signs of truncal obesity (BMI 32.9 kg/m^2), abdominal and upper limb striae rubrae, and a moon face with thin, flushed facial skin.
A low-dose dexamethasone suppression test (2 mg) was performed under close blood pressure and glycemic monitoring, which showed persistently elevated and non-suppressible cortisol levels.
An abdominal MRI supported the diagnosis of ACTH-independent Cushing's syndrome, revealing a solid mass in the left adrenal gland measuring 30x30 mm. The patient was therefore referred for left adrenalectomy.
In the weeks following the surgery, the patient—who also reported a family history of scarlet fever in his child—developed fever and fatigue. He presented to the emergency department with a worsening clinical picture. Initial blood tests showed CRP at 190 ng/l, procalcitonin >100 ng/ml, leukocytosis, elevated lactate, marked hypotension (70/45 mmHg), and acute kidney injury superimposed on chronic kidney disease (creatinine 3.09 mg/dl), compatible with a severe septic state.
The hospital stay lasted about a month and included initial antibiotic therapy with meropenem 1000 mg and tigecycline 50 mg, followed by antifungal therapy with fluconazole 200 mg. Due to a likely polymicrobial infection, the patient was discharged on continued antibiotic therapy and oral fluconazole 200 mg.
After fourteen days, the patient returned to our outpatient clinic with severe fatigue, nausea, arterial hypotension and marked dehydration. The suspicion of postoperative adrenal insufficiency was further supported by the history of prolonged fluconazole use. Laboratory tests confirmed the clinical suspicion, revealing severe hyponatremia and hypotension (Na 130 mmol/l, K 5.5 mmol/l). Intravenous hydrocortisone was administered promptly, correcting both the volume deficit and the electrolyte imbalance. Following stabilization, the patient was discharged on oral cortisone acetate therapy for confirmed adrenal insufficiency, evidenced by low serum and urinary cortisol levels.
This clinical case highlights the challenges in managing patients with severe hypertension resistant to common antihypertensive drugs and underscores the importance of early identification of secondary causes. Postoperative management of secondary hypertension, particularly in Cushing's syndrome, can be complex due to potential autoimmune rebounds and increased infection risk, which may precipitate adrenal insufficiency. In this patient, the development of psoriatic arthritis and transient autoimmune hypothyroidism further complicated the clinical course. Finally, this case also emphasizes the importance of monitoring adrenal function during antifungal therapy, particularly with agents as Ketoconazole, which inhibit enzymes as 11beta-hydroxylase, and Fluconazole, which has been implicated in similar cases.
The patient is currently in good general health, with mild hypertension and is in the process of permanently discontinuing Cortisone acetate replacement therapy for resumption of contralateral adrenal function.

A RARE DISEASE THAT PRESENTS WITH COMMON SYMPTOMS: KIKUCHI-FUJIMOTO DISEASE

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We report the case of a 52-year-old caucasian male with a past medical history significant for nephrolithiasis. In July 2023, he was admitted to the internal medicine department due to a two-month history of recurrent fever of unknown

origin, marked asthenia, cough, diffuse arthromyalgias, and erythema nodosum. Two months prior, he experienced two episodes of renal colic and an infectious bronchopneumonia with bilateral pleural effusion, managed on an outpatient basis, with a subsequent chest X-ray yielding normal results. In May 2023, he received his third dose of the SARS-CoV-2 vaccine.
Laboratory investigations revealed elevated inflammatory markers (ESR 120 mm/h) without leukocytosis (WBC 10,350/μL), mild eosinophilia (710 eosinophils/μL), and elevated total IgE (357.69 IU/mL). Infectious etiologies were explored through serological testing for TORCH pathogens, EBV IgM and IgG, Quantiferon-TB Gold, and hepatitis viruses; all results were negative. Urinalysis and sputum cultures were unremarkable. Imaging studies, including chest X-ray and abdominal ultrasound, did not reveal any pathological findings. Given the exclusion of infectious diseases such as tuberculosis, infectious mononucleosis, cytomegalovirus, and toxoplasmosis, an autoimmune etiology was considered. Autoantibody testing showed borderline ANA titers (1:80), with negative p-ANCA, c-ANCA, and ENA screening. In August 2023, multiple bilateral laterocervical lymphadenopathies were detected, the largest measuring 27 mm × 17 mm on the left side, with an oval shape. Contrast-enhanced neck CT scan revealed small hypodense areas suggestive of liquefactive necrosis. A lymphoproliferative disorder was suspected, and a biopsy of the largest lymph node was planned. However, blood count values did not support this diagnosis, as there were no alterations in the leukocyte formula, cytopenias, lymphocytosis, or elevated LDH levels. Tumor markers, including CEA, alpha-fetoprotein, and CA 19.9, were within normal limits. The absence of anti-dsDNA and anti-Sm antibodies, along with the lack of joint manifestations and cutaneous rash, led to the exclusion of systemic lupus erythematosus. Although the patient exhibited diffuse arthralgias, particularly in the knees and ankles, lymphadenopathy, fever, and erythema nodosum, adult-onset Still's disease was ruled out due to the absence of the characteristic salmon-colored rash and lack of hyperferritinemia. Castleman disease, a rare non-neoplastic lymphoproliferative disorder associated with nonspecific symptoms such as fever, asthenia, splenomegaly, and weight loss, was considered. However, the absence of anemia, hypergammaglobulinemia, and histological evidence of lymph node necrosis led to its exclusion. Kikuchi-Fujimoto disease (KFD), a rare form of necrotizing lymphadenitis, has been increasingly reported in association with SARS-CoV-2 infection and vaccination. The disease typically presents with fever and cervical lymphadenopathy, often involving tender, elastic lymph nodes with areas of necrosis. Additional findings may include splenomegaly, cutaneous involvement, leukopenia, and elevated erythrocyte sedimentation rate. The etiology remains unknown, but associations with infectious and autoimmune conditions have been noted. The course is generally benign and self-limiting. Histopathological examination of the excised lymph node revealed lymphoid parenchyma with aggregates of CD68-positive histiocytes and areas of necrosis, consistent with necrotizing granulomatous lymphadenitis. The absence of S100-positive histiocytes and emperipolesis excluded Rosai-Dorfman disease. No neoplastic cells were identified, ruling out Hodgkin and non-Hodgkin lymphomas. The presence of necrosis, along with the absence of pulmonary, mediastinal, hepatic, or splenic involvement, made sarcoidosis unlikely. The patient received anti-inflammatory therapy, leading to complete remission of symptoms and normalization of inflammatory markers within three months.
Since 2020, over 15 cases of KFD associated with SARS-CoV-2 infection or vaccination have been documented. Although more prevalent in Asian populations and females, KFD should not be excluded in Caucasian individuals. In suspected cases, lymph node biopsy remains essential for differential diagnosis.

CLINICAL, FUNCTIONAL, AND MICROVASCULAR FEATURES IN THE EARLY DIAGNOSIS OF PULMONARY HYPERTENSION IN SYSTEMIC SCLEROSIS: THE VALUE OF MULTIMODAL SCREENING STRATEGIES IN INTERNAL MEDICINE

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Introduction: Pulmonary hypertension (PH) is one of the most severe complications in patients with systemic sclerosis (SSc), an autoimmune disease characterized by widespread fibrosis and systemic vascular dysfunction. SSc-associated PH (SSc-PH) has a variable prevalence ranging from 5% to 19% and is associated with poor prognosis, with a three-year survival rate below 62%. Timely and accurate diagnosis is essential to improve clinical management and outcomes. This study aimed to assess the prevalence of SSc-PH in a tertiary care center and analyze the associated clinical, functional, echocardiographic, and microvascular factors, with particular focus on nailfold videocapillaroscopy (NVC) as a non-invasive screening tool.
Materials and methods: A retrospective analysis was conducted on 77 consecutive patients with SSc diagnosed according to the 2013 ACR/EULAR criteria. Patients were assessed for age, sex, disease duration (since Raynaud's onset), comorbidities, and organ involvement. Pulmonary function parameters (DLCO, FVC, FEV1), HRCT findings, echocardiographic data (TAPSE, PASP, chamber diameters), and NVC patterns (capillary density, megacapillaries, avascular areas) were analyzed. Patients were stratified by presence or absence of PH.
Results: The prevalence of SSc-PH was 27% (21/77 patients). Patients with PH had significantly longer disease duration (10.8 vs. 8.7 years; $p < 0.001$) and higher BMI (26.3 vs. 24.1 kg/m²; $p = 0.049$). Lung function testing showed lower DLCO (62.2% vs. 71.7%; $p = 0.044$) and a restrictive pattern with reduced FVC (2.8 L vs. 3.2 L; $p = 0.005$). Interstitial lung involvement was more frequent in PH patients (65% vs. 33.3%; $p = 0.018$), as was musculoskeletal involvement (20% vs. 3.5%; $p = 0.037$).
Echocardiography revealed significant signs of right ventricular dysfunction: lower TAPSE (22.2 mm vs. 24.7 mm; $p = 0.013$), increased RV diameter (32.7 mm vs. 31.1 mm), and larger inferior vena cava diameter (19.1 mm vs. 17.1 mm; $p < 0.001$). Mean PASP in PH patients was 41.7 mmHg, confirming hemodynamic compromise.
NVC showed a higher prevalence of "active" and "late" scleroderma patterns in PH patients (35% with late pattern), with capillary rarefaction, megacapillaries, and avascular areas. These microvascular changes correlated significantly with lower DLCO and worsened spirometry, suggesting a link between peripheral microangiopathy and pulmonary vascular damage.
Discussion: The findings support the clinical value of a multimodal, non-invasive diagnostic approach in the early identification of PH in SSc. Disease duration, lung involvement, and functional deterioration are significant predictors. NVC, when integrated with pulmonary function tests and echocardiography, proves to be a reliable tool for risk stratification and early detection of patients at higher risk. Echocardiography remains a cornerstone in PH screening and is enhanced by emerging techniques like right ventricular strain imaging and 3D echocardiography.
Although current international guidelines identify right heart catheterization (RHC) as the gold standard for the diagnosis of pulmonary hypertension, its routine use in clinical practice is often limited. This is due to its invasive nature, logistical constraints in non-tertiary care settings, and the difficulty in selecting appropriate candidates for referral. Additionally, many patients with SSc present with clinical frailty or comorbidities that increase procedural risk, leading to underutilization of this important diagnostic tool. These barriers may result in missed or delayed diagnoses, particularly in the early stages of disease. Therefore, the adoption of non-invasive, accessible, and repeatable tools such as echocardiography, pulmonary function testing, and videocapillaroscopy becomes crucial for preliminary assessment and to guide decisions regarding the need for invasive confirmation.
The integration of these diagnostic modalities enables a more comprehensive and earlier identification of patients with SSc at risk for developing PH. Capillaroscopy, in particular, offers a simple and reproducible method for evaluating microvascular involvement that may reflect early pulmonary vascular changes. Although correlations between peripheral and pulmonary microangiopathy are still under investigation, the associations found in this study reinforce the relevance of systemic microvascular assessment in this context.
Conclusions: In the context of Internal Medicine, SSc-PH is a common and severe complication, and its early detection is critical to improving outcomes. A multimodal diagnostic strategy combining spirometry, HRCT, echocardiography, and NVC is essential. Capillaroscopy, in particular, emerges as a practical, accessible, and repeatable tool even in outpatient settings.

A CASE REPORT OF HIT-T, WITHOUT THE FIRST T: MASSIVE THROMBOSIS DUE TO HIT IN THE ABSENCE OF SIGNIFICANT THROMBOCYTOPENIA.

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Heparin-induced thrombocytopenia (HIT) is a potentially life-threatening complication of heparin therapy, characterized by a marked prothrombotic state. Early recognition is crucial to prevent major thromboembolic events.
We report the case of a 44-year-old man admitted for acute pneumonia who developed extensive venous thrombosis and bilateral pulmonary embolism during prophylactic treatment with low molecular weight heparin (LMWH). Despite a significant drop in platelet count, HIT was not initially suspected, and the continuation of heparin therapy contributed to the worsening of the thromboembolic burden and the patient's overall clinical status.

The patient had initially been hospitalized for left basal pneumonia and was started on LMWH (4,000 IU/day) in accordance with current guidelines. Approximately seven days after starting LMWH, he experienced a syncopal episode and underwent CT pulmonary angiography, which revealed bilateral pulmonary embolism and thrombosis of the inferior vena cava extending to the iliac and femoral veins. He was transferred to the intensive care unit. Despite systemic thrombolysis and therapeutic anticoagulation with LMWH, his clinical condition progressively deteriorated, with recurrent presyncope and worsening respiratory failure. Given the critical scenario, mechanical thrombectomy was performed; however, anticoagulation with LMWH was continued.

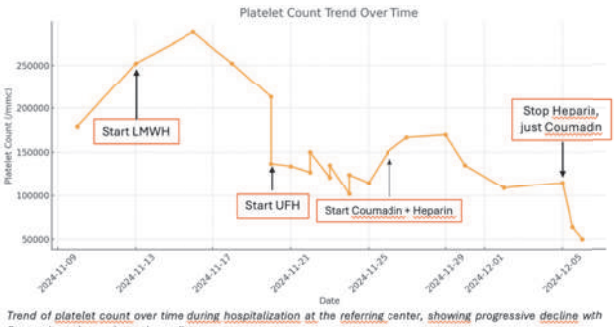
The patient was considered "resistant" to pharmacologic thrombolysis (tPA and LMWH) and thrombectomy and was subsequently started on warfarin after appropriate bridging with heparin. After three days of vitamin K antagonist (VKA) therapy, his condition worsened again, and he was transferred to our center.

Upon admission on 06/12/2024, he presented with deep vein thrombosis extending from the lower limbs to the right atrium, severe pulmonary embolism, and thrombocytopenia (PLT 47,000/mm^3). Heparin therapy had been initiated on 12/11 at the referring hospital, and a first >50% drop in platelet count (to 137,000/mm^3 from a baseline of 287,000/mm^3) was already evident by day 8. However, platelet levels showed a fluctuating course, with partial recovery up to 150,000/mm^3, creating an aspecific and misleading laboratory picture. The nadir (47,000/mm^3) was reached only on 06/12. Although this course was compatible with classical-onset HIT, the fluctuation in platelet count—and likely, the concomitant corticosteroid therapy—may have delayed the development of an absolute thrombocytopenia. The absence of moderate-to-severe thrombocytopenia likely contributed to the missed diagnosis, despite worsening thrombosis. Therefore, HIT-T without the "first T"—that is, without overt thrombocytopenia—was not recognized, and persistent heparin exposure maintained a prothrombotic state.

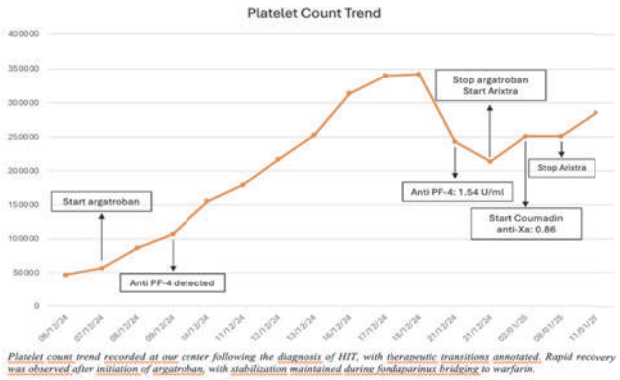
After nearly 20 days of heparin exposure, on 07/12, HIT was clinically suspected and both immunologic and functional assays confirmed the presence of anti-PF4 antibodies. The patient had already been on warfarin for four days, with an INR of 3.4. In accordance with ASH guidelines, which contraindicate VKA therapy in early HIT due to the associated risk of protein C depletion and transient prothrombotic state, warfarin was discontinued, and continuous infusion of argatroban was initiated, titrated according to aPTT. The clinical picture improved rapidly, with platelet count exceeding 150,000/mm^3 within 3–4 days. After 24 days of IV argatroban, therapy was transitioned to therapeutic-dose fondaparinux, with monitoring of anti-Xa activity.

In this case, HIT remained unrecognized for at least two weeks. Ongoing heparin exposure exacerbated the thrombosis, which appeared "resistant" to thrombolysis, anticoagulation, and thrombectomy, placing the patient's life at risk. The early introduction of warfarin (with PLT <150,000/mm^3) may have further worsened the clinical picture, as previously described in the literature, due to the hypercoagulable state associated with early protein C reduction.

The patient's condition stabilized only after switching to non-heparin anticoagulants. This case highlights the importance of suspecting HIT even in the absence of moderate or severe absolute thrombocytopenia, with careful evaluation of relative platelet drop after 5 days of heparin exposure. In the presence of progressive thrombosis despite adequate anticoagulation, HIT-T must always be considered. Management requires immediate heparin discontinuation and the use of alternative anticoagulants. Diagnosis is based on immunologic and functional testing for anti-PF4 antibodies. The patient is currently in good general condition and is on chronic warfarin therapy. However, total-body CT imaging shows a significant residual thrombotic burden involving both the lower limbs and pulmonary circulation.



Trend of platelet count over time during hospitalization at the referring center, showing progressive decline with fluctuating values prior to the nadir.



Platelet count trend recorded at our center following the diagnosis of HIT, with therapeutic transitions annotated. Rapid recovery was observed after initiation of argatroban, with stabilization maintained during fondaparinux bridging to warfarin.

AS FRAGILE AS HER BALANCE: DKA, SEPSIS, AND DIC ON SGLT2i

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Case report: A 83-year-old woman presented to the emergency department with fever associated with nausea, vomiting and anorexia. Her past medical history included hypertension, hypercholesterolemia, type 2 diabetes mellitus, and chronic vascular cerebropathy. She had also recently been admitted to the Cardiology department for acute heart failure secondary to atrial fibrillation with high ventricular response and tachycardiomyopathy (EF 40%). At the time of discharge, she was prescribed therapy with ACE inhibitor, beta blocker, SGLT2i, mineralocorticoid receptor antagonist, and anticoagulant therapy with DOAC. She was also taking statin therapy. Due to nausea, vomiting and anorexia, the patient was not taking any therapy. On physical examination, she presented fever (38°C), BP 100/60, HR 120/min, SPo2 95% in room air, HGT 652 mg/dl. The patient presented in very serious general conditions. Tachyfrequent arrhythmic heart sounds, diffusely reduced vescicular murmur, manageable abdomen, not painful, ECT, peristalsis present and severe mucocutaneous dehydration. Initial investigations revealed Hgb 8.6 g/dl, WBC 12 X1000/microL and PLT 184 x1000/microL. CRP was 125 mg/L (reference range, < 5 mg/L) PCT 3 ng/mL (r.r., < 0.5 ng/mL). Clotting studies were within the reference ranges. Na was 158 mmol/L (r.r. 136-145mmol/L), K 5.1mmol/l (r.r. 3.5-5.0 mmol/L), urea 42 mg/dL (r.r. 7-18 mg/dL), and creatinine 8 mg/dl (r.r. 0.67-1.17 mg/dL). Liver function tests were normal. Serum amylase and creatine kinase were normal. The patient underwent ECG with evidence of atrial fibrillation with rapid ventricular response, heart rate 145/min, left anterior hemiblock. She underwent the following blood tests: blood cultures 2 sets and urine culture. A hemogasanalysis was also performed showing pH 7.29, HCO3 8, AG 23, Glucose 659, Na 155, K 4.9. Finally, a chest x-ray was performed and was negative for inflammatory foci. A diagnosis of DKA secondary to probable urosepsis, acute kidney injury and atrial fibrillation with rapid ventricular response was made. A double-lumen central venous catheter was placed in the left jugular vein to start intravenous therapy in the absence of intraprocedural complications. Therapy with saline solution and insulin aspart 50 IU in 500 cc of saline solution at a rate of 40 ml/hour (estimated weight of the patient approximately 45 kg) was started. The patient also underwent Metoprolol 5mg in 100cc of saline solution 0,9% over 30 minutes with good heart rate control (100 bpm) and empiric antibiotic therapy with Piperacillin/Tazobactam and Levofloxacin. Prophylaxis of VTE with fondaparinux had also been introduced.The day after admission, the patient was better hydrated with improving renal function. Blood gas analysis was repeated showing pH 7.36, HCO3 22, AG 14, Na 149, K 3.5. On the third day after admission, the patient presented with monolateral edema of the right upper limb. She underwent US of the upper limbs which documented in situ thrombosis of the central venous catheter extending to the left subclavian vein. Blood tests revealed persistent neutrophilic leukocytosis, high inflammation indices (PCR >100 mg/L), thrombocytopenia (69,000/mm^3), incoagulable PT and aPTT, fibrinogen 37 mg/dL and D-dimer 9,770 ng/mL. All blood and urine cultures performed at the time of admission were positive for Enterococcus Faecium VRE. A sepsis induced DIC diagnosis was made. Antibiotic therapy was therefore started according to the antibiogram with Linezolid 600 mg x 2. In the presence of manifest thrombosis and absence of active bleeding, it was decided to start low molecular weight heparin (LMWH) at a therapeutic dose, with close monitoring. After a few days of anticoagulant and antimicrobial therapy, progressive resolution of Sepsis and DIC was bserved, with improvement and normalization of haemocoagulative parameters.

Discussion: Sodium-glucose cotransporter 2 inhibitors (SGLT2i) are widely used in the treatment of type 2 diabetes and heart failure. SGLT2i function by decreasing glucose reabsorption from the proximal convoluted tubule and increasing urinary glucose excretion. Consequently, this leads to reduced carbohydrate usage and prompts a shift toward the utilization of fatty acids, resulting in ketogenesis, a process observed as diabetic ketoacidosis (DKA) in diabetic patients. Studies in rats have shown that SGLT2is can increase plasma concentrations of catecholamines and cortisol due to hypovolemia, leading to insulinopenia and subsequently augmenting hepatic ketogenesis. SGLT2i are also associated with an increased risk of urinary and genital tract infections, which can become clinically significant in predisposed individuals. While offering significant metabolic and cardiovascular benefits, they can pose considerable risks in vulnerable populations, particularly the elderly and frail. This case demonstrates how SGLT2i determined, through the above-mentioned mechanisms, a cascade of potentially fatal events culminating in the development of VRE sepsis and DIC.

HEPARIN-INDUCED-THROMBOCYTOPENIA IN THE SHADOW OF RENAL FAILURE: A COMPLEX CASE MANAGED WITH DANAPAROID

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Heparin-induced thrombocytopenia (HIT) type II is a rare but potentially life-threatening complication of heparin exposure, caused by the production of antibodies against platelet factor 4 (PF4)-heparin complexes. These immune complexes activate platelets and monocytes leading to potentially catastrophic thrombotic events. One of the most challenging aspects in the management of HIT is the paradoxical need for anticoagulation despite thrombocytopenia. While low platelet count usually raise concern for bleeding, in HIT it indicates a pro-thrombotic state that requires immediate anticoagulant therapy. Ideally, the best way to prevent HIT would be to limit heparin exposure. However, this is not always feasible, especially in hemodialyzed patients, in whom heparin is still widely used to prevent intra-circuit blood clotting during dialysis. In these patients the risk of HIT is always present and management is challenging since many alternative anticoagulants are renally cleared.
We report a case of a HIT in a dialysis-dependet patient; management was complex due to the coexistence of severe thrombocytopenia, ongoing thrombosis and end-stage kidney disease (ESKD).
An 88-years-old female was admitted to our Internal Medicine Ward for a severe Escherichia coli urosepsis. Her past history included chronic renal disease, but she had no previous hospitalizations or heparin exposure. Due to sepsis, her renal function deteriorated rapidly (eGFR 6 mL/min), requiring empiric antibiotic therapy with piperacillin-tazobactam, later confirmed by antibiogram.Initial platelet count was 358 x 109/L, reasing transiently to 450 x 109/L, mostly due to the infection.On day 12 due to persistent renal failure with oligoanuria the patient was started on hemodialysis. Unfractioned heparin (UFH) was used in the circuit.Seven days after the start of the hemodialysis the platelet count started to drop (day 20: 274 x 109/L) rapidly reaching a nadir of 54 x 109/L on day 26. This decline was unexplained, as the infection was resolving and antibiotic had already been discontinued on day 21.
A strong suspicion of HIT arose. We used the 4T score (figure 1) which assessed a high-risk condition for this worrisome complication. Despite the absence of overt symptoms, a Doppler US was performed, revealing thrombosis of the right femoral vein, near the dialysis catheter. We were dealing with a severe case of HIT already complicated by thrombosis. Anti-PF4 antibodies tested positive with the enzyme immunoassay EIA (7.4 U/mL, positivity > 1 U/mL).UFH was immediately discontinued. However, since the patient still required dialysis, an alternative anticoagulant was necessary. Given the rarity of the case, we carefully reviewed the literature. The choice of drug was complicated by the fact that in our peripheral hospital access to certain medication is limited, as is the ability to monitor their activity in the laboratory.
We consulted a thrombosis expert and sought the help of the "HIT-THE-HIT" network. The choice fell on danaparoid. In patients on hemodialysis, danaparoid dosing depends on weight and session frequency. In our case, 3750 units of danaparoid were administered before each session. To monitor for potential accumulation (due to impaired renal clearance), anti-Xa activity was measured before each session, showing no evidence of drug buildup.Following UFH discontinuation, platelet count began to recover, normalizing within five days. Clinical stability improved and total body CT scan showed no signs of venous or arterial thrombosis elsewhere. As platelet levels rose – likely reflecting decreased anti-PF4 activity – warfarin was initiated on day 5. By day 11, danaparoid was discontinued upon achieving therapeutic INR. Figure 2 illustrates the progression of platelet counts throughout the patient's hospital stay.
Unfortunately, the patient later died of septic shock unrelated to HIT. Nonetheless, thrombocytopenia and thrombosis were successfully managed without further complication.
We have described a complex case of HIT in a patient with ESKD. Thrombosis had already occurred by the time of diagnosis and this is usually associated with high morbidity and mortality. Prompt recognition using the 4T score and immediate discontinuation of UFH were crucial. Despite limited access to certain treatments in our peripheral hospital, danaparoid proved to be a safe and effective alternative in this context. High clinical suspicion remains essential, especially in dialysis patients with unexplained thrombocytopenia. Our experience reinforces the role of Internal Medicine in complex, high-risk scenarios, where timely clinical judgment can alter the course of potentially fatal complications.
References: Hamadi R, Sakr F, Aridi H, Alameddine Z, Dimachkie R, Assaad M, Asmar S, ElSayegh S. Heparin-Induced Thrombocytopenia in Chronic Hemodialysis Patients. Clin Appl Thromb Hemost. 2023 Jan-Dec;29:
Hogan M, Berger JS. Heparin-induced thrombocytopenia (HIT): review of incidence, diagnosis, and management. Vasc Med. 2020;25(2):160-173.

4T SCORE	
Platelet count fall >50% AND platelet nadir ≥20	+2 points
Clear onset between days 5–10	+2 points
New thrombosis	+ 2 points
No other causes for thrombocytopenia	+ 2 points

Figure 1

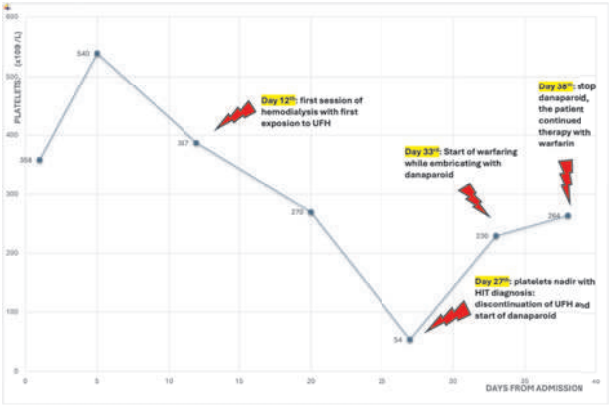

Figure 2

HEPARIN-INDUCED THROMBOCYTOPENIA (HIT): A MONOCENTRIC EXPERIENCE WITH DANAPAROID

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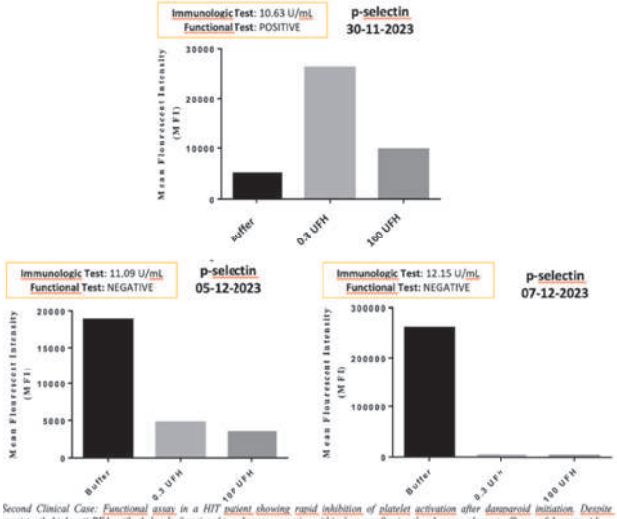
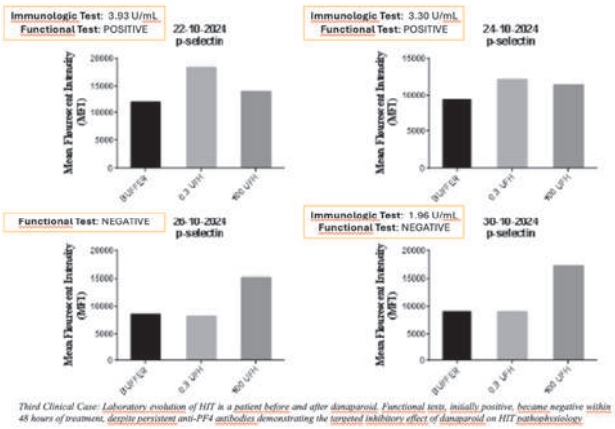
Heparin-induced thrombocytopenia (HIT), with or without thrombosis (HIT-T), is a potentially severe immune-mediated condition characterized by a high risk of arterial and venous thrombotic events. The prevalence of anti-PF4 antibodies among patients exposed to heparin can reach up to 8%, but only 1–5% progress to clinically significant HIT. Early diagnosis and prompt discontinuation of heparin, combined with the initiation of a non-heparin anticoagulant, are essential to prevent fatal outcomes. Sodium danaparoid, a low molecular weight heparinoid with a high anti-Xa/anti-IIa ratio, minimal interference with the fibrinolytic system, and low cross-reactivity with anti-heparin antibodies, represents a safe and effective therapeutic option. It is the only drug also approved for venous thromboembolism (VTE) prophylaxis in patients with a history of HIT without active thrombosis and can be used during pregnancy and breastfeeding.
We present a series of three patients admitted to the cardio surgery unit at the A. Gemelli University Hospital, all diagnosed with HIT-T based on clinical criteria (4T score ≥4), positive anti-PF4 immunoassay [HemosIL Acustar HIT

IgG assay], and positive functional test performed by flow cytometry.
In all cases, heparin therapy was discontinued, and treatment with sodium danaparoid was initiated—initially via intravenous infusion and subsequently subcutaneously, followed by transition to oral anticoagulation.
The first case involves a 74-year-old woman who underwent biological mitral valve replacement and developed thrombocytopenia (nadir 48,000/mmc) after sequential exposure to sodium, calcium heparin, and enoxaparin. HIT was confirmed by positive anti-PF4 antibodies (1.89 → 2.71 U/mL) and a positive functional test. She was started on danaparoid (bolus + continuous IV infusion), followed by subcutaneous administration for approximately 15 days. Platelet count exceeded 150,000/mmc within 5 days and reached 254,000/mmc at discharge (day 14). She was successfully transitioned to warfarin with appropriate overlap, without adverse events.
The second case is a 74-year-old woman with a history of mitral valvuloplasty, who underwent valve replacement and tricuspid repair. Following exposure to unfractionated heparin during cardiopulmonary bypass and postoperative calcium heparin, she developed severe thrombocytopenia (nadir 18,000/mmc) with high-titer anti-PF4 antibodies (25.25 U/mL) and a positive functional test. After an initial attempt with fondaparinux (discontinued due to further platelet decline), she was treated with corticosteroids and subsequently with intravenous argatroban. Once clinically stable, danaparoid was introduced subcutaneously, resulting in gradual platelet recovery and eventual transition to warfarin. At discharge, platelet count was consistently >130,000/mmc, and follow-up confirmed stable clinical control.
The third case is a 60-year-old man who underwent emergency cardiac surgery for papillary muscle rupture during an inferoposterior STEMI. Following treatment with UFH during cardiopulmonary bypass and subsequent exposure to low molecular weight heparin, he developed early prosthetic valve thrombosis and thrombocytopenia with anti-PF4 positivity (3.93 U/mL) and a positive functional test. Danaparoid was initiated with a bolus and continuous IV infusion, followed by subcutaneous administration. Platelet count rose progressively (from 126,000 to 202,000/mmc over 8 days), with an effective clinical response and safe transition to warfarin.
All patients treated with danaparoid achieved a stable platelet recovery (PLT >150,000/mmc) within 5–10 days, without thrombotic or hemorrhagic complications. No treatment modifications were required due to cross-reactivity or inefficacy.
Literature data confirm the supportive profile of danaparoid in HIT-T, with clinical success rates exceeding 90%, resolution of thrombocytopenia in 91% of cases, and a lower bleeding risk compared to other anticoagulants. Beyond its efficacy, danaparoid stands out for its pathogenetically targeted mechanism: its heparinoid structure with low cross-reactivity to anti-PF4/heparin antibodies allows it to interfere with the immune-mediated process underlying HIT by inhibiting the formation and stabilization of pathogenic complexes. This makes it particularly suitable in the acute phase, when rapid interruption of the thrombotic cascade is crucial. Initial doses below 2,250 IU/day are associated with a higher risk of treatment failure, underscoring the importance of appropriate IV dosing in early management.
Although recommended by major international guidelines, its use in Italy remains limited, despite being officially approved for HIT for approximately two years.Given its targeted mechanism, clinical efficacy, and favorable safety profile, danaparoid should be considered a first-line therapy for HIT.



Second Clinical Case: Functional assay in a HIT patient showing rapid inhibition of platelet activation after danaparoid initiation. Despite persistently high anti-PF4 antibody levels, functional tests became negative within days, confirming the pharmacodynamic efficacy of danaparoid.



Third Clinical Case: Laboratory evolution of HIT in a patient before and after danaparoid. Functional tests, initially positive, became negative within 48 hours of treatment, despite persistent anti-PF4 antibodies demonstrating the targeted inhibitory effect of danaparoid on HIT pathophysiology.

HOSPITAL-ACQUIRED INFECTIONS AND ANTIMICROBIAL RESISTANCE: ANALYSIS OF PREVALENCE AND APPROPRIATE ANTIBIOTIC USE IN A GENERAL MEDICINE WARD OF A TERTIARY CARE HOSPITAL

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Background: Infections represent one of the leading causes of morbidity and prolonged hospital stay in Internal Medicine wards, particularly among frail patients with multiple comorbidities. In recent years, the spread of multidrug-resistant (MDR) microorganisms has made the clinical and therapeutic management of these patients increasingly complex. The World Health Organization has emphasized the urgent need to implement effective measures to contain the spread of MDR pathogens, including the adoption of antimicrobial stewardship principles.
Objective: This study aims to analyse the prevalence and clinical-epidemiological characteristics of infections, with a specific focus on those caused by MDR microorganisms, in a cohort of patients admitted to an Internal Medicine ward of a tertiary care hospital in Lombardy, Italy.
Methods: This is an interim analysis of the data gathered through the prospective observational clinical study MED-Cli recruiting patients admitted to the General Medicine Unit for Metabolic Health and Aging at IRCCS San Raffaele Hospital in Milan. Admissions with recorded discharge dates between February 1st, 2024, and January 31st, 2025 were included in the analysis. Data were collected on the institutional Cohort Genomic Platform via a case report form which recorded demographic and clinical information, comorbidities, chronic medications, functional assessment scales (Charlson Comorbidity Index, Cumulative Illness Rating Scale, Barthel, Braden), reasons for admission, administered therapies, laboratory and microbiological results, and clinical parameters at admission and discharge.
Results: The analysis included 392 patients, for a total of 407 admission events. The median age of the cohort was 76 years, with males accounting for 54% of patients. At admission, the median number of comorbidities was 7, and the median number of home medications was 11. Infections were one of the reasons for hospitalization in 49.26% of cases. The most frequently isolated microorganisms at admission were Staphylococcus spp (19.46%, including S. aureus 6.19%), Enterococcus spp (13.27%), and E. coli (10.61%).
During hospitalization, 837 blood culture samples were collected, with a positivity rate of 68.3%. Analysis of the isolated pathogens showed a predominance of Staphylococcus spp (49.15%, 58 patients), with S. aureus detected in 15.5% of these cases (9 patients). Other isolated microorganisms included Enterococcus spp, E. coli, Pseudomonas spp, and Streptococcus spp (each found in 6.77%, 8 patients), Klebsiella pneumoniae (0.84%, 1 patient), and Candida spp (2.54%, 3 patients). Overall, 73.95% of the patients in the cohort received antimicrobial therapy during their hospital stay. Preliminary analysis showed that 12.5% of patients developed a nosocomial infection (onset >72 hours after admission), some of which were associated with MDR microorganisms. These infections were linked to increased length of stay and more complex clinical management.
Conclusions: Infections - especially those caused by multidrug-resistant organisms - are an increasingly significant challenge in Internal Medicine wards. Targeted strategies for prevention, surveillance, and antimicrobial stewardship are essential to contain the spread of these pathogens and improve clinical outcomes.

FEVER, CYTOPENIA AND SPLENOMEGALY: WHEN THE DIAGNOSIS IS HIDDEN IN THE BONE MARROW

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An 18-year-old male patient-obese, a smoker, and a habitual consumer of high-alcohol-content beverages and cannabis, was admitted to our Department for cholecystitis associated with severe trilinear cytopenia (Hb 8 g/dL, WBC 3740/µL, PLT 85,000/µL) and marked splenomegaly (25 cm), both already under diagnostic investigation.Three months earlier, the patient had undergone blood tests due to persistent asthenia, which revealed positive Epstein-Barr virus (EBV) serology. A bone marrow (BM) examination conducted following the detection of splenomegaly yielded inconclusive results, showing only erythroid hyperplasia.A lymphoproliferative disorder was initially suspected; however, both total-body CT and PET scans excluded the presence of hematological malignancies.Despite antibiotic therapy, the patient continued to present with multiple daily fever spikes. A strongly positive direct Coombs test suggested an immune-mediated hemolytic process, prompting further serologic testing for EBV, CMV, HIV, HCV, HBV, and Parvovirus B19, all of which were negative. A peripheral blood smear showed no schistocytes, ruling out intravascular hemolysis.Given the constellation of hepatosplenomegaly (Figure 1), cytopenias, intermittent fever, and polyclonal hypergammaglobulinemia (on electrophoresis), visceral leishmaniasis was suspected. The diagnosis was confirmed by both serological testing and PCR analysis of the bone marrow aspirate.
The patient was treated with Amphotericin B (17 mg/kg) for 3 weeks, resulting in hematologic improvement (Table 1), although he subsequently developed severe hypokalemia due to an iatrogenic tubulopathy.Additionally, bone marrow examination at admission revealed marked activation of the reticulo-histiocytic system with evidence of hemophagocytosis.
These findings supported a concurrent diagnosis of hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS) triggered by Leishmania infection. First-line treatment included dexamethasone and intravenous immunoglobulin (IVIG).

	Admission	Before Amphotericin B	After Amphotericin B	3 days before discharge	Discharge	Two weeks after Discharge
Hemoglobin (g/dL)	8.3	7.9	8.7	9.9	10.7	13.2
White Blood cells (U/µL)	2450	2090	5080	4970	5040	6880
Platelets (U/µL)	84 000	75 000	125 000	77 000	76 000	220 000

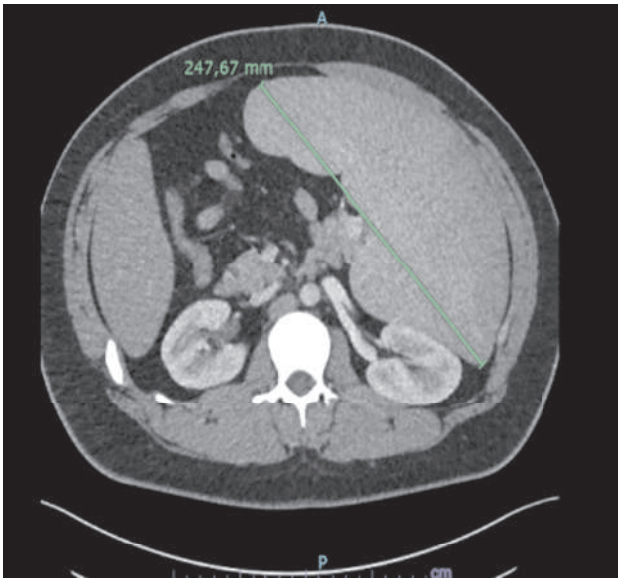

Figure 1. Abdominal CT scan showing marked splenomegaly (maximum diameter: 25 cm), in the absence of focal lesions.

PREDICT-HF: PREDICTIVE VALUE OF PULMONARY AND SYSTEMIC CONGESTION AFTER HOSPITALIZATION IN PATIENTS WITH HEART FAILURE. PRELIMINARY DATA OF A MULTICENTRIC OBSERVATIONAL STUDY

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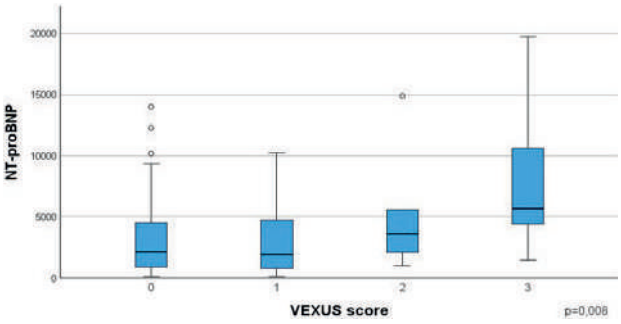
Background: Heart failure (HF) is a leading cause of hospitalization in Cardiology and Internal Medicine units, with rising incidence in recent years. It carries a high mid-term mortality and risk of readmission, especially shortly after discharge. Despite the known influence of factors such as age, comorbidities, blood markers, and residual venous congestion, there are currently no reliable integrated models to predict clinical deterioration post-discharge.
Purpose: This study aims to develop a predictive model for mortality or need for acute care in discharged HF patients, using clinical, laboratory, and ultrasound variables.
The main purpose of this study is to assess how different indicators of pulmonary and systemic congestion (clinical, laboratory, and ultrasound-based) can individually and collectively (via a multimodal approach) predict mortality, readmission or the need for intravenous diuretic treatment within 90 days in patients discharged after an episode of acute heart failure.
Methods: The PREDICT-HF study is a prospective multicenter nonpharmacological observational study, involving two Internal Medicine Wards (Ospedale Universitario L. Sacco,ASST Fatebenefratelli Sacco, Milano and Hospital Universitario Infanta Leonor, Madrid). The study includes patients admitted to hospital for acute heart failure, with evidence of a structural or functional cardiac disease. At discharge clinical, laboratory and ultrasound parameters were recorded - lung ultrasound, splanchnic vein Doppler sampling according to VExUS (Venous Excess UltraSound score), CA 125, NT-proBNP, Everest scale.
Primary outcome consists of a composite of 90-days mortality, readmission, need for urgent intravenous diuretic therapy.
The planned sample size is 200 patients; to date, a total of 131 patients have completed the study.
Results: The cohort is characterized by older patients with significant comorbidities (table 1); 28% have left ventricle reduced ejection fraction. A total of 33 patients experienced the primary outcome (26%).
The only factor associated with the endpoint is NT-proBNP (3549 pg/ml ± 3549 pg/ml vs 6772 pg/ml ± 8219 pg/ml, p 0,002).
Ischaemic heart disease is at the threshold of statistical significance (20.4% vs 36.4%, p 0,06).
On the contrary CA-125, ultrasound parameters of lung and splanchnic congestion (B lines, pleural effusion, IVC diameter and collapsibility, VExUS score) don't show any correlation with the outcome. Not even identifying congested patients by combining LUS with VexUS score has shown any prediction of the endpoint.
However VExUS score severity is observed to be significantly related to NT-proBNP values (VExUS 0 - NT-proBNP 3819 pg/ml ± 5640 pg/ml; VExUS 1 - NT-proBNP 2979 pg/ml ± 2837 pg/ml; VExUS 2 - NT-proBNP 5419 pg/ml ± 5563 pg/ml; VExUS 3 - NP-proBNP 7916 pg/ml ± 5952 pg/ml; p 0,008).
This is also true for significant lung congestion (defined by total B lines at LUS ≥ 15 and/or presence of pleural effusion) vs NT-proBNP (No significant lung congestion - NT-proBNP 3405 pg/ml ± 5212 pg/ml; presence of significant lung congestion - NT-proBNP 4844 pg/ml ± 5244; p 0,005).
Conclusions: Considering the preliminary nature of the data obtained so far, although the ultrasound assessment (lung ultrasound and VEXUS) is consistent with NT-proBNP levels in identifying congested patients, only NT-proBNP at discharge correlates with the primary endpoint.
Reaching the planned sample size will enhance the statistical power of the study to identify any potential predictor of the outcome.

Study population characteristics	
Age	80,93 yr ± 9.39
Sex	48% F
Arterial hypertension	86%
Diabetes	47%
Ischaemic heart disease	25%
COPD	35%
CKD	43%
eGFR	55 ml/min ± 21
Pulmonary hypertension	55%
LVEF < 50%	28%
Charlson Score	6,47 ± 2,01
Everest score	1,39 ± 1.85
Outcomes	26%
Total population	131 patients



THE ROLE OF POINT OF CARE ULTRASOUND (POCUS) IN EVALUATION OF HYPERTENSION MEDIATED ORGAN DAMAGE SCREENING AND DETECTION

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Introduction: European Society of Hypertension (ESH) guidelines for Arterial hypertension management suggest the evaluation of hypertension mediated organ damage (HMOD) to stratify cardiovascular risk, even if routine echocardiography is not suggested for all patients. Point of Care Ultrasound might be an alternative faster method first evaluation of HMOD.
Aim: to evaluate diagnostic accuracy of cardiac Point of Care Ultrasound with pocket size device (POCUS) for the identification of HMOD compared to standard echocardiographic assessment. Evaluate concordance of POCUS performed by non-trained operators and exert operator.
Methods: We designed a cross-sectional study in a population of hypertensive patients that access for the first time to the Hypertension Centre of Federico II University Hospital in Naples, Italy. Every patient underwent full clinical visit, cardiac-POCUS (c-POCUS) performed by a non-trained operator and by an expert and then full echocardiographic examination.. We evaluate with standard echocardiography presence of left ventricular hypertrophy (LVH) (defined as LV mass > 47 g/m2.7 in women and >50 g/m2.7 in men) and Left atrial (LA) dilatation defined as LA volume> 34 ml/m2. Furthermore, systolic function was also evaluated as ejection fraction (EF) and define preserve if > 55%. Visual estimation of LVH, LA dilatation and EF was performed with c-POCUS by non-trained and exert operators.
Results: We recruited 193 consecutive hypertensive patients with characteristics reported in table 1. We analyze performance of c-POCUS in HMOD detection using standard echocardiography as reference test. Diagnostic accuracy of c-POCUS for evaluation of LVH was 81.5 (95%CI 75-86) for expert and 70 (95%CI 63-77) for non-trained operator. For LA accuracy of c-POCUS was 88.9 (95%CI 84-93) for expert and 80 (95%CI 74-86) for non-trained operator. For evaluation of systolic function accuracy of c-POCUS for preserved EF was 91 (95%IC 86-35) for expert and 89 (95%CI 83-93) for non-trained operator.
Conclusion: As shown by our data, c-POCUS could be suggested as HMOD screening test in hypertensive patients to refine their cardiovascular risk, even if executed by a non-expert operator.

Table 1: Patients characteristics at Baseline	
Patients (N=193)	
Age (years)	55.4 ± 15.6
Male (n, %)	101 (52.6%)
BMI (kg/m^2)	28 ± 5
PAS (mmHg)	137.5 ± 12.4
PAD (mmHg)	81.8 ± 12.4
FC (bpm)	70.6 ± 11.3
Dyslipidaemia (%)	42.2 %
DM2 (%)	11.7 %
Stroke (%)	1.1 %
Ischemic Heart disease (%)	5.7 %
Atrial Fibrillation (%)	4.2 %
OSAS (%)	2.6 %
Smoking habits (%)	28.6 %

DRUG-INDUCED PNEUMONIA IN ONCOLOGY: NOT ONLY IMMUNE CHECKPOINT INHIBITORS

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A 66-year-old male presented to the Emergency Department of "S. Croce e Carle" Hospital in Cuneo with persistent low-grade fever for approximately one month and progressively worsening dyspnea. The patient had a known diagnosis of oligometastatic pancreatic adenocarcinoma, under active chemotherapy with gemcitabine and nab-paclitaxel. His medical history included arterial hypertension and type 2 diabetes mellitus.
A contrast-enhanced chest-abdominal CT performed in the preceding weeks had ruled out pulmonary embolism but revealed bilateral upper lobe ground-glass opacities, interpreted as nonspecific. Concurrently, a reduction in both the primary pancreatic tumor and the hepatic metastasis was observed. Despite two empirical courses of antibiotic therapy initiated by the attending physicians, no clinical improvement was noted.
On presentation, arterial blood gas analysis indicated type I respiratory failure, with mildly elevated inflammatory markers and negative procalcitonin. Chest radiography showed multiple confluent opacities, predominantly on the right side. The patient was subsequently admitted to the High-Intensity Internal Medicine Unit.
During hospitalization, a chest CT scan demonstrated diffuse bilateral consolidations with a peripheral distribution and multiple peribronchial microfoci in the lower lobes, consistent with atypical pneumonia. Bronchoalveolar lavage did not reveal any pathogens, and blood and urine assays for specific antigens and antibodies were negative. Given the ongoing chemotherapy and the clinical-radiological findings, a diagnosis of drug-induced pneumonitis—likely gemcitabine-related—was considered.
Systemic corticosteroid therapy with methylprednisolone (1 mg/kg/day) was initiated, leading to rapid clinical improvement, discontinuation of oxygen supplementation, and resolution of fever. The patient was discharged with a tapering corticosteroid regimen, pulmonology follow-up, and resumed oncological monitoring at the referral center. At two months post-discharge, he remained clinically asymptomatic and was continuing chemotherapy with an alternative regimen.
Gemcitabine, although widely used, is associated with pulmonary toxicity in approximately 5% of patients. Clinical manifestations range from mild dyspnea to acute respiratory distress syndrome (ARDS). Symptoms may appear weeks or months after therapy initiation, though rare cases have been reported after a single dose1. The mechanism is believed to be non–dose-dependent and may involve endothelial dysfunction or cytokine-mediated inflammation. Recognized risk factors include concurrent treatment with taxanes2 (as in this case), prior thoracic radiotherapy, preexisting pulmonary fibrosis, pulmonary malignancies, and asbestos exposure. Management typically involves systemic corticosteroids, such as methylprednisolone or prednisone at 1 mg/kg/day, followed by gradual tapering. This case highlights the importance of considering pulmonary toxicity even in patients treated with conventional cytotoxic agents like gemcitabine, not solely those receiving immune checkpoint inhibitors, which are more frequently associated with similar presentations.
1 Umemura S, Yamane H, Suwaki T, et al. Interstitial lung disease associated with gemcitabine treatment in patients with non-small-cell lung cancer and

pancreatic cancer. J Cancer Res Clin Oncol. 2011
2 Belknap SM, Kuzel TM, Yarnold PR, et al. Clinical features and correlates of gemcitabine-associated lung injury: findings from the RADAR project. Cancer. 2006

WHEN A STROKE TELLS A DEEPER STORY: CARDIAC AMYLOIDOSIS REVEALED THROUGH A NEUROLOGICAL EVENT

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All patients presenting with stroke should undergo a thorough diagnostic work-up, beginning with a detailed history and physical examination, to identify the precise etiology of the neurological event. While the majority of ischemic strokes are attributed to cardioembolism, large vessel atherothromboembolism, or small vessel disease, a subset remains cryptogenic. In other cases, stroke may serve as a sentinel event, unveiling a more complex systemic condition.
Our case is worthy of attention as, at the end of our diagnostic work-up, the patient was discovered to suffer from cardiac amyloidosis (CA).
A 82 year-old woman arrived at the Emergency Department with sudden-onset global aphasia and right hemiparesis. Not eligible for thrombolysis, she was admitted to our Internal Medicine Ward due to unavailability of beds in the Neurology Unit. Her past medical history was notable for heart failure with reduced ejection fraction (EF), long-standing arterial hypertension, hypercholesterolemia, atrial fibrillation (AF) and microvascular angina. Since 2017 she had been followed for suspected hypertrophic cardiomiopathy, but this feature was not further evaluated. Additional relevant history included bilateral carpal tunnel syndrome and progressive hearing loss – two red flags that would later prove significant. Her home medication included sacubitril-valsartan, potassium canrenoate, furosemide, apixaban, diltiazem, atorvastatin.
On arrival, she was apyretic with stable vital signs. ECG confirmed the presence of AF (75 bpm) with a left anterior fascicular block. Physical examination confirmed the neurological deficit of right hemiparesis. Macroglossia was also observed. Cranial CT revealed a cortico-subcortical hypodensity in the left fronto-insular region. The hypothesis of a trivial cardioembolic stroke was supported by the anamnestic information of AF and by low adherence to treatment, in particular apixaban and sacubitril-valsartan, reporting episodes of pre-syncope after taking sacubitril-valsartan. However, several additional findings prompted broader evaluation.
Laboratory data revealed elevated hemoglobin (16.6 g/dL) and hematocrit (47,5%) as well as a monoclonal protein spike on serum electrophoresis. The presence of an IgG lambda monoclonal band (0,5 g/dL) was confirmed by immunofixation. The free light chain ratio was within normal limits (1,18) and no CRAB criteria for multiple myeloma were met, supporting a diagnosis of monoclonal gammopathy of undetermined significance (MGUS). Testing for JAK2 mutation was negative, reducing the likelihood of a myeloproliferative disorder. Transthoracic echocardiography revealed concentric ventricular hypertrophy, thickened atrioventricular valves, and a characteristic apical sparing on left ventricle global longitudinal strain, the so-called "cherry-on-top" pattern, suggestive of amyloid infiltration (**figure 1**).
The constellation of findings – macroglossia, bilateral carpal tunnel, orthostatic hypotension, echocardiographic pattern– raised strong suspicion for cardiac amyloidosis (CA). A 99mTc-labeled bone scintigraphy demonstrated intense cardiac uptake with a Perugini score of 3 (**figure 2**), highly suggestive of transthyretin-related (ATTR) CA. Subsequent investigation, in particular cardiac MR and periumbilical fat pad biopsy were concordant with the hypothesis of cardiac amyloidosis ATTR wild-type (wt). As a matter of fact, a preliminary salivary test for common mutations was negative; definitive genetic testing is ongoing. In line with Gilmore's diagnostic algorithm, the presence of a serum monoclonal component required hematologic evaluation, which ruled out the coexistence of AL amyloidosis.Unfortunately, assessment of functional capacity (6MWT and KCCQ) revealed severe impairment, and the patient was not deemed suitable for initiation of targeted therapies at that stage.
Nonetheless, our diagnostic efforts proved clinically valuable for at least two key reasons:
This case highlights the pivotal role of Internal Medicine in managing complex, multisystemic presentations. During the diagnostic work-up of a suspected cardio-embolic stroke some red-flags appeared and their correct interpretation led us to an overlooked diagnosis (**figure 3**). It is worth noting that thrombotic events are increasingly recognized in ATTR amyloidosis, not only due to the high prevalence of AF but also as a consequence of mechanical dysfunction, atrial myopathy and altered hemodynamics.

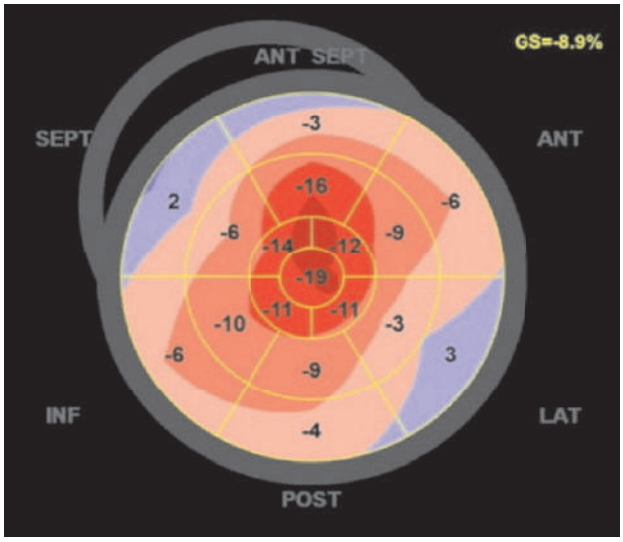

Figure 1

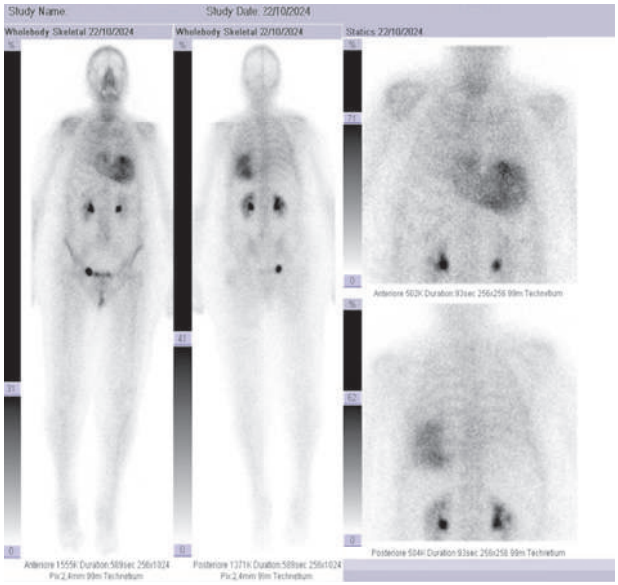

Figure 2

Extracardiac and cardiac amyloidosis red flags according to literature vs our case		
	Our patient	Amylodosis where it is most frequently found
Polyneuropathy	No	ATTRv, AL, AA, AGel
Dysautonomia	No	ATTR, AL
Skin bruising	No	AL
Macroglossia	Yes	AL
Deafness	Yes	ATTRwt
Bilateral carpal tunnel syndrome	Yes	ATTRv, ATTRwt
Ruptured biceps tendon	No	ATTRwt
Lumbar spinal stenosis	No	ATTRwt
Vitreous deposits	Not evaluated	ATTRv
Corneal lattice dystrophy	Not evaluated	AGel
Family history	No	ATTRv, AApoAI, AApoAII
Renal insufficiency	No	AL, AA
Proteinuria	No	AL, AA
Orthostatic hypotension	Yes	ATTR, AL
Low/decreased QRS voltage to degree of LV thickness	Yes	All
Granular sparkling of myocardium	Yes	All
Increased right ventricular wall thickness	Yes	All
Increased valve thickness	Yes	All
Reduced longitudinal strain with apical sparing pattern	Yes	All
Pericardial effusion	No	All

Figure 3

CRITICAL GAPS IN CONTEMPORARY CARDIOVASCULAR RISK ASSESSMENT: UNDERESTIMATION OF OBESITY-ASSOCIATED RISK IN CURRENT CLINICAL ALGORITHMS

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Background: Obesity is a major independent risk factor for cardiovascular disease (CVD), acting through multiple mechanisms including insulin resistance, hypertension, dyslipidaemia and chronic inflammation. Despite this, SCORE2, the 10-year cardiovascular risk algorithm endorsed by European guidelines, does not account for adiposity, omitting measures such as body mass index (BMI). This limitation may result in systematic underestimation of risk in individuals with obesity. We evaluated the agreement between SCORE2-estimated cardiovascular risk and clinically established CVD and investigated whether BMI provides additional predictive value in an obesity-predominant population.
Methods: We retrospectively analysed 115 adults referred for cardiometabolic assessment; 88% had obesity (BMI ≥30 kg/m²). All participants had complete data for SCORE2, lipid profile, blood pressure and anthropometrics. CVD was defined as documented coronary or atherosclerotic vascular disease. High-risk status was defined as SCORE2 ≥7.5%. Multivariable logistic regression examined associations between CVD and SCORE2 or BMI (standardised as z-scores), adjusting for sex and smoking. Odds ratios (OR) with 95% confidence intervals (CI) were calculated.
Results: SCORE2 identified only 16% of patients as high risk, despite a high prevalence of obesity and cardiometabolic burden. Among obese individuals classified as low risk (SCORE2 <7.5%), several had established CVD. SCORE2 was not significantly associated with CVD presence (β = 0.03; OR 1.03, 95% CI: 0.29–3.71; p = 0.935). In contrast, BMI showed a stronger, though non-significant, association (β = 0.93; OR 2.53, 95% CI: 0.80–8.01; p = 0.122). Smoking was not predictive (p = 0.849), and male sex showed a borderline inverse association (OR 0.08, 95% CI: 0.01–1.23; p = 0.080).
Conclusion: These findings highlight the limited discriminatory power of SCORE2 in obesity, potentially misclassifying high-risk individuals. SCORE2 may underestimate cardiovascular risk in patients with obesity, failing to capture adiposity-driven risk in clinical practice. Although not statistically significant, BMI showed a stronger association with CVD than SCORE2, suggesting it may reflect risk in this population. Incorporating adiposity-related metrics into future risk algorithms could improve the identification of high-risk individuals and support more equitable, tailored prevention strategies.

WHEN HISTORY MISLEADS: A CHALLENGING CASE OF FEVER OF UNKNOWN ORIGIN

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Introduction: Fever of unknown origin (FUO) is defined as a temperature > 38.3°C for at least three weeks, which remains undiagnosed after one week of extensive medical evaluation. The potential etiology can be grouped into: infectious, inflammatory, malignant and miscellaneous. Given the diagnostic and management complexities, the classification of FUO has been revised to create four classes: classic FUO, healthcare-associated FUO, immunodeficiency-related FUO, and travel-associated FUO. [1]
Case report: A 62-year-old woman was admitted to our medical department with a two-month persistent fever, night sweats, asthenia and palpitations. One week before, she attended the Emergency Room exhibiting similar symptoms: no definitive etiology was identified. Suspecting an infectious disease, she was subsequently discharged with a course of antibiotic therapy consisting of Levofloxacin.
Her past medical history included:
- Follicular lymphoma, in remission since 2019. A recent total body computed tomography scan showed slight enlargement of axillary and mammary lymph nodes;
- Myocarditis in 2019;
- Symptomatic paroxysmal supraventricular tachycardia (PSVT) with lipothymia;
- Splenic thrombosis, managed with DOAC;
- Anxious depressive syndrome on treatment;
Despite fever, she was hemodynamically and respiratory stable, and her symptoms were initially treated only with acetaminophen. Subsequent microbiological investigations, including blood and urine cultures, a nasal swab for Methicillin-resistant *Staphylococcus aureus* (MRSA) and samples for the detection of respiratory bacteria and viruses resulted negative.
To exclude a potential recurrence of the patient's oncohematological disease, a chest CT scan was performed. It revealed a 55x45 mm pulmonary consolidation in the right superior lobe, without enlargement of lymphadenopathies, thereby rendering a lymphoma recurrence less likely.
Considering the presence of pulmonary emphysema related to the long-term history of smoking, and suspecting oncological versus infectious disease, a bronchoscopy with bronchoalveolar lavage was performed. A transthoracic echocardiogram excluded endocarditis.
During hospitalization, second-line microbiological tests were performed. The QuantiFERON test was positive, leading us to a further hypothesis. The patient was placed in isolation and additional tests were carried out on stool, urine and broncho-alveolar lavage to confirm active tuberculosis; all of them returned negative.
Patient's laboratory results progressively worsened, with white blood cell count rising to 14400/mmc and C-reactive protein at 186 mg/L, and the recurrent fever was debilitating the patient. Therefore, we introduced empirical antibiotic therapy with ceftazidime and clindamycin, without significant clinical improvement.
Finally, tests on bronchoalveolar lavage did not confirm mycobacteria or malignant tumor cells. BAL culture was positive for methicillin-sensitive Staphylococcus aureus (MSSA) and Fusobacterium nucleatum resistant to clindamycin. Targeted antibiotic therapy was started using cefazolin plus metronidazole. Moreover, to further support the diagnosis and rule out a neoplastic mass superinfection, a fine needle aspiration biopsy was performed, revealing fibrotic tissue and neutrophilic leukocytosis, confirming the absence of neoplasia.
Starting the specific antibiotic therapy, patient's condition improved with stable apyrexia and normalization of the inflammatory markers. The patient was discharged on oral antibiotic therapy. Given the patient's home antidepressant therapy, it was suggested a course of delafloxacin, a quinolone that is not associated with QTc prolongation.
One week after the discharge, the patient was asymptomatic and biochemistry remained in the normal range. A chest CT scan showed a reduction of the pulmonary lesion at three weeks.
Discussion: In Europe, tuberculosis is still the leading cause of FUO. In our patient, we suspected tuberculosis due to the QuantiFERON test and the presence of a pulmonary lesion. Non-Hodgkin lymphoma is another potential cause of FUO that we needed to rule out, given the patient's past medical history. FUO related to solid tumors is less common, but we still must take it into account due to the patient's history of tabagism and suggestive imaging findings.
During hospitalization, we searched for an infectious cause: the failure of broad-spectrum antibiotic treatment made the infectious etiology less likely. The positivity of the broncho-lavage fluid culture provided us with an unexpected diagnosis that fortunately allowed for an appropriate management with a resolution of fever.
Conclusion: Fever of Unknown Origin (FUO) remains a challenging clinical entity due to its complexity and the wide array of underlying etiologies that necessitate sequential exclusion to reach a diagnosis.
Additionally, it is important to recognize that while the patient's clinical history is essential, it can sometimes lead to a misleading diagnosis, delaying accurate identification of the underlying case.
[1] Haidar, G. et al. Fever of Unknown Origin. N Engl J Med. 2022

SINDROME IPEREOSINOFILA LINFOCITARIA VARIANTE LGL/NK LIKE CON POLISIEROSITE EOSINOFILICA E COINVOLGIMENTO MULTIORGANO

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Background: lymphocytic variant hypereosinophilic syndrome (L-HES) is a rare form of HES in which an aberrant T-cell clone produces IL-5. The $CD3^-CD4^+$ phenotype predominates; in fewer than 10 % of cases, LGL/NK-like clones ($CD3^+CD8^+CD56^+CD57^+$) emerge. Although numerical criteria, namely an absolute eosinophil count (AEC) ≥ 1 500 cells/mm³ for ≥ 6 months have been established, recent guidelines also recognize chronic tissue eosinophilia with organ damage as a diagnostic equivalent. Primary differential diagnoses include ANCA-associated vasculitis and myeloproliferative forms.
Case report: a 64-year-old man with a history of schizophrenia and adult-onset bronchial asthma with nasal polyposis underwent esophagogastroduodenoscopy for abdominal pain, anorexia, and recurrent diarrhea, revealing findings consistent with eosinophilic gastroenteritis. In the following months, he developed extensive polyserositis characterized by:
Peripheral AEC remained moderate (800–1 100 cells/mm³, 18 %), without other abnormalities in complete blood count, vitamin B_{12}, LDH, or tryptase. Serologies for parasites, ANCA, and IgE levels were negative, as were tests for FIP1L1-PDGFRA and the KIT D816V mutation. Further evaluation by peripheral-blood flow cytometry demonstrated reduced $CD4^+$ lymphocytes (207 cells/mm³), an inverted CD4:CD8 ratio (~1:1.8) and a 25 % expansion of lymphocytes with the $CD3^+CD8^+CD56^+CD57^+$ phenotype. BIOMED-2 PCR for T-cell receptor β revealed dominant, reproducible incomplete Dβ–Jβ rearrangements, confirming T-cell clonality. Cardiac MRI excluded eosinophilic myocarditis. CT of the facial massif, performed to investigate nasal polyps for possible biopsy, was negative, as was PET/CT for disease staging to assess potential progression toward high-grade peripheral T-cell lymphoma.
A diagnosis of L-HES, LGL/NK-like variant, was made based on:
The patient was treated with methylprednisolone 40 mg/day for 5 days, then 20 mg/day with gradual tapering, combined with mepolizumab 300 mg subcutaneously every 4 weeks. At 3 weeks: AEC < 300 cells/mm³, resolution of ascites and serous effusions, no recurrence of cardiac tamponade, and
LGL clone < 5 %.
This case report highlights that the LGL/NK-like variant of L-HES (an exceedingly rare entity not previously described in association with extensive polyserositis) can present with moderate peripheral eosinophilia but severe polyserositis and cardiac tamponade. An integrated diagnostic approach using flow cytometry, TCR clonality assessment and demonstration of tissue eosinophilia permits diagnosis even in the absence of an AEC ≥ 1 500 cells/mm³ for 6 months. Treatment with corticosteroids and anti–IL-5 offers a rapid and effective therapeutic option, obviating the need for cytotoxic chemotherapy.

ORAL ALLERGY SYNDROME AS A MARKER OF FOOD ALLERGY IN A MONOCENTRIC COHORT OF ATOPIC PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Background: Eosinophilic esophagitis (EoE) is a chronic, immune-mediated disease of the esophagus frequently associated with atopic conditions. The role of food allergy, particularly IgE-mediated mechanisms, remains unclear. Oral allergy syndrome (OAS), commonly observed in atopic individuals, may serve as a clinical marker for food allergy and offer insight into disease phenotypes within EoE.
Objective: This study aimed to evaluate the prevalence and clinical significance of OAS in a monocentric cohort of atopic and non-atopic adult patients with EoE, examining its potential as a marker of food allergy and a tool to distinguish EoE phenotypes.
Methods: A retrospective analysis was conducted on adult patients with confirmed EoE diagnosis, followed at the Allergy Unit of San Raffaele Hospital between January 2022 and August 2024. Clinical, endoscopic, histologic, and allergy data were collected and analyzed. Patients were divided into atopic and non-atopic groups based on clinical history and sensitization profiles. Statistical analysis was performed to compare clinical features and diagnostic markers between the groups.
Results: Of 44 patients included, 31 were atopic and 13 non-atopic. OAS was reported in 67.7% of atopic patients and in none of the non-atopic group ($p<0.05$). Atopic patients showed a shorter diagnostic delay and more frequent proximal esophageal eosinophilic infiltration. Despite similar endoscopic severity scores (EREFS), non-atopic patients had higher mean eosinophil counts per high-power field. Sensitization to cow's milk proteins was observed in 71% of atopic patients, though often asymptomatic.
Conclusions: OAS is highly prevalent in atopic EoE patients and may serve as a useful clinical marker for identifying food allergy and guiding phenotypic stratification. The findings highlight the heterogeneity of EoE and underscore the need for personalized diagnostic and therapeutic approaches. Larger, prospective studies are warranted to validate these observations and further explore the immunopathogenic role of atopy in EoE.

RAPID EFFECTIVENESS OF ANIFROLUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH HEMATOLOGICAL INVOLVEMENT

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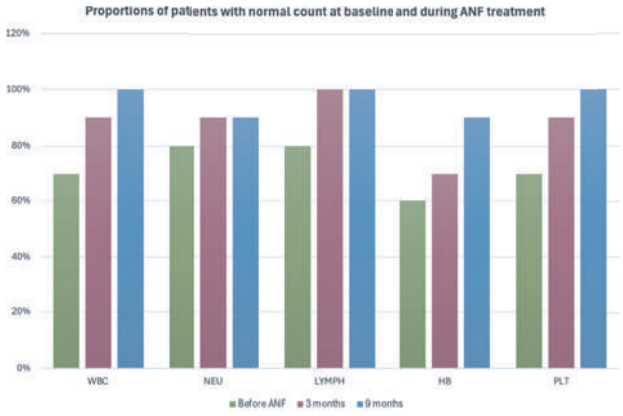
Introduction: Systemic lupus erythematosus (SLE) is a multi-system autoimmune disease of variable severity and course, characterized by a tendency for flare and progressive organ damage. Hematological manifestations in SLE include anemia, leukopenia, lymphopenia, and thrombocytopenia which are commonly associated with other organ manifestations and an active state of SLE. Anifrolumab (ANF) is a type I interferon receptor inhibitor recently approved for the treatment of adults with SLE, particularly in patients affected by cutaneous and musculoskeletal manifestations. However, its efficacy in patients with hematologic manifestations is not well established.
Methods: This monocentric retrospective study aims at assessing the effectiveness of anifrolumab in normalization of white blood cell counts, hemoglobin [Hb], and platelets in SLE patients with hematological manifestations. Response to treatment was evaluated at different time points [before ANF beginning (T0), three months from ANF introduction (T1) and last available follow-up at nine months (T2)].
Results: Among the ten patients who received anifrolumab 300 mg monthly, patients who had low baseline levels of white blood cells (WBC) were 3/10 (30%), while 4/10 (40%) had low Hb levels and 3/10 (30%) had low platelet count. At Week 12, WBC normalized in 2 patients (all patients have normalized lymphocyte levels, while one patient normalizes neutrophil count). Concomitantly, Hb levels normalized in one patient, while platelet counts normalized in two patients. During last follow-up at nine months, the improvement in laboratory

values persisted and lymphocyte levels and platelet counts returned to normal in all patients, while Hb levels normalized in two additional patients (90%).
Conclusion: Despite our preliminary data on small size population of SLE patients with hematological manifestations, type I IFN blockade with ANF appears to be effective in inducing sustained and rapid improvement of hematological parameters. Prospective studies are warranted to corroborate these data.



NOT JUST A SYNCOPE: SIADH DUE TO CRANIAL TRAUMA

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Background: The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a disorder of water and electrolyte balance characterized by an impaired ability to dilute urine and hypotonic hyponatremia secondary to excessive water retention in the absence of renal disease or other identifiable non-osmotic stimuli known to trigger antidiuretic hormone (ADH) release.
Clinical Presentation: A 68-year-old man presented to the emergency department with lethargy and altered mental status. Laboratory tests revealed severe hyponatremia (109 mEq/L). Approximately 45 days earlier, he had been admitted to the ED for a syncopal episode of cardiogenic origin complicated by head trauma. On that occasion a cranial CT scan revealed a small left frontotemporal subdural hematoma, subarachnoid hemorrhage and a small intraparenchymal hemorrhagic focus with no indication for neurosurgical intervention. During that hospitalization prophylactic treatment with Levetiracetam was initiated.
Differential Diagnosis: The patient was admitted to our department and underwent blood and urine chemistry tests which revealed hypotonic hyponatremia (260 mOsm/L) with elevated urine osmolality (604 mOsm/kg) and increased urinary sodium excretion (119 mMol/L). On physical examination the patient appeared euvolemic with normal skin and mucosal hydration supported by normal hematocrit, BUN/creatinine ratio, serum potassium, BNP and inferior vena cava diameter with no evidence of peripheral edema. This clinical picture allowed us to exclude, as a first hypothesis, cerebral salt-wasting syndrome (CWS) which is characterized by hypovolemic hyponatremia secondary to central nervous system disorders. TSH, ACTH, cortisol and aldosterone levels were subsequently measured and found to be within normal limits, thereby ruling out hyponatremia due to hypothyroidism or primary/secondary adrenal insufficiency. Given the hypothesis of SIADH, the patient underwent contrast-enhanced total-body CT scan for investigation of an underlying cause and Levetiracetam therapy was discontinued.
Results: The contrast-enhanced total-body CT scan was negative for oncological pathology and, despite discontinuation of antiepileptic therapy, hyponatremia persisted. A diagnosis of SIADH secondary to the previous cranial trauma, which had not yet fully resolved, was established. Given the impossibility of eliminating the underlying cause, the lack of a surgical option and the contraindication to fluid restriction due to cerebral hemorrhage, the patient started Tolvaptan 15 mg/day with dose titration based on serum sodium levels and clinical response.
Pathophysiology: The condition is characterized by an absolute increase in total body water resulting from excessive intake relative to the kidney's limited ability to dilute urine and produce an appropriate compensatory diuresis. ADH is secreted by the neurohypophysis and exerts its physiological effects at the level of the collecting ducts in the distal renal tubule by regulating water excretion through V2 receptors and aquaporin-2 channels. In the absence of ADH, these cells are impermeable to water. Various pathophysiological models of osmotic regulation in SIADH have been described, ranging from elevated ADH levels to mutations in V2 receptors leading to an exaggerated response to ADH. Underlying causes should primarily be sought among neoplastic diseases, pulmonary disorders, central nervous system abnormalities, and certain medications.
Discussion and Conclusion: This case highlights the importance of properly evaluating hyponatremia by following a diagnostic algorithm that initially involves distinctive among pseudohyponatremia, hypertonic hyponatremia and hypotonic hyponatremia. In cases of hypotonic hyponatremia, it need further differentiation based on urine osmolality, urinary sodium concentration and volume status. SIADH is a diagnosis of exclusion and needs investigation of the underlying cause. The only definitive treatment is removal of the causal factor. When this is not possible, one of the new therapeutic options includes non-peptide vasopressin receptor antagonists-vaptans or aquaretics.

DESIGN AND INITIAL IMPLEMENTATION OF A "VERY" FAST-TRACK FOR GIANT CELL ARTERITIS: THE EXPERIENCE OF FATEBENEFRATELLI-SACCO

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Introduction: Giant Cell Arteritis (GCA) is the most frequent idiopathic vasculitis of the elderly, characterised by robust systemic inflammation and patchy large vessel vasculitis. Suspected GCA is considered a medical urgency due to the risk of abrupt onset of ocular involvement, which occurs in up to a quarter of subjects and results in persistent visual loss in about 80% of them. Ocular involvement by GCA represents the most frequent medical emergency in ophthalmology.
Importantly, early diagnosis and adequate steroid treatment reduce the risk of ocular ischemia and blindness. Therefore, it is recommended to develop a fast-track pathway for rapid referral of new suspected patients to a specialist in charge of GCA diagnosis and therapy. In literature, different studies have demonstrated the utility of the fast-track pathway to reduce the risk of blindness and the cumulative dosage of steroids.
The ophthalmic Emergency Room (ER) at Fatebenefratelli-Oftalmico Hospital of Milan naturally represents a collector of severe GCA with ocular involvement that requires emergent work-up. Therefore, we aimed at implementing a "very" fast-track at our center that could answer to clinical requirements of patients with or without visual involvement and represent a backbone facility for i) referring physicians in the territory as well as neighbouring hospitals, and ii) translational research studies requiring biologic specimens collected before steroid therapy. A secondary objective was to verify the feasibility of the process.
Methods: The "very" fast-track pathway for GCA was activated at our center in January 2024. Briefly, trigger figures of the process are i) internal physicians suspecting GCA, mostly in both the ophthalmic and general ERs, but also in the clinics and wards, and ii) external physicians in the territory (eg, general practitioners and territorial specialists) or specialists from other Hospitals. These figures contact a "clinical GCA team" to verify the initial suspicion for GCA and confirm the activation of the "very" fast-track. This is based in the Ophthalmic ER, and includes biochemistry, temporal artery biopsy by an on-call "bioptic team" and a specialist assessment by the "clinical GCA team" which may perform temporal artery ultrasonography and defines the provisional diagnosis and treatment, which includes emergent steroid pulse in the case of ischemic complications. Similarly, in the case of suspected ocular involvement, ophthalmologic assessment is performed in parallel. After the acute setting, patients are directed to a specific vasculitis clinic in the hospital or return to their referring center. This "very" fast track is active every working day, but the clinical team is available on call 7 days/week and designed to be implemented as much as possible within a few hours (typically, less than 3 hours) after its activation: to perform intra-day temporal artery biopsies, patients are required to arrive in the ER by 2:30 PM. For no reason, steroid therapy has been withheld for more than 60 minutes to perform a temporal artery biopsy.
Results: Since January 2024, 67 patients with suspected GCA have been managed by our "very" fast track. The final diagnosis of these was GCA in 62 patients. Biopsy was not performed in nine patients due to contraindications, denying of consent to the procedure. Temporal artery biopsies were performed before steroid therapy in 28 cases, and after steroids in 26 (ie, in the case of initiation of steroid therapy during late afternoons, nights, or weekends). Compared to the conventional pathway before 2024, we observed a higher in-

cidence of GCA diagnoses with this fast-track pathway, especially during the latter half of 2024 and the first four months of 2025 (see Figure 1). In fact, in 2022, 15 suspected GCA cases were evaluated, while in 2023, GCA was suspected in 12 patients.
Conclusion: A "very" fast track is feasible in selected academic Hospitals, fostering an increase in the incident cases at our center. Clinical and translational implications appear obvious, although future epidemiologic studies should verify the impact of such organization on the prognosis of GCA in our territory.

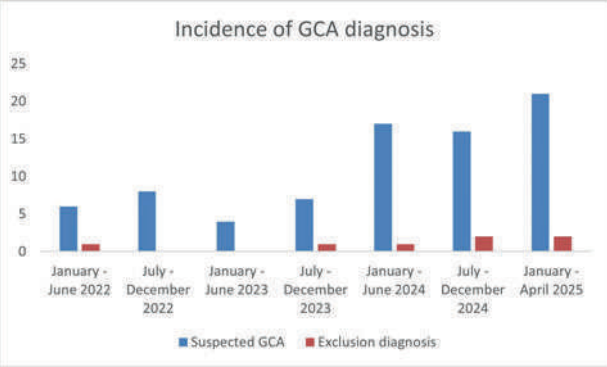

Figure 1. Incidence of GCA diagnosis before and after 2024

INTERSTITIAL LUNG DISEASE ASSOCIATED WITH COMMON VARIABLE IMMUNODEFICIENCY (CVID): A CASE SERIES

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Background: Common variable immunodeficiency (CVID) is a rare disease characterized by decreased immunoglobulin levels and heterogeneous clinical features, ranging from infections to non-infectious manifestations due to immune dysregulation. Interstitial lung disease (ILD) is a non-infectious complication found in approximately 10-20% of patients with CVID. This condition increases morbidity and mortality and, therefore requires early diagnosis and management.
Methods: We review the clinical data of three patients with CVID-ILD (2 males, 1 female; median age 37.3 years), referred to the Department of Rheumatology and Clinical Immunology of the University of Salerno, from August 2022 to March 2025. They represent about 20% (3/14) of all CVID patients in our centre (4 males, 10 females, median age 67.8 years). The diagnosis of ILD was based on clinical and radiological findings. A HRCT and lung function tests with DLCO were performed in all patients of our cohort.
Results: The demographic characteristics of our patients are shown in Table 1. Notably, the mean diagnostic delay is 13.3 years, higher than the group of CVID without ILD (3.9 years); this is probably because in CVID-ILD the disease often begins early with autoimmune manifestations than infections. In 2/3 patients the diagnosis of ILD was made at the same time as the diagnosis of CVID. All patients started immunoglobulin replacement therapy (IRT) at the CVID diagnosis. Infections and non-infectious complications are listed in Table 2. The most frequent infections, found in all patients, are upper respiratory tract infections (URTI) such as sinusitis, otitis and pharyngitis, and lower respiratory tract infections (LRTI) such as bronchitis and pneumonia. In our cohort, there is no significative difference in the frequence of respiratory tract infections between the CVID-ILD group and that without ILD, before starting IRT; this could mean that the development of ILD is a distinct phenomenon, not primarily driven by recurrent infections. Interestingly, in all patients with CVID-ILD the first manifestation of immunodeficiency was a hematological autoimmune disease, mostly immune thrombocytopenia (ITP). Splenomegaly is found in all cases. No gastrointestinal complications are recorded in these patients. The most common respiratory symptoms were dyspnea (patient 1) and persistent cough (patients 1, 2). Table 3 shows the pulmonary function tests. A mild or moderate DLCO impairment is present in all three cases, as expected in the ILDs. On global spirometry, total lung capacity (TLC) is reduced in 2/3 patients and it is indicative of a restrictive respiratory deficit. Dynamic lung volumes are variable among our patients: no one present an obstructive pattern while a mild reduction in forced vital capacity (FVC) is present in patients 1 and 3, as a possible indirect indicator of restrictive pattern. HRCT scan findings are represented in Table 4. All patients show bronchiectasis, ground glass opacity and adenopathy. In 2/3, small nodules and consolidation are found.
Conclusions: In this case series, CVID-ILD is associated with splenomegaly, autoimmune cytopenias and lymphoadenopathy, with a more complicated course of the disease. Our patients received a diagnosis of ILD based on clinical presentation, pulmonary function tests and characteristic imaging features. Currently, there is still a lack of consensus guidelines for the diagnosis of CVID-ILD; in some cases, it is necessary to perform a bronchoalveolar lavage or a lung biopsy to exclude other differential diagnosis (e.g. infections, sarcoidosis, lymphoma). ILD developed despite IRT in patient 3; in patient 1 and 2 IRT was started at the diagnosis of ILD. Patients with CVID-ILD often require immunosuppressive treatment for their lung disease, which complicates the management of the immunodeficiency.

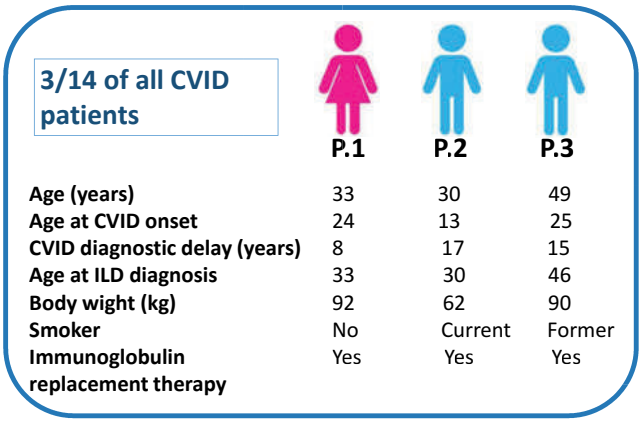

Table 1: Characteristics of the patients

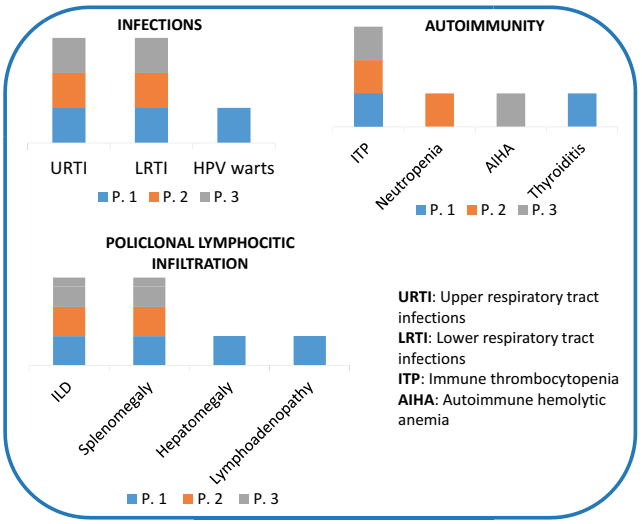

Table 2: Clinical features of CVID*Evans syndrome consists of autoimmune hemolytic anemia and thrombocytopenia

	P. 1	P. 2	P. 3
FEV1/FVC	78	91	75
FEV1 (% of predicted)	69	93	76
FVC (% of predicted)	74 ↓	84	76 ↓
TLC (% of predicted)	86	79 ↓	76 ↓
DLCO (% of predicted)	51 ↓	69 ↓	58 ↓

Table 3: Lung function parameters

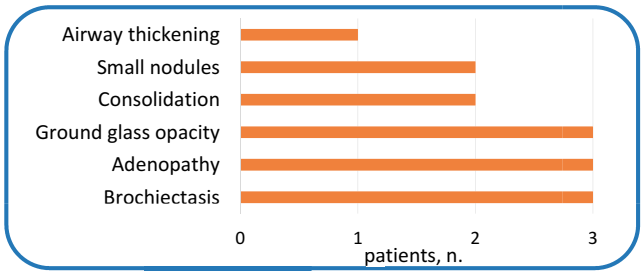

Table 4: HRCT scan findings

DIAGNOSTIC ACCURACY OF POCUS IN ACUTE ABDOMINAL PAIN IN THE EMERGENCY DEPARTMENT: A PROSPECTIVE OBSERVATIONAL STUDY

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Obiettivo: L'ACUTE ABDOMEN (Ali, 2019) è stato proposto come protocollo di ecografia point of care (POCUS) in grado di evidenziare le cause principali di addome acuto. L'obiettivo di questo studio è validare in maniera prospettica il protocollo, valutandone accuratezza diagnostica in confronto al gold standard, nei pazienti che accedono in Pronto Soccorso (PS) per dolore addominale acuto severo.
Metodo: Si tratta di uno studio prospettico osservazionale monocentrico che ha incluso pazienti maggiorenni che accedevano in PS per addome acuto sottoposti a POCUS secondo ACUTE ABDOMEN e TC con MDC.
Risultati: Lo studio ha incluso 215 pazienti (116 donne, 54%), con età mediana 64 anni (IQR 50-80), Il protocollo ACUTE ABDOMEN veniva eseguito in una mediana di 6 minuti (IQR 5-8), ad 8 minuti dall'ingresso in ambulatorio (IQR 5-14), Nei confronti di aneurisma dell'aorta addominale, segni di perforazione viscerale, versamento addominale libero, appendicite acuta, colecistite, dilatazione delle vie biliari, distensione patologica delle anse intestinali e diverticolite, ostruzione ureterale, torsione testicolare, il protocollo mostrava accuratezza del 100%, 94.8%, 80.5%, 96.6%, 92.8%, 97.1%, 91.4%, 94.3%, 96.2%, 100% rispettivamente. Non sono stati osservati casi di torsione gonadica, gravidanza ectopica. La TC con MDC veniva eseguita a circa 120 minuti in mediana dall'ingresso in ambulatorio (IQR 80-180).
Discussione: I nostri risultati dimostrano un'eccellente accuratezza della POCUS, con valori > 92% nella quasi totalità dei quadri patologici addominali considerati, specificità > 92% e +LR > 12.I risultati si dimostrano in linea con quelli della letteratura internazionale recente, in particolare per quanto concerne l'occlusione intestinale (Rosano, 2021), l'appendicite acuta (Cho, 2023), la diverticolite acuta (Shokoohi, 2023; Nazerian, 2021).
Tuttavia, abbiamo registrato valori di sensibilità rispettivamente del 66.7%, 64,.5%, 57.1% nei confronti del riscontro di appendicite acuta, liquido libero addominale e perforazione intestinale, rispettivamente, per cui il protocollo non ha dimostrato sufficiente valore predittivo negativo per poter escludere la presenza di patologia. Tuttavia, appare significativo il valore predittivo negativo del 98% della POCUS nell'occlusione intestinale, con valori di specificità significativamente maggiori che Rx diretta addome (Rosano et al., 2021).
La mancanza di sufficienti dati per l'inclusione nello studio dei riscontri ecoscopici per i quadri di patologia annessiale, gravidanza ectopica, torsione testicolare, aneurisma aortico addominale è in linea con la prevalenza globale delle patologie in oggetto (10‰ delle donne in età fertile per la patologia annessiale (Weström, 1980); 1-2% di tutte le gravidanze per la gravidanza ectopica (Van Den Eeden, 2015); 0.25‰ per la torsione testicolare (Lacy, 2023); 0.5-1.4% per AAA (Song, 2023)).
Conclusioni: La POCUS si conferma uno strumento diagnostico estremamente accurato e di impatto significativo nella gestione del percorso diagnostico-terapeutico del paziente con presentazione di dolore addominale acuto in PS, specificamente per quanto riguarda un approccio sistematico secondo protocollo "ACUTE ABDOMEN", mostrando in questo studio pari o maggiore attendibilità e campi di applicazione rispetto a quanto pubblicato finora, in particolare nei casi di idroureteronefrosi e colecistite acuta.

UNVEILING CARDIAC ATTR AMYLOIDOSIS: A CASE REPORT

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Introduzione: L'amiloidosi rappresenta un gruppo eterogeneo di malattie caratterizzate dall'accumulo extracellulare di fibrille proteiche insolubili, derivanti dalla deposizione anomala di subunità proteiche a basso peso molecolare. Queste fibrille, organizzate tipicamente in strutture a β-foglietto, si aggregano nella matrice extracellulare causando danni tissutali progressivi. A seconda della proteina coinvolta, si distinguono diverse forme cliniche, tra cui la forma AL (catene leggere di immunoglobuline), AA (proteina sierica A) e ATTR (transtiretina). Quest'ultima, in particolare, può manifestarsi come forma ereditaria, legata a mutazioni genetiche (ATTRm), o come forma wild-type (ATTRwt), associata all'invecchiamento. Il cuore è uno degli organi più frequentemente colpiti, portando a cardiomiopatia restrittiva, insufficienza cardiaca a frazione di eiezione preservata, aritmie e disturbi della conduzione. La diagnosi è spesso ritardata, a causa della varietà e aspecificità dei sintomi e della necessità di esami diagnostici avanzati per la conferma.
Caso clinico: Presentiamo il caso di una paziente di 84 anni, con anamnesi di ipertensione arteriosa, dislipidemia non trattata per intolleranza alle statine, pregresso carcinoma mammario e gastrico trattati con successo, e plurimi carcinomi basocellulari asportati. Negli anni precedenti la paziente aveva avuto ripetuti episodi di palpitazioni e lipotimie, per i quali si era sottoposta a monitoraggi elettrocardiografici e valutazioni cardiologiche, senza rilevazione di aritmie significative. Nel settembre 2024 giungeva in Pronto Soccorso per una caduta accidentale con trauma cranico, riferendo diplopia e confusione. L'esame obiettivo mostrava disorientamento, eloquio impastato e instabilità posturale. L'ECG documentava fibrillazione atriale di nuova insorgenza a bassa frequenza ventricolare; veniva effettuata una telemetria, che segnalava episodi di bradicardia notturna fino a 32 bpm. Gli esami ematochimici risultavano nella norma e la TC encefalo escludeva lesioni acute. Durante la degenza presso il nostro reparto, veniva effettuata una ecocardiografia che mostrava un ventricolo sinistro non dilatato con ipertrofia concentrica, funzione sistolica ipernormale (FE 77%) con obliterazione medio-apicale e pattern "granular sparkling" del miocardio, altamente suggestivo per amiloidosi e confermato alla successiva cardioRM. La scintigrafia con Tc-99m HMDP confermava l'accumulo di radiofarmaco a livello delle pareti miocardiche, orientando verso una diagnosi di amiloidosi ATTR, verosimilmente wild-type. Gli esami per discrasie plasmacellulari (elettroforesi sieroproteica e urinaria, immunofissazione e dosaggio delle catene leggere libere) risultavano negativi. Il monitoraggio ECG nelle 24 ore documentava flutter atriale persistente con frequenze tra 49 e 119 bpm, senza pause significative, escludendo l'indicazione al posizionamento di pacemaker. La gestione terapeutica ha previsto l'avvio di anticoagulanti orali diretti (DOAC), terapia diuretica modulabile secondo clinica e follow-up cardiologico ravvicinato, inclusa valutazione genetica (del cui risultato siamo ancora in attesa nel momento di stesura di questo articolo). Alla dimissione, la paziente risultava in buone condizioni generali, stabile emodinamicamente, senza segni di scompenso congestizio né alterazioni neurologiche.
Discussione: Il caso descritto riflette pienamente le caratteristiche dell'amiloidosi cardiaca ATTR, spesso diagnosticata tardivamente a causa della natura insidiosa dei sintomi. Nel nostro caso, la paziente aveva presentato negli anni precedenti sintomi compatibili con aritmie misconosciute e disfunzione di conduzione, che non avevano destato sospetto per una malattia infiltrativa, anche per la normalità degli esami eseguiti. La diagnosi è emersa solo grazie al sospetto clinico generato dall'aspetto ecocardiografico e alla conferma tramite imaging avanzato. Questo evidenzia come, soprattutto nei pazienti anziani, l'ipertrofia ventricolare inspiegata, le aritmie di nuova insorgenza e i sintomi aspecifici come lipotimie e palpitazioni debbano indurre il clinico a considerare l'amiloidosi tra le ipotesi diagnostiche. Il riconoscimento precoce della malattia è cruciale per impostare una gestione terapeutica adeguata, prevenire complicanze e migliorare la qualità di vita.
Conclusioni: L'amiloidosi cardiaca ATTR, sebbene rara, rappresenta una causa importante di cardiomiopatia restrittiva e scompenso cardiaco nell'anziano, spesso sotto-diagnosticata a causa della presentazione clinica sfumata. La nostra esperienza sottolinea l'importanza di mantenere un alto livello di sospetto diagnostico nei pazienti anziani con aritmie e segni di disfunzione cardiaca non spiegabili da altre cause. Solo attraverso un approccio multidisciplinare, integrando cardiologia, medicina interna, radiologia e genetica, è possibile raggiungere una diagnosi definitiva e offrire al paziente le migliori opzioni terapeutiche disponibili. Speriamo che questo caso stimoli i colleghi a riconoscere più precocemente i segni di questa patologia, migliorando così gli esiti clinici.

IDIOPATHIC INCESSANT EFFUSIVE-CONSTRICTIVE PERICARDITIS PROGRESSING TO CONSTRICTIVE PERICARDITIS OVER ONE YEAR DURING ANTI-INTERLEUKIN 1 THERAPY: A CASE REPORT

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Case presentation: A 32-year-old male presented to the Emergency Department in March 2024 complaining of dyspnea, fever, cough and malaise over the past few days. His medical history was remarkable solely for an autism spectrum disorder. Laboratory tests revealed an elevated C-reactive protein (245 mg/L) without leukocytosis and with a normal procalcitonin. Upon admission the ECG showed sinus tachycardia (HR 104 bpm) with mild diffuse ST-segment elevation and electrical alternans.
Both chest X-ray and thoracic ultrasound (US) revealed a left basal pleural effusion. A contrast-enhanced chest CT confirmed the pleural effusion but detected a large circumferential pericardial effusion, with thickened and contrast-enhancing pericardial leaflets (Fig. 1).

Despite initial signs of cardiac tamponade on transthoracic echocardiography, pericardiocentesis was not performed due to the predominantly posterolateral location of the effusion and the patient's hemodynamic stability. Because of persistent dyspnea, a thoracentesis of the left hemithorax was performed, yielding400mL of yellow-brown serohematic exudate, on which microscopic analysis, *M. tuberculosis* DNA testing, cytology and cultural tests all turned back negative. An extensive rheumatological (ANA, ANCA, ENA, RF, anti-CCP, C3, C4) and infectious disease (Quantiferon; serologies for Echovirus, Coxsackievirus, Parvovirus B19, HIV, CMV, EBV, *T. gondii, C. burnetii, M. pneumoniae, C. pneumophila*; blood cultures and *S. pneumoniae* and L. *pneumophila* urinary antigens) work-up was negative. Abdominal US showed no abnormalities.
Given the poor clinical and laboratory response to initial oral non-steroidal anti-inflammatory drugs (NSAIDs, Ibuprofen 600 mg tid) combined with colchicine (1 mg/die), the patient was switched to intravenous indomethacin and oral prednisone (25 mg/die), with slow symptomatic improvement. At discharge, CRP had decreased to 56 mg/L. A new echocardiogram showed persistent circumferential pericardial effusion with significant fibrinous organization (extensive fibrin strands adherent to the visceral pericardium and freely floating within the pericardial cavity)(Fig. 2) and features suggestive of constriction (diastolic reversal flow in the suprahepatic veins, septal bounce, and inferior vena cava dilation), without overt clinical picture of constrictive pericarditis.

One week later, the patient was readmitted due to worsening pleural effusion. At that time, C-reactive protein (CRP) levels were 30 mg/L and signs of constrictive physiology had resolved. After ruling out autoimmune and infectious etiologies, treatment with anti-interleukin 1 (anakinra) was started and the patient was discharged.
Since then, the patient had been followed up at the Pericardial Diseases Outpatient Clinic of Fatebenefratelli Hospital. Two months after the initial episode NSAIDs, colchicine, and prednisone were gradually withdrawn based on the resolution of clinical symptoms and the normalization of inflammatory markers (CRP), while maintaining anakinra.
The patient was on anakinra six days per week when, one year since the first episode (in April 2025), he developed symptomatic pericardial constriction, showing jugular vein turgor, peripheral edema and ascites, requiring increasing doses of diuretics. Echocardiographic features of constrictive pericarditis were more evident. We therefore referred him for pericardiectomy.
Discussion: We described a case of a patient with idiopathic pleuro-pericarditis who, despite treatment with anakinra, progressed to symptomatic pericardial constriction requiring pericardiectomy. Evolution to constrictive pericarditis is a rare complication of acute idiopathic pericarditis and occurs in less than 1% of cases. A recognized risk factor for progression to constrictive pericarditis is incessant course, defined as persistent pericarditis without an asymptomatic interval despite therapy. In such cases, corticosteroid dependence and colchicine resistance appear to be associated with a possible progression to constrictive pericarditis (within months, compared to years in other forms).
After reviewing the case, it is possible to hypothesize that our patient had an acute idiopathic effusive-constrictive pericarditis with an incessant course, which progressed directly to the constrictive form without clinical recurrences during follow-up. On the other hand, the presence from the onset of pericardial effusion with a fibrotic component and the persistence of an elevated CRP after initial therapy could have favored progression. In conclusion, although scientific literature suggests that anakinra treatment might be able to revert echocardiographic signs of pericardial constriction in patients with incessant pericarditis, our case shows that it's efficacy in preventing progression to chronic constrictive pericarditis is, unfortunately, not guaranteed in all cases.

END OF LIFE IN THE EMERGENCY DEPARTMENT: TRAJECTORY AND CARE APPROACH. A RETROSPECTIVE STUDY

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Rationale and objective of the study: Correctly identifying end-of-life patients is crucial for the best ethical and care approach. The objective of this study is to evaluate the prevalence of end-of-life trajectories in the Emergency Department (ED) and their correlation with the diagnostic and therapeutic pathways.
Materials and methods: Monocentric retrospective observational study on adult patients who died in the ED between 2018 and 2022. Five end-of-life trajectories were defined: 1) healthy patients with an acute event (Charlson Comorbidity Index (CCI) <4, absence of comorbidities); 2) terminal cancer

patients or in palliative therapy (PT); 3) acute exacerbation of chronic disease; 4) frail with dementia or other degenerative conditions; 5) unclassifiable.
Results: A total of 657 patients were included: 38 in trajectory 1 (6%), 68 in trajectory 2 (11%), 63 in trajectory 3 (10%), 310 in trajectory 4 (49%), and 149 (24%) in trajectory 5.
Patients in trajectory 1 undergo Advanced Cardiovascular Life Support (ACLS) in 66% of cases, followed by patients in trajectory 5 (43%), 3 (32%), 2, and 4 (24%) (p<0.001).
The initiation of an exclusive palliative approach occurred in 35% of patients on trajectory 2, 13% on trajectory 5, 11% on trajectories 3 and 4, and 2.6% on trajectory 1. The explicit discussion of end-of-life occurred more frequently in patients on trajectory 2 (51%), compared to 34% on trajectories 4 and 5, 32% on trajectory 3, and 21% on trajectory 1 (p=0.019).
Among the CCI criteria, ischemic heart disease increases the probability of ACLS (OR 2.372, p<0.001), while dementia (OR 0.324, p<0.001), hemiplegia (OR 0.224, p 0.002), metastatic tumours (OR 0.458, p 0.026), and leukaemia (OR 0.104, p 0.036) reduce it. Access with a request for PT (OR 0.071, p 0.007), difficulty in home management (OR 0.45, p 0.038), the total SIAARTI score (OR 1.244, p 0.045), and being affected by a terminal disease (OR 4.106, p 0.022) predicted the recognition of immediate death and initiating a palliative approach.
Discussion: Identifying the correct end-of-life trajectory in the ED allows for the differentiation between patients for whom life-sustaining treatment must necessarily be associated with aggressive etiological treatment and those for whom intensive curative treatment is no longer clinically and ethically appropriate due to the inability to modify the disease progression. Although the four trajectories ideally describe end-of-life trajectories, some patients do not fit into any of the classical classifications (Lunney et al., 2002) and offering the best end-of-life care may be difficult (Zambrano et al., 2025). Patients with a high chance of survival must undergo an intensive palliative and curative approach; however, in frail, terminally ill patients, balancing a curative approach with an exclusively palliative approach may be difficult (SIAARTI 2013). Especially in patients admitted for a disease exacerbation or a new disease and even in patients in trajectory 2, identifying this latest event as terminal may not be simple without additional tools for a correct evaluation (Huang et al., 2020).
Conclusions: Despite recent best practice guidelines to guide intensive care unit care (ICU) admission (SIAARTI 2018), further instruments should be developed that, by integrating clinical and ethical information, help the physician decide how to intervene, balancing the respect for human dignity and the necessity of intervention.

A DIAGNOSTIC CHALLENGE SIMULATING AN IGG4-RELATED DISEASE

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Keywords: fever of unknown origin (FUO), differential diagnosis, retroperitoneal masses, liposarcoma, IgG4 syndrome.
Introduction: Fever is one of the most common signs observed every day in clinical practice from the origin of medicine itself. Countless medical conditions can cause fever, ranging from non-serious to life-threatening ones.
Case presentation: We report a case of dedifferentiated retroperitoneal liposarcoma initially mimicking IgG4-related disease. The patient presented with prolonged fever, back pain and unilateral leg swelling. Imaging revealed a retroperitoneal mass, and extensive laboratory workup, including autoimmune and infectious panels, was inconclusive. Histopathological analysis after surgical biopsy confirmed the diagnosis of liposarcoma.
Conclusion: This case underscores the importance of including rare malignancies in the differential diagnosis. The purpose of this report is to highlight the importance of rare diseases in the diagnostic process of fever of unknown origin, and their typical and atypical presentations. High index of suspicious, while analysing vague symptoms, can lead to early diagnosis, prompt treatment and, at the end, better patient outcomes. A vigilant clinical approach and thorough investigation, including histological confirmation, are essential for timely diagnosis and optimal management.

MASTICATORY PERFORMANCE AS A MARKER OF MUSCLE FUNCTION AND NUTRITIONAL STATUS IN OLDER ADULTS UNDERGOING DENTAL TREATMENT

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Rationale: Individuals with impaired chewing strength often alter the quality and quantity of food intake, thereby increasing their risk of malnutrition and sarcopenia, defined as the progressive loss of muscle mass and function(s).
To identify the clinical impact of muscle function on masticatory performance, the aims of this study were to i) evaluate the relationship between Maximum Bite Force (MBF) and skeletal muscle (SM) function, and ii) investigate how these parameters relate to nutritional status in a group of older adults undergoing either conservative or surgical dental treatment.
Methods: Subjects undergoing either mild (MILD) or limited/extended (LIM/EXT) dental surgery were studied. Nutritional assessment was performed with Mini Nutritional Assessment - Short Form (MNA-SF). Changes in body weight, either weight loss (WL) or weight stability (WS), during the previous 6 months were recorded. Changes in body composition were estimated via bioelectrical impedance analysis (BIA). SM function was evaluated by Hand Grip Test (HGT) and 6-Minutes Walking Test (6MWT). MBF was measured using a gnathodynamometer. Sex-specific internal cut-off for fat-free mass index (FFMI) were defined as ≤16.8 kg/m2 for females and ≤19.1 kg/m2 for males.
Results: Participants who were classified as normally nourished (NS, n=30) exhibited significantly higher MBF compared to those either at risk or malnourished (RM, n=8) (p=0.028). The combined effects of surgery type, nutritional status and body composition were further evaluated. Significant reductions in HGT (p=0.029), 6MWT (p=0.047) and MBF (p=0.004) were observed in LIM/EXT + RM (n=7) compared to MILD + NS (n=18). Additionally, MBF was significantly reduced in LIM/EXT + low FFMI (n=9) compared to MILD + high FFMI (n=8) (p=0.036). Furthermore, both HGT (p=0.003) and MBF (p=0.014) were significantly reduced in LIM/EXT + WL (n=6) compared to MILD + WS (n=15).
Conclusion: Measurement of MBF appears to be a promising, cost-effective, and accessible clinical tool for identifying subjects at risk of sarcopenia and muscle function impairment. Further studies are warranted to validate these preliminary yet compelling findings.

LOW VON WILLEBRAND FACTOR LEVELS IN A CASE WITH ANTIPHOSPHOLIPID ANTIBODIES

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Background: Von Willebrand factor (vWF) is a blood glycoprotein involved in platelet aggregation and the stabilization of coagulation factor VIII. A deficiency of vWF causes a bleeding disorder characterized by a tendency to bleed. Antiphospholipid antibodies are a heterogeneous group of autoantibodies, including anti-β2-glycoprotein I (aβ2GPI), anticardiolipin (aCL) antibodies, and antibodies that prolong plasma clotting time in in vitro tests, known as lupus anticoagulant (LAC). These are part of the laboratory criteria for the diagnosis of antiphospholipid syndrome (APS), a rare systemic autoimmune disease characterized by recurrent pregnancy morbidity or thrombosis.
Case presentation: A 55-year-old female patient presented to our center for evaluation of hemorrhagic and thrombotic disorders after a prolonged activated partial thromboplastin time (aPTT) was detected during preoperative testing prior to a total hysterectomy for uterine fibromatosis. The patient had a mild, non-significant personal history of bleeding manifestations (bleeding score 2). She had previously undergone total thyroidectomy and radioiodine therapy for papillary thyroid carcinoma without any complications. Further laboratory investigations were requested, including a mixing test (partially corrected, baseline 37.6 s, mixing 35 s), and testing for the presence of lupus anticoagulant (LAC), which was found to be positive. Given the patient's clinical history, which included mild bleeding diathesis, we investigated the intrinsic pathway of coagulation and found low levels of von Willebrand factor (Ag 27%, Ricof 56%). Simultaneously, we requested antiphospholipid antibody testing, which was positive at high titers (ACA IgG 688, IgM 79.5, anti-β2GP1 IgG 1759, IgM 47.7). In accordance with the Sydney criteria, the tests were repeated after 3 months, with confirmation of the results. During follow-up, the patient reported arthralgia, and an expanded autoimmune screening was performed to exclude a secondary form, which returned negative. In accordance with current recommendations, considering the triple positivity for high-titer antibodies, we recommended antithrombotic prophylaxis with 100 mg/day of acetylsalicylic acid. Over the 8-month follow-up period, the patient did not experience any thrombotic events or hemorrhagic complications.
Conclusion: According to published studies, antiphospholipid antibodies can increase the risk of arterial thrombosis by inducing an overactivation of vWF

and promoting platelet activation, but the mechanism underlying the correlation between aPL antibodies and vWF remains unclear. Therefore, in our case, it can be hypothesized that the low levels of vWF may have played a protective role, as no thrombotic events occurred despite the high-titer triple positivity for antiphospholipid antibodies. However, further studies are required to investigate and elucidate the precise biological mechanism of action of elevated vWF in patients with autoimmune diseases.

RECLASSIFYING CARDIOVASCULAR RISK BASED ON LIPOPROTEIN(A) LEVELS: TIME TO RE-EVALUATE LDL-C TARGETS?

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Lipoprotein(a) (Lp(a)) is a low-density-lipoprotein (LDL)-like Apolipoprotein B-containing lipoprotein, covalently bound to an additional apolipoprotein called apolipoprotein(a). Elevated Lp(a) levels are an independent significant additional risk factor for cardiovascular (CV) diseases, including coronary artery disease (CAD) and stroke. A linear increase in cardiovascular risk has been observed, and a threshold of Lp(a) concentrations of 50 mg/dL has been suggested. Lp(a) levels are largely genetically-determined and marginally-influenced by lifestyle and diet. Since there are no specific drugs available to lower Lp(a) to date, the higher the Lp(a) level, the lower LDL-C-level should ideally be to minimize the CV risk. The recently-developed tool "Lp(a) clinical guidance risk ristratification tool" allows to estimate lifetime CAD/stroke risk. However, little is understood about how to effectively incorporate Lp(a)values into 10-year cardiovascular (CV) risk stratification and how to adjust LDL-C targets.
Our study aimed to: 1) explore Lp(a) distribution in moderate, high and very-high CV risk patients; 2) reclassify CV risk based on Lp(a) levels; 3) assess the concordance of different validated clinical scores for CV risk estimation; 4) determine if current CV risk scores underestimate risk in individuals with high Lp(a).
We selected 422 patients (55±15 years, 51% female) attending our tertiary-care outpatient clinics. We collected: biometric parameters; data on smoking habits, diabetes, hypertension and ASCVD; renal, glycemic and lipid profiles - including Lp(a). The following scores were calculated when appropriate: SCORE2/SCORE2-OP/SCORE-2 Diabetes, ESC U-prevent 10 years/lifetime score, Lp(a) Clinical Guidance tool.
Lp(a) distribution in our patients' cohort mirrored that of Caucasians. The cohort's average estimated lifetime CV risk increased after adjustment for Lp(a) values (22.36%±18.82 vs. 28.38%±22.04). A concordance between SCORE-2/SCORE2-OP/SCORE2-Diabetes and the 10-year ESC-U-prevent score, and between the lifetime ESC-UPrevent and the lifetime Lp(a) Clinical Guidance tool -before and after adjustment for Lp(a) – was found. Interestingly, Lp(a) values > 50 mg/dL were detected in a significant number of patients at moderate cardiovascular risk according to the validated scores. Finally, a significant number of patients in the fourth quartile of Lp(a) values did not fall within the top quartile of the ESC-U Prevent Lifetime Score.
In conclusion, the most used scores to estimate CV risk not considering Lp(a) values were unable to appropriately classify the patients at their CV risk, thus underestimating the actual global CV risk. While it is easier to focus on lipid targets in high/very-high CV risk patients -with ambitious therapeutic goals leading to low circulating levels of LDL poor in cholesterol content- it seems mandatory to consider Lp(a) contribution in patients classified at lower CV risk. This will help avoid the underestimation of the actual risk level of each patient and guide the selection of the most appropriate diagnostic, therapeutic, and follow-up strategies.

625. CARDIOVASCULAR RISK STRATIFICATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: THE ROLE OF NON- INVASIVE IMAGING AND TRADITIONAL RISK SCORES

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Background: Patients with inflammatory bowel disease (IBD) have an increased cardiovascular risk (CVR) and cardiovascular disease (CVD) is the leading cause of mortality in IBD patients. A more in-depth screening of patients has become important with the EMA warning for JAK-inhibitors. The current CV risk stratification algorithms are based on traditional risk factors not considering subclinical atherosclerosis. This study aimed to stratify the CVR of IBD patients according to the European Society of Cardiology (ESC 2021/23) and European Society of Atherosclerosis (EAS), together with the evaluation of the presence of previously subclinical atherosclerosis by carotid ultrasound.
Methods: Demographic and disease-related data were collected from consecutive IBD patients aged over 40 years, including systolic blood pressure, body mass index (BMI), lipid panel, and cardiovascular comorbidities. Asymptomatic atherosclerotic disease was assessed by carotid ultrasound in order to measure the carotid intima-media thickness (cIMT) and to detect the presence of plaques. CVR was stratified based on the latest guidelines on dyslipidemias (EAS/ESC 2019), cardiovascular prevention (ESC 2021), and the management of cardiovascular disease in patients with diabetes (ESC 2023). Moreover, additional IBD-related parameters potentially associated with an increased CVR were investigated, such as disease activity, current therapies, duration of disease, and extraintestinal manifestations.
Results: A total of 120 IBD patients were included (UC: 67 patients, CD: 53 patients) Baseline characteristics are presented in Table 1. Patients with UC had significantly higher mean values of total cholesterol (C-TOT) and low-density lipoprotein cholesterol (C-LDL) ($p<0.001$ and $p=0.001$ respectively). At baseline, 48% of patients were classified as having intermediate CVR, 34% as high risk, and 18% as very high risk (Table 2). Following carotid ultrasonography, subclinical atherosclerosis was diagnosed in 48.3% of patients. Based on these findings, CVR re-stratification was performed in 21% of patients resulting in 71% of patients with high and very high risk, compared to 50% at baseline. Additional risk factors for an increased CVR identified by multivariate regression analysis were having active disease ($p=0.047$) and concomitant spondiloathropathies ($p=0.03$)
Conclusion: Our study demonstrates that carotid ultrasound contributed to re-classify the CVR in patients who were previously considered to be in lower risk categories confirming that the use of traditional risk scores underestimates CVR in IBD patients. Having active intestinal disease and concomitant spondiloarthritis increases further the CV risk.

	Tot N=120	UC N=67	CD N=53	p
Sex (male); n (%)	58 (48.3)	29 (43.3)	29 (54.7)	0.223
Median age (range)	59 (51-66)	59 (52-67)	59 (51-65)	0,888
Body Mass Index (BMI, Kg/m²); median (range)	24,7 (22.4-27.6)	25,3 (23.2-27.7)	24,5 (21,9-25,8)	0.146
Smokers; n (%)	32 (26.7)	8 (11.9)	24 (45.3)	<0.001
SBD (mmHg) median (range)	125 (115-135)	125 (120-135)	120 (110-135)	0.122
DBP (mmHg) median (range)	75 (70-80)	80 (70-80)	75 (70-80)	0.325
Hypertension; n (%)	50 (41.6)	29 (43.3)	21 (39.6)	0.689
Total cholesterol (mg/dL); median (range)	208.5 (169.3-230.5)	219 (190-237.5)	172 (146-218)	<0.001
HDL (mg/dL); median (range)	54 (46-62.5)	57 (48.6-69.5)	50 (44-57)	0.002
Triglycerides (mg/dL); median (range)	106.5 (82.8-151.3)	99 (81-147.5)	120 (89-155)	0.125
LDL (mg/dL) median (range	126.1 (96.5-147.2)	135 (109.7-152.7)	103 (76.8-145.2)	0.001
Diabetes n (%)	13 (10.8)	10 (14.9)	3 (5.7)	0.012
Moderate or severe CKD; n (%)	6 (5)	1 (0.8)	5 (4.2)	0.219
Disease-related variables				
Disease duration (yrs); median (range)	11 (6-22)	12 (7-24)	9 (5-20)	0.143
Clinical disease activity; n(%)				
Remission	87 (72.5)	54 (80.5)	33 (62.3)	0.029
Mild	16 (13.3)	5 (7.5)	11 (20.7)	0.040
Moderate	12 (10)	6 (9)	6 (11.3)	0.716
Severe	5 (4.2)	2 (3)	3 (5.7)	0.424
Conventional therapy; n (%)	86 (71.7)	66 (98.5)	20 (37.8)	< 0.001
Anti-TNFs n (%)	35 (29.1)	16 (34.8)	19 (54.3)	0.037
Vedolizumab n (%)	8 (6.7)	7 (15.2)	1 (2.9)	0.028
Ustekinumab n (%)	17 (14.1)	7 (15.2)	10 (18.9)	0.561
Anti-JAKs n (%)	16 (13.3)	16 (34.8)	0 (0)	<0.001
Risankizumab n (%)	5 (4.1)	0 (0)	5 (14.3)	0.001
Spondyloarthropathy; n (%)	26 (21.7)	13 (19.4)	13 (24.5)	0.502

Table 1. Baseline characteristics of patients. PMS=partial Mayo score; HBI = Harvey Bradshaw Index; SBP= Systolic blood pressure; DBP= diastolic blood pressure; CKD chronic kidney disease

	Tot	UC	CD
Current CV risk stratification algorithms			
Very high CVR; n (%)	24 (20)	15 (22.4)	9 (17)
High CVR; n (%)	61 (50.8)	31 (46.3)	30 (56.6)
Moderate CVR; n (%)	35 (29.1)	21 (31.3)	14 (26.4)
Carotid US evaluation			
Plaque; n (%)	67 (55.8)	40 (59.7)	27 (50.9)
Carotid stenosis; >50% n (%)	3 (2.5)	3 (4.5)	0 (0)
CVR re-classification after carotid US			
Reclassified CVR; n (%)	26 (21.7)	17 (25.4)	9 (17)
From high to very high; n (%)	3 (2.5)	3 (1.5)	0 (0)
From moderate to high; n (%)	23 (19.1)	14 (20.9)	9 (17)

Table 2. Risk stratification with current algorithms and reclassification of CV risk after Carotid Ultrasound

CATHETER-RELATED RIGHT ATRIAL THROMBOSIS IN CANCER PATIENTS: A PROSPECTIVE OBSERVATIONAL ANALYSIS

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Background and aims: Literature data on catheter-related right atrial thrombosis (CRAT) are scarce and based only on case reports or case series1-2. Data mostly concern dialysis patients while reports on oncological patients are poor2. In this prospective observational study, we investigated characteristics at baseline, management, and outcomes of patients with cancer and CRAT, to provide a better characterisation and improve the knowledge of this disease.
Methods: We analysed data of 25 consecutive outpatients with cancer and CRAT that referred to our Thrombosis Unit over a period of 4 years.
Of these patients we collected epidemiological and clinical data and evaluated the efficacy (resolution of the thrombotic process and recurrences) and safety (major and clinically relevant non-major bleedings) of the different treatments used.
Results: In our study, the median age was 60 years, with 4 (16%) males and 21 (84%) females. The mean BMI was 26,7 Kg/m2, and the mean eGFR was 88 mL/min sec Cockcroft-Gault, with 5 (20%) patients with eGFR <60 mL/min. All patients had active malignancy and were undergoing active therapy: the localization was: 12 (48%) ovarian, 4 (16%) colorectal, 4 (16%) uterine, 3 (12%) breast cancer, and 2 (8%) had synchronous cancer (ovarian and uterine; kidney and squamocellular carcinoma); among them, 19 (76%) were metastatic, with 2 (8%) patients with cerebral metastasis. All patient had a central venous catheter: In 7 (28%) patients, atrial thrombosis occurred concomitantly with a thromboembolic event at a second site, i.e., Pulmonary Embolism (PE) (2), Deep Veins of the Upper Extremities (UEDVT) or superior vena cava. The diagnosis of CRAT was made mostly by contrast enhanced CT (88%), with further confirmation by echocardiography or cardiac MRI in 15 patients. The mean follow-up was 21 ±12 months. During the first month after diagnosis, one patient underwent surgical thrombectomy, one patient received a subtherapeutical dose of Low Molecular Weight Heparin (LMWH), while 23 patients were treated with a full dose anticoagulant therapy: 22 (91%) with a parenteral therapy, either LMWH or Fondaparinux, and one with a Direct Oral Anticoagulant (DOAC). During the first three months of follow-up, 21 out of the 24 patients (87,5%) underwent a full dose anticoagulant therapy, either with DOAC or LMWH. At 6 months of follow-up, 19 out of 24 patients (79%) continued a full dose anticoagulant therapy, Finally, 8 out of 22 patients (36%) underwent up to 1 year of full dose therapy, and only 3 out of 19 patients (16%) continued a long term full dose anticoagulant therapy after a year. After completion of the treatment period with full dose anticoagulation, a dose reduction was prescribed in 14 patients (87,5%): 13 (81%) with a DOAC and 1 (6%) with LMWH; 2 patients (12,5%) suspended any anticoagulant therapies. In the first month, 3 (12%) complete resolution of the CRAT, 1 (4%) partial resolution and 3 (12%) thrombus stability were documented; between 1 and 3 months 7 (29%) complete resolution, 8 (33%) partial resolution, and 3 (12,5%) thrombus stability were documented; between 3 and 6 months, 13 (54%) complete resolution, 4 (17%) partial resolution, and 3 (12,5%) thrombus stability were documented; between 6 and 12 months 16 (70%) complete resolution and 4 (17%) partial resolution, with 1 (4%) stable CRAT. 2 (8%) patients didn't undergo any radiological follow-up exam. 5 (20%) patients experienced one or more thromboembolism recurrences: 2 (8%) PE, 1 (4%) Deep Vein Thrombosis (DVT), 1 (4%) extension of the atrial thrombus; 1 patient (4%) developed an UEDVT, and later a proximal DVT with concomitant PE. Regarding patients who presented a thromboembolic recurrence, one had suspended the anticoagulant therapy, 2 were on prophylactic anticoagulation, and 2 were receiving full dose anticoagulation. No major bleedings occurred during follow-up with only 1 (4%) clinically relevant non major bleeding. Four (16%) patients died during follow-up.
Conclusions: With the increase of patients with central venous catheters, CRAT is becoming less uncommon than previously thought. Early treatment may lead to complete thrombosis resolution in more than half of patients. Nevertheless, the risk of recurrence appears to be higher than expected for thrombosis in usual sites in cancer patients3-4. Moreover, in this population both full and low dose anticoagulants seem to be a safe therapeutic option with low risk of bleeding. Accordingly, long term full dose anticoagulation could be considered a suitable treatment in this population, but more evidence is needed to support these findings.
References: Stavroulopoulos A, Aresti V et al. Right atrial thrombi and haemodialysis catheters: meta-analysis and management proposal. Nephrol Dial Transplant, 2012.
Tran MH, Wilcox T et al. Catheter-related right atrial thrombosis. J Vasc Access, 2020.
Prandoni P et al. VTE and bleeding in cancer. Blood, 2002.
Wang TF, Li A et al. Thrombosis in cancer. Res Pract Thromb Haemost, 2018.

WITCHING THE DOSE OF MEPOLIZUMAB IN PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA): A EUROPEAN RETROSPECTIVE MULTICENTRE REAL-WORLD STUDY

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Background: and rationale: Eosinophilic Granulomatosis with Polyangiitis (EGPA, former Churg-Strauss) is a rare multisystemic disease classified within Anti-Neutrophil Cytoplasmatic Antibody (ANCA)-associated vasculitis. Mepolizumab, an anti-IL-5 monoclonal antibody is approved for the treatment of EGPA at a dose of 300 mg every four weeks, based on the MIRRA trial. However, in clinical practice, both 100 mg and 300 mg dosing regimens are used, with limited data available on their comparative effectiveness and optimal dosing strategies.
Aim of the study: The aim of this study is to evaluate the effectiveness of switching mepolizumab dosage from 100 mg to 300 mg every four weeksand and viceversa in patients with EGPA.
Materials and Methods: In this retrospective observational study, we included patients with EGPA, classified according to the ACR and/or the MIRRA trial criteria, who were treated with mepolizumab followed at 50 referral centres across Europe. Eligibility required a minimum follow-up of three months and a documented dosage switch from 100 mg to 300 mg every four weeks, and viceversa. The reasons for switching, as well as key clinical outcomes and oral corticosteroid (OCS) after dosage change were collected. Complete response (CR) was defined as a Birmingham Vasculitis Activity Score (BVAS) of 0 with a prednisone dose ≤ 4 mg/day, while partial response (PR) was defined as BVAS = 0 with prednisone dose > 4 mg/day.
Results: The final cohort included 145 patients with EGPA, of whom 138 (95%) switched mepolizumab dosage from 100 mg to 300 mg every four weeks, while 7 patients (5%) switched from 300 mg to 100 mg. The most common reason for dose escalation was suboptimal clinical response (n = 44, 32%); asthma worsening prompted the change in 39 patients (39%) and ENT symptom deterioration in 22 cases (16%). Thirtyone patients (22%) increased dosage for other reasons, primarily to facilitate OCS tapering. In contrast, among those who de-escalated to 100 mg every 4 weeks, remission was the main reason (n=3, 43%), followed by a planned de-escalation strategy in two patients (29%) and cost issues in the remaining two (29%). Among patients who switched from 100 mg to 300 mg, 62 (45%) achieved CR, 24 (17%) had PR, and 34 (25%) remained clinically stable. The median time to clinical response following dosage adjustment was 4.3 months (IQR 3–6). Only 7 patients (5%) experienced worsening of asthma or ENT symptoms. Among those who de-escalated to 100 mg, 3 patients (43%) achieved CR, 3 remained stable, and one reported worsening ENT symptoms due to a concurrent infectious complication. The median time to clinical response in this group was 4.6 months (IQR 3–6). Three months after dose change OCS daily dosage was decreased in both subgroups, from 9 to 4 mg in patients switching from 100 to 300 mg and from 10 to 5 mg in those who switched from 300 to 100 mg. Moreover, BVAS score improved in both subgroups (Table 2)
Conclusions: in real world clinical practice switching mepolizumab dose from 100 to 300 mg provides an adjunctive clinical benefit in achieving remission in patients with EGPA. Although based on a limited cohort, dose de-escalation from 300 to 100 mg does not seem to compromise clinical control and may be considered as a strategy following sustained remission.

SEVERE HYPOTHYROIDISM COMPLICATED BY STATUS EPILEPTICUS AND MULTISYSTEM FAILURE: A CASE STUDY

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Severe hypothyroidism (SH) is a rare but life-threatening medical emergency, with an estimated incidence of about 1 to 2 cases per million persons per year. The majority of affected patients are older women. The most common triggers include discontinuation of levothyroxine therapy, drug-induced hypothyroidism, and acute events (i.e. sepsis) in patients with poorly controlled hypothyroidism. Clinical presentation may involve coma, hemodynamic instability, hypothermia, hypoglycemia, bradycardia, heart failure, and seizures. In-hospital mortality ranges from 30% to 40%. Treatment involves the administration of levothyroxine, preferably intravenously, although oral therapy may also be used.
The Case: An 87-year-old woman — in past medical history atrial fibrillation and hypothyroidism of unknown origin— was admitted to the emergency department due to worsening consciousness and walking difficulties, following a fall. Initial neurological evaluation revealed slowed psychomotor responses, facial hypomimia, ideomotor slowdown, extrapyramidal signs, and upper limb myoclonus. Imaging showed moderate bilateral pleural effusion, and ECG revealed atrial fibrillation with a low ventricular rate. A toxicology screen was negative. Brain CT scans excluded acute ischemic or hemorrhagic events. Cerebrospinal fluid analysis ruled out central nervous system infection. Blood tests showed TSH > 100 mU/L and pancytopenia. Due to severe hypothyroidism and altered mental status, levothyroxine was administered via nasogastric tube. During hospitalization, there was a progressive decline in cognitive status, leading to a comatose state (GCS 3). An Electroencephalography (EEG) was performed and revealed a slowed and periodic pattern, consistent with non-convulsive status epilepticus. Intravenous diazepam was administered with seizure resolution. EEG activity and neurological status improved during treatment with levothyroxine and levetiracetam. A whole-body CT scan was performed to exclude the possibility of a paraneoplastic encephalitis. Empiric glucocorticoid was administered as part of initial therapy based on suspicion of concurrent adrenal insufficiency. The patient showed gradual neurological improvement: she regained alertness, began to respond to questions, and followed commands, though with persistent disorientation and depressed mood. Melevodopa/carbidopa was added for suspected preexisting parkinsonism. During early hospitalization, the patient developed multiple hypothyroidism-related systemic complications: severe bradycardia (requiring isoprenaline), severe hypotension, marked hypothermia, and transfusion-requiring pancytopenia — all of which improved with hormone replacement. Generalized edema, likely from hypothyroidism and fluid support, responded to low-dose diuretics. She was treated with piperacillin/tazobactam for inhalation pneumonia.
Discussion: Our patient presented with numerous neurological, metabolic and hemodynamic alterations that were due to severe hypothyroidism. This case illustrates the challenge of recognizing those clinical manifestations, linking them together, identifying hypothyroidism as the origin, and excluding other potential concomitant causes. The trigger of severe hypothyroidism of this patient could not be definitely identified, as relatives claimed she was correctly assuming the prescribed therapy and no clear acute event was reported, nor change in medications. SH is a rare condition associated with complications that are often seen in other diseases as well. Therefore, a multidisciplinary approach with close collaboration between internists, neurologists, and endocrinologists was essential.
Identification of status epilepticus in absence of convulsions was particularly challenging, as the progressive deterioration of cognitive status could have been generally attributed to worsening of myxedema coma. It is important to remember that neurological complications of SH may include manifestations like seizures that require prompt identification and life-saving specific interventions.
Managing multiple hypothyroidism-related systemic complications was difficult, especially in the absence of intensive care monitoring. Levothyroxine was administered enterally because the intravenous formulation wasn't available. The initial levothyroxine dose was 125 mcg, based on the patient's age and weight, to reduce the risk of myocardial infarction and arrhythmias, although literature suggests a higher starting dose.
Bibliografia: Somoza-Cano, F.J., Al Armashi, A.R., Patell, K., Hammad, F., & Ravakhah, K. (2022). *Status Epilepticus as a Life-Threatening Manifestation of Myxedema Crisis*. Cureus,14(1), e21155.Bourcier, S., Coutrot, M., Ferré, A., et al. (2023). *Critically ill severe hypothyroidism: A retrospective multicenter cohort study*. Annals of Intensive Care,13,15.Ono, Y., Ono, S., Yasunaga, H., Matsui, H., Fushimi, K., & Tanaka, Y. (2017). *Clinical characteristics and outcomes of myxedema coma: Analysis of a national inpatient database in Japan*. Journal of Epidemiology,27(3),117–122

NOCARDIA FARCINICA AND OTHER ENEMIES OF IMMUNOCOMPROMISED HOST: A COMPLEX CHALLENGE

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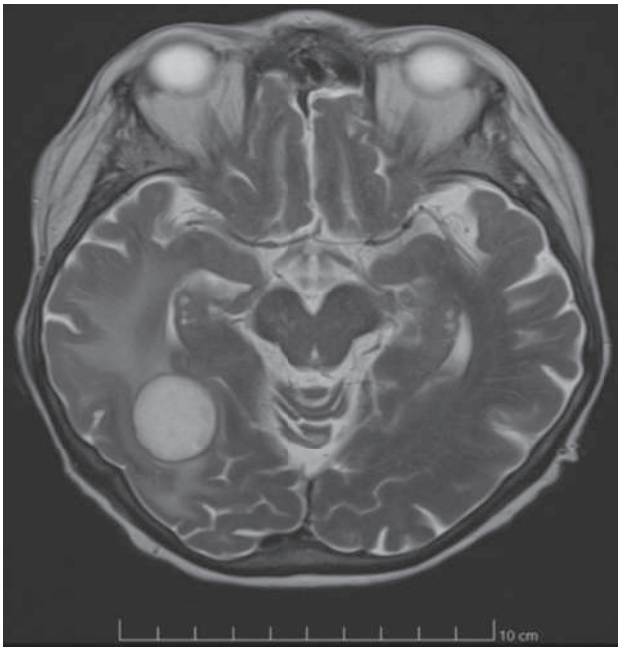
Introduction: This case highlights the diagnostic and therapeutic challenge posed by *Nocardia farcinica*, opportunistic pathogen known for causing disseminated infections in immunocompromised patients as lung transplant recipients.
Case report: A 62-year-old woman, bilateral lung transplant recipient for one year due to pulmonary fibroelastosis, was admitted to our Unit for fever, bradyphrenia and bradykinesia. She had a history of type 2 Diabetes Mellitus, Chronic Kidney Disease and recent invasive fungal infection by *Aspergillus fumigatus* involving left frontal cerebral cortex lobe, left orbital cavity and paranasal sinuses successfully treated with Voriconazole. Her immunosuppressive therapy included tacrolimus and mycophenolate. Blood tests evidenced increased inflammatory markers and moderate anemia; blood cultures were negative. A digital-rectal exam revealed a perianal mass, confirmed by ultrasound. A whole body CT scan, performed considering previous invasive fungal infection, revealed a left ischiorectal abscess and an oval fluid-corpuscolar lesion in the

right parieto-temporo-occipital cerebral cortex (Figure 1), whose characteristics were suggestive of an abscess on a subsequent brain MRI scan.



MRI DWI image of cerebral abscess: A cultured collected fluid, obtained by ultrasound-guided gluteal abscess drainage, resulted positive for *Nocardia farcinica*. Due to the possibility of disseminated nocardiosis, we started intravenous antibiotic therapy with imipinem/cilastatin and amikacin, avoiding cotrimoxazole to prevent further bone marrow and renal toxicity. The scenario was complicated by reactivation of Cytomegalovirus (CMV) infection treated with Valganciclovir and anti-CMV immunoglobulins. Patient's clinical conditions suddenly worsened with acute respiratory distress, disseminated intravascular coagulation and multiorgan failure leading to sudden cardiorespiratory arrest meanwhile a nasopharyngeal swab revelead a positivity for SARS-CoV2.
Summary: In our case the challenge is unfortunately lost due to the complexity of managing disseminated *Nocardia farcinica* infection, especially when associated to multiple opportunistic infections. This case underscores the importance of vigilant monitoring, early diagnosis and treatment, although these measures are not always sufficient to avoid fatal outcome.

UNLOCKING THE PREDICTIVE POWER OF NUTRITIONAL SCORES IN SEPTIC PATIENTS

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Sepsis is a critical condition characterized by severe immune dysregulation, ranking among the leading causes of morbidity and mortality in intensive care and internal medicine units. Nutritional status plays a pivotal role in modulating these responses, as when inadequate it can compromise immune defenses, the body's ability to handle stress and inflammation, and the clinical course. Malnutrition is frequently observed in septic patients and is strongly associated with worse clinical outcomes, including increased mortality, prolonged hospital stays, and greater complication rates. In this context, nutritional scoring systems have emerged as valuable tools to evaluate patients' nutritional status and predict clinical trajectories.
Objectives: Given the absence of a direct comparison of their performance in an internal medicine setting, this study aimed to assess the effectiveness of various nutritional scores as predictive tools for clinical outcomes in septic patients, emphasizing their application within the field of internal medicine.
Methods and Results: A retrospective analysis was conducted on 143 patients diagnosed with sepsis or septic shock who were admitted to an internal medicine unit. Key variables included clinical and laboratory parameters, comorbidities, and nutritional scores at the time of diagnosis. The modified Glasgow Prognostic Score (mGPS), the Prognostic Nutritional Index (PNI), the Controlling Nutritional Status (CONUT) score, the modified Nutrition Risk in Critically Ill (mNUTRIC) score, and the blood urea nitrogen-to-albumin ratio (BAR) were evaluated in forecasting mortality and clinical outcomes in patients with sepsis. Among them, the mNUTRIC score emerged as the strongest independent predictor of in-hospital mortality, with a good performance and a reasonable threshold for risk stratification.
Conclusions: The study highlights the mNUTRIC score's practicality and reliability in assessing nutritional and inflammatory risks in septic patients, particularly in non-ICU settings. These findings suggest its potential utility in guiding nutritional interventions and improving clinical outcomes, emphasizing the importance of integrating nutritional assessment into sepsis management.

TROPONIN IN PATIENTS WITH PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA: WHAT ROLE?

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Introduzione e obiettivi: La tachicardia parossistica sopraventricolare (TPSV), per l'esordio improvviso e la frequenza elevata, è spesso sintomatica e induce i pazienti a rivolgersi al Pronto Soccorso (PS), soprattutto se persistente. In assenza di comorbidità o recidive frequenti, è considerata una condizione benigna. Tuttavia, nei pazienti valutati in PS, la troponina viene frequentemente dosata nel sospetto di sindrome coronarica acuta (SCA), soprattutto in presenza di dolore toracico o alterazioni ECG (ST depresso o blocco di branca sinistro). Non è chiaro se l'elevazione della troponina in questo contesto indichi effettiva ischemia miocardica o se abbia valore prognostico. Obiettivi dello studio: 1) identificare i fattori associati alla troponina elevata e la correlazione con cardiopatia ischemica; 2) valutare se la troponina positiva si associ a un endpoint combinato (morte e/o ricovero per patologia cardiovascolare diversa dalla TPSV) entro almeno 6 mesi.
Materiali e metodi: Studio osservazionale, retrospettivo, monocentrico presso il PS dell'IRCCS Fondazione Policlinico Universitario "A. Gemelli" di Roma. Inclusi pazienti 18–80 anni giunti in PS con TPSV tra gennaio 2012 e luglio 2023. Esclusi: altre tachicardie a QRS stretto (sinusale, fibrillazione/flutter, tachicardia atriale) e gravi comorbidità (neoplasie attive, insufficienza renale/epatica/cardiaca severa). Raccolti dati anamnestici (cardiopatia ischemica, fattori di rischio), ECG durante TPSV (frequenza cardiaca, segni ischemici), ECG post-cardioversione (se disponibile), esami laboratoristici (troponina, emoglobina, creatinina) e strumentali (ecocardiogramma, test per ischemia). Analisi statistica con SPSS 26.
Risultati: Dei 581 pazienti valutati per TPSV, 364 sono stati inclusi (61% donne; età media 56,4 ±13,9). In 216 casi (59,3%) è stata dosata la troponina, risultata positiva in 84 (40,8%). Solo 50 pazienti (13,7%) hanno eseguito test per ischemia; 5 (10%) con conferma di cardiopatia ischemica. In questi, la troponina era stata dosata in 46 (92%) e positiva in 31 (67,4%). I pazienti troponina-positivi erano più anziani e presentavano più frequentemente ipertensione e dislipidemia. Nessuna differenza significativa per sesso o altri fattori di rischio. L'elevazione della troponina era associata al dolore toracico, ma non correlava con frequenza cardiaca, durata dell'aritmia, alterazioni ECG (in fase acuta o dopo cardioversione), ecocardiogramma, emoglobina o creatinina. All'analisi multivariata, l'età (OR 1,04; IC 95%: 1,01–1,07) e il dolore toracico (OR 2,5; IC 95%: 1,3–4,8) erano associati indipendentemente alla troponina positiva. Non c'erano associazioni significative tra troponina positiva e cardiopatia ischemica. L'unico fattore associato a cardiopatia ischemica era la presenza di alterazioni ECG post-cardioversione (p=0,02). La troponina positiva non risultava associata all'endpoint combinato. Età (p=0,02), storia di cardiopatia ischemica (p=0,002) e ipertensione (p=0,001) erano associati all'endpoint. Non è stata eseguita analisi multivariata per bassa numerosità del campione relativo all'outcome.
Conclusioni: Nel nostro studio, sintomi e alterazioni ECG durante TPSV non erano indicativi di ischemia miocardica. La prevalenza di cardiopatia ischemica era bassa e l'elevazione della troponina comune ma non predittiva di SCA né di esiti sfavorevoli a distanza. In PS, il dosaggio della troponina appare poco utile in pazienti senza fattori di rischio o comorbidità significative, e può portare a degenze prolungate, ricoveri e accertamenti non necessari. La TPSV è spesso benigna e trattabile in PS: il paziente senza comorbidità dovrebbe essere dimesso rapidamente dopo cardioversione. I limiti principali sono la natura retrospettiva, il singolo centro e il basso numero di pazienti con ischemia doc-

umentata o eventi avversi. Sono necessari studi prospettici per definire meglio i predittori di cardiopatia ischemica e il ruolo dei biomarcatori di danno miocardico in questi pazienti.

A SNEAKY CASE OF SUBACUTE ENDOCARDITIS

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Introduzione: L'endocardite infettiva (IE) è un'infezione endovascolare delle strutture miocardiche native (valvole, endocardio atriale o ventricolare) o impiantate chirurgicamente. Può presentarsi come endocardite batterica acuta (ABE) che si sviluppa all'improvviso e progredisce rapidamente o come endocardite batterica subacuta (SBE) che, sebbene aggressiva, progredisce lentamente nell'arco di settimane o mesi, con febbricola o addirittura senza. La IE può anche manifestarsi direttamente come una delle sue complicanze (scompenso cardiaco acuto, aritmia, stroke ischemico, emorragia intracranica, embolia polmonare o splenica…). Pertanto in presenza di febbre di origine sconosciuta in pazienti con uno o più fattori di rischio, per orientare la gestione ottimale del paziente si raccomanda fortemente di coinvolgere tempestivamente l'Endocarditis Team. **Caso clinico.** Donna, testimone di Geova, 69 anni, ricoverata per febbre recidivante comparsa da circa 4 mesi (TC max 38°C), artralgie diffuse (anca e caviglia) e quadro di scompenso cardiaco congestizio III-IV classe NYHA. In anamnesi: IPA II grado ESC/ESH, stenosi aortica severa, scompenso cardiaco cronico, anemia sideropenica, RCU e celiachia. Alla valutazione: piressia (TC 38.5°C), emodinamica stabile eccetto tachicardia sinusale (PA: 130/70 mmHg, FC 150 bpm con soffio sistolico 4/6 mesocardiaco, SpO2 97% in AA), segni di congestione periferica (rumori umidi polmonari ed edemi declivi) e numerosi elementi dentari con carie destruenti e con lesioni parodontali severe. Agli esami ematochimici: rialzo di TnI (425,2 ng/L), D-dimero (3173 ng/ml), ferritina (1040 ng/ml) e PCR (61,90 mg/L), proBNP (12300 pg/ml); all' emocromo: Hb 9.2 g/dl, PLT 229000/uL GB 10290/uL, N% 80.5%. Negative: urinocoltura, emocoltura basale eseguita in ingresso ed emocoltura su 3 set al picco febbrile. Ab Tot anti Treponema pallidum, VDRL e Widal-Wright: negativi. Ra TEST, ANA, DS DNA, ENAS e ANTI-CCP: negativi. ECG: Tachicardia sinusale a 106 bpm. Ecocardiogramma: ventricolo sinistro di normali dimensioni, moderatamente ipertrofico a FE 55%; atrio sinistro dilatato; stenosi aortica di grado severo, cuspidi ispessite calcifiche stenotiche, insufficienza tricuspidalica di grado moderato-severo con segni di ipertensione polmonare, insufficienza mitralica di grado severo, versamento pericardico moderato senza segni di tamponamento. RX torace: marcati segni di edema interstizio-alveolare, marcata cardiomegalia. Per la persistenza di febbre (in corso di antibioticoterapia con Ceftriaxone 2g/die, impostata in ingresso), si decideva in team multidisciplinare di escludere una endocardite eseguendo un ETE da cui: Prolasso mitralico anteriore scallop a1 a2,a3 e posteriore p2 determinante insufficienza mitralica valvolare di grado severo con presenza di jet multipli; valvola aortica con stenosi di grado severo ampiamente rimaneggiata da vegetazioni endocarditiche diffuse con presenza di ampia perforazione della cuspide coronaria sinistra, ampio flusso in entrata e uscita; presenza di pseudoaneurisma in corrispondenza della continuità mitro-aortica. Conclusione: endocardite infettiva con ascesso cavato della radice aortica, rifornito al doppler. Posta indicazione ad intervento cardiochirurgico di sostituzione valvola aortica (SVA) associato a riparazione aortica, rifiutato dalla paziente per il rischio intraoperatorio e postoperatorio di anemizzazione severa con necessità di supporto emotrasfusionale. Veniva impostata terapia medica con Ceftriaxone (2gr 2vv/die) ed Ampicillina (3gr 4vv/die) per 4 settimane. Dopo 7 giorni: paziente stabile, apiretica; agli esami ematochimici: indici di flogosi e di sepsi negativi. Dimessa con indicazione a proseguire terapia con Cefditoren Pivoxil (400mg 2vv/die) e Amoxicillina/Acido Clavulanico (1gr 3 vv/die) per 4 settimane. Alla valutazione a 30 giorni: paziente apiretica da 7 giorni, stabile clinicamente, persiste alto il rischio di embolizzazione settica. Nei giorni seguenti comparsa di disartria e parestesie a carico dell'arto superiore destro, della durata di pochi minuti a regressione spontanea. Seguiva accesso in PS. Risultati negativi indici di flogosi ed emocolture; eseguita TC encefalo con reperto di emorragia subaracnoidea (iperdensità emorragica di alcuni solchi in sede fronto-parietale sinistra alla convessità). Posta nuovamente indicazione ad intervento di SVA e/o sostituzione e riparazione della valvola mitralica, rifiutato dalla paziente. Veniva intrapreso ciclo di antibioticoterapia con Amoxicillina/Acido Clavulanico (1 gr 3vv/die) da proseguire per ulteriori 30 giorni. Dopo le dimissioni, la paziente non è più tornata al follow-up. **Conclusioni:** Appare evidente l'importanza della valutazione multidisciplinare del paziente con sospetta o confermata endocardite mediante l'apporto di più specialisti al fine di garantire l'individuazione tempestiva della diagnosi, di fornire le migliori strategie terapeutiche mediche e/o chirurgiche e di prevenire l'insorgenza di complicanze migliorando così la prognosi dei pazienti, soprattutto di quelli con rischio più elevato di mortalità.

SARCOPENIA ASSESSED BY CT-BASED CRITERIA PREDICTS MORTALITY AND NUMBER OF HOSPITAL ADMISSIONS IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: (1); Aim (2); Material and Methods (3); results (4); conclusion (5)
1) Sarcopenia, the progressive loss of muscle mass and function, significantly affects the prognosis and, ultimately, mortality of patients with liver cirrhosis, but a standard definition is still lacking. Several studies have tried to identify potential tools to aid diagnosis of sarcopenia in cirrhotics and guide clinical decision-making by using different imaging approaches. However, the correlation between the magnitude of muscle mass loss and clinical outcomes has not yet been clearly defined
2) Our study aimed to assess whether the psoas muscle area (PMA) and the transverse psoas muscle thickness (TPMT), especially their temporal changes (delta values), could be used as predictive markers of number of hospital admission and mortality in patients with liver cirrhosis.
3) For this study, we enrolled 205 patients with liver cirrhosis. For each patient, we assessed both clinical variables (including sex, age, etiology of cirrhosis, laboratory tests, prognostic indices and drugs) and radiological features (CT scan). The latter included serial changes on CT scans performed every six months for 2 years, focusing on the psoas muscle area (PMA) at the inferior margin of the L4 vertebral body and the transverse psoas muscle thickness (TPMT), the maximum transverse diameter of the psoas muscle. Rather than considering absolute PMA and TPMT measurements over time, we recorded delta changes between baseline and follow-up CT scans.
4) We observed a progressive increase in delta changes over time, reflecting a gradual reduction in TPMT and PMA between baseline and last follow-up (24 months). We analyzed the association between ΔPMA and ΔTPMT and mortality at 12 and 24 months. PMA assessed at baseline versus 12 months, PMA assessed at baseline versus 24 months, and TPMT at baseline versus 24 months, showed statistically significant correlation with mortality ($p < 0.001$,$p < 0.05$ and $p < 0.05$, respectively). As well, ΔPMA (baseline versus 24 months) was significantly associated with the number of hospital admissions.
5) Our results highlight the value of dynamic muscle loss assessment into routine imaging follow-up, offering a practical and objective tool to identify sarcopenia and guide timely clinical interventions.

DEVELOPMENT AND INTERNAL VALIDATION OF AN INTEGRATED PREDICTIVE SCORE FOR THE DIAGNOSIS OF ACUTE PYELONEPHRITIS

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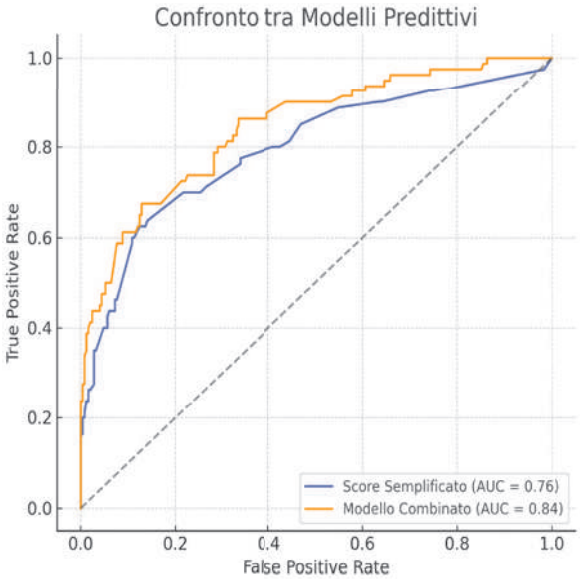
Introduction: Timely diagnosis of pyelonephritis remains a clinical challenge, particularly in hospitalized patients with comorbidities. This study aimed to develop and internally validate an integrated predictive score—based on clinical, B-mode ultrasound, laboratory, and anamnesis data—to improve diagnostic accuracy for acute pyelonephritis.
Methods: A single-center prospective study was conducted (Departmental Ultrasound Program "Serra" – Sant'Orsola Malpighi University Hospital, Bologna) involving 329 patients with suspected acute pyelonephritis. The diagnosis was confirmed using contrast-enhanced ultrasound (CEUS). Included parameters were clinical symptoms (e.g., flank pain), ultrasound findings (hypo-/hyperechoic cortex, globular renal shape, perirenal fluid, hydronephrosis/ureteral dilatation), laboratory markers (CRP, leukocyte esterase), and comorbidities (e.g., immunosuppression, hypertension). A weighted dichotomous score was built using multivariable logistic regression. Predictive performance was assessed via ROC curve and AUC.
Results: Among the 329 patients, 80 (24.3%) had a confirmed diagnosis of acute pyelonephritis. The mean age was 58.4 years (SD ± 21); 47% were male. Multivariate analysis identified several independent predictors significantly associated with the diagnosis. Flank pain increased the risk of pyelonephritis more than threefold (OR 3.30; 95% CI: 1.60–6.79; $p = 0.001$), while a globular renal appearance on ultrasound showed one of the strongest associations (OR 8.26; 95% CI: 1.86–36.67; $p = 0.005$). B-mode cortical alterations were also relevant: hyperechoic cortex was associated with a tripled risk (OR 3.31; 95% CI: 1.27–8.59; $p = 0.014$), while hypoechoic cortex showed the strongest association (OR 11.68; 95% CI: 3.37–40.45; $p < 0.001$). The final predictive

score included 11 variables and achieved an AUC of 0.84, with an optimal cut-off of ≥3 points (sensitivity 63.8%, specificity 80.3%). Independent predictors included flank pain (β = 0.86, p = 0.005), hypoechoic cortex (β = 2.63, p < 0.001), immunosuppression (β = 0.66, p = 0.017), and CRP >10 mg/L (β = 0.03, p = 0.027). Integrating comorbidities significantly improved discriminative performance compared to clinical-ultrasound models alone (AUC 0.76).
Conclusions: The integrated score may serve as a practical and accurate tool for diagnosing acute pyelonephritis. Its application could optimize patient stratification and reduce the need for contrast-enhanced imaging, thus preserving healthcare resources.



PAI-1 GENE HOMOZYGOSITY AND RENAL ARTERY THROMBOSIS. A CASE REPORT.

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Case presentation: A 40-year-old man with renal artery thrombosis was admitted to the Internal Medicine Department of the University of Naples "Federico II" with severe back pain. After excluding muscle skeletal pain, abdominal ultrasound and angio-CT revealed an opacification of a polar branch of the left renal artery, leading to ischemia of a significant portion of the renal parenchyma. The patient's medical history was notable only for cephalgia, frequently managed with NSAIDs, and a family history of early-onset coronary artery disease (CAD). On physical examination, the patient's temperature was 37.0°C, heart rate was 90 bpm, and blood pressure was 110/90 mmHg. Pulmonary and cardiac auscultation were unremarkable, but tenderness was elicited in the left lumbar region. Laboratory findings included evidence of marked inflammation (white blood cell count 13.67 x 10^3 U/L, C-reactive protein 306 mg/L), slight prolongation of baseline coagulation tests (PT INR 1.47; aPTT ratio 1.21, fibrinogen 659 mg/dL), mild hypertransaminasemia (ALT 2-3 times the upper limit of normal), and elevated renal injury parameters (24-hour proteinuria: 0.7 g). ECG findings and a negative echocardiography and bubble test on echocardiography excluded a cardioembolic origin. Transcranial Doppler, brain angio-MRI, carotid ultrasound, and lower limb color Doppler examinations were also performed. Autoimmune investigation showed positivity for AbTPO. The patient was screened for polymorphisms in factor V, Leiden factor, HR2, prothrombin, and PAI-1 genes, given their prevalence as causes of thrombophilia in the general population. Homozygosity for the 4G/4G polymorphism of the PAI1 gene was detected. The patient was treated with fondaparinux 7.5 mg/day for 3 weeks and then with aspirin 100 mg/day.
Discussion: PAI-1, or plasminogen activator inhibitor-1, is a key regulator of fibrinolysis, the process of dissolving blood clots. It primarily inhibits the activity of tissue plasminogen activator (tPA) and urokinase plasminogen activator (uPA), enzymes that convert plasminogen into plasmin, which then breaks down fibrin clots. Consequently, elevated levels of this enzyme impede fibrinolytic action and promote thrombosis. Polymorphisms in the PAI-1 gene, as well as in other genes encoding proteins in the fibrinolytic pathway, the protein C promoter region, and the tissue factor pathway inhibitor gene, may increase the risk of venous thromboembolism (VTE), although the evidence remains inconclusive. The literature contains no solid evidence to support an important relationship between the PAI-1 defects and the risk of arterial thrombosis. Still, arterial and venous thrombosis share some pathophysiological mechanisms, including inflammation, endothelial damage, and hypercoagulability. . Although early studies explored the role of thrombophilias in arterial thrombosis, these publications have several important limitations. First, the literature is largely retrospective, lacking prospective randomized trials to determine the clinical importance or optimal management of thrombophilias in arterial disease. Second, the infrequent occurrence of both thrombophilias and truly unexplained arterial thrombosis makes it difficult to confirm or deny a link. Third, most studies only assess the risk of the initial thrombotic event, leaving the recurrence risk unknown.
Conclusions: This case of renal artery thrombosis in a young man without typical risk factors, but with identified homozygosity for the 4G/4G polymorphism of the PAI1 gene, highlights the potential role of inherited thrombophilia in seemingly unexplained arterial events. Although a direct causal link between PAI-1 homozygosity and renal artery thrombosis requires further investigation in larger studies, this case supports the consideration of thrombophilic risk factors in the diagnostic workup of such cases.

HYPERTRIGLYCERIDAEMIA IN THE METABOLIC CLINIC: DIABETES DRIVEN VERSUS STEATOSIS DRIVEN PHENOTYPES IN A PROSPECTIVE 102 PATIENT COHORT

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Background: Hypertriglyceridaemia (HTG) is increasingly recognized as a residual cardiovascular-metabolic risk factor, although its clinical heterogeneity complicates risk stratification in everyday practice. We prospectively explored the phenotypic spectrum of HTG in a real-world cohort consecutively attending our tertiary Metabolism & Dyslipidaemia Out-patient Clinic over a single month.
Methods: From 1 to 30 April 2025 we enrolled 102 consecutive, treatment-naïve adults at their first visit. Standardized data were collected at baseline: anthropometry, fasting lipids, glucose, thyroid function, renal and liver function biochemical tests, liver ultrasonography, and structured comorbidity flags (diabetes; hypertension; steatosis; obesity). HTG was defined as triglycerides (TAG) ≥ 150 mg dL^{-1}.
First, the prevalence of HTG was quantified. Second, we modelled a composite "high-risk lipid status" (HRLS) outcome—HTG positivity—by multivariable logistic regression including age, gender, diabetes, hypertension, body-mass index (BMI), glucose, steatosis and fT4. Continuous predictors were entered per 1 SD. Third, we performed an unsupervised K-means cluster analysis restricted to HRLS patients, using the same predictors but excluding fT4 in a sensitivity analysis. Continuous features were z-standardised while binary flags were kept as 0/1; the optimal number of clusters was determined by silhouette criterion and visualised with principal-component analysis.
Results: Among the 102 patients (55 % women, mean ± SD age 59 ± 14 y, BMI 28.4 ± 4.2 kg m^{-2}) the prevalence of HTG was 42 % (n = 43).
In the logistic model (McFadden R^2 = 0.434), the strongest independent predictors of HRLS were diabetes (OR 6.80, p < 0.001) and fasting glucose (OR 2.63 per SD, p < 0.001). Steatosis showed an inverse association (OR 0.42, p = 0.028), while BMI had a borderline effect (OR 1.64, p = 0.049). Age, gender, hypertension and fT4 were non-significant.
The first phenotype (Cluster 0), comprising 23 patients, was characterized by moderate hypertriglyceridaemia (average triglycerides 178 mg/dL), combined with a predominant presence of hepatic steatosis (affecting 83% of subjects). These patients had relatively mild glucose disturbances (mean glucose level of 110 mg/dL) and a lower prevalence of diabetes (22%).
Conversely, the second phenotype (Cluster 1), involving 20 patients, presented a significantly more severe metabolic profile, including marked hypertriglyceridaemia (average triglycerides 276 mg/dL), frequent diabetes (60%), elevated fasting glucose (155 mg/dL on average), and the highest BMI among clusters (average 31 kg/m^2). This "hyperglycaemic diabetic" phenotype underscores the crucial role of glucose metabolism in driving severe dyslipidaemic conditions. PCA confirmed clear separation chiefly along the glucose/diabetes versus steatosis axis.
Discussion:
In a single-centre month-long snapshot, more than one-third of first-visit dyslipidaemic patients already exhibited HTG, underscoring its early prevalence

in referral populations. Diabetes and ambient hyperglycaemia emerged as the principal drivers of HRLS, multiplying risk nearly seven-fold even after adjustment for adiposity, whereas hepatic steatosis (though common) was paradoxically associated with lower odds of high-risk lipid status. Clustering refined this picture into a glucose-centred, diabetes-dominated phenotype and a liver-fat-centred steatosis phenotype, suggesting different pathophysiological routes to HTG that may require tailored interventions. Validation in the forthcoming expanded cohort of > 1000 patients will clarify whether these phenotypes confer distinct long-term cardio-metabolic risk and response to targeted therapy.

PHEOCHROMOCYTOMA: A CLINICALLY CHALLENGING DIAGNOSIS

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Background: Pheochromocytoma is a rare neuroendocrine tumor arising from the chromaffin cells of the adrenal medulla, often characterized by excessive secretion of catecholamines. It is typically associated with paroxysmal or sustained hypertension, but it may also present with nonspecific symptoms or atypical complications, making diagnosis particularly challenging. When associated with systemic vascular involvement, it may mimic vasculitis or connective tissue disorders, further delaying appropriate management.
Discussion: We report the case of a 77-year-old woman admitted in May 2024 with a hypertensive crisis (systolic BP >200 mmHg) and acute upper abdominal pain. Her medical history included autoimmune hypothyroidism and HCV-related cirrhosis in remission. Initial evaluation revealed mild troponin elevation, increased lactate levels, and nonspecific ECG changes. The patient was initially admitted to the cardiology department, where she underwent a chest CT scan negative for pulmonary thromboembolism, as well as serial troponin testing and an echocardiogram, both considered non-significant. Intravenous nitroglycerin therapy was required due to severely elevated blood pressure.
Because of the persistent abdominal pain, an abdominal CT scan was performed, revealing a complex vascular pattern: dissection of the proper hepatic artery with multiple intrahepatic pseudoaneurysms, thrombosis of the inferior mesenteric artery, and post-stenotic dilation of the celiac trunk, likely due to compression by the median arcuate ligament. With cardiac causes ruled out, the patient was transferred to the internal medicine department.
A comprehensive vascular assessment, including angio-CT and brain MRI, identified chronic cerebrovascular disease, bilateral non-significant carotid stenosis, and a small anterior communicating artery aneurysm. Additional dissections and pseudoaneurysms were observed in the splenic and gastric arteries. Extensive autoimmune testing—including AMA, ASMA, ANCA, ENA, anti-DNA, MPO, PR3, anti-CL, and HLA-B51—was negative. PET imaging ruled out active vasculitis. The overall picture suggested secondary vascular damage due to hypertension rather than primary vasculopathy.
At this point, the patient's medical history was reassessed: since the age of 20, she had reported episodes of headaches associated with nausea and vomiting, and high blood pressure triggered particularly by the intake of chocolate, Parmigiano Reggiano cheese, and wine. These findings, together with her elevated blood pressure at admission, medical history, and CT imaging-which also revealed a previously overlooked lesion in the left adrenal gland-were considered.
Hormonal assays revealed elevated urinary metanephrines (1163 mcg/24h), normetanephrines (497–1116 mcg/24h), and chromogranin A (406 ng/mL), with suppressed renin and aldosterone. Tests were repeated after beta-blocker withdrawal, while maintaining doxazosin and a PPI, which may interfere with biochemical interpretation. Nevertheless, the findings remained consistent with pheochromocytoma. I-123 MIBG scintigraphy showed focal uptake in the left adrenal gland.
Outpatient follow-up in late 2024 confirmed that the adrenal lesion was stable (16×13 mm), and vascular imaging showed resolution of the pseudoaneurysms and regression of the intramural hematoma. These improvements enabled surgical intervention.
On February 21, 2025, the patient underwent robot-assisted left adrenalectomy. The surgery was uneventful, with a rapid postoperative recovery: early resumption of oral intake, stable vital signs, good pain control, and autonomous mobilization.
At discharge, the patient was in good clinical condition, on optimized antihypertensive and endocrine therapy. Histopathological examination is currently ongoing, and an endocrinological reassessment is scheduled in the coming weeks.
This case illustrates the diagnostic complexity of pheochromocytoma, particularly when it presents with vascular abnormalities mimicking systemic vasculitis or connective tissue disorders. It underscores the importance of a multidisciplinary approach, combining advanced imaging, hormonal assays, nuclear medicine, and careful clinical judgment. A conservative vascular strategy and appropriate alpha- and beta-blockade were key to achieving surgical eligibility and favorable outcomes. Clinicians should maintain a high index of suspicion for pheochromocytoma in patients presenting with hypertensive crises and adrenal incidentalomas, especially when vascular anomalies are also present.

INCLISIRAN AND TYG: A PROMISING CORRELATION IN HIGH CARDIOVASCULAR RISK PATIENTS

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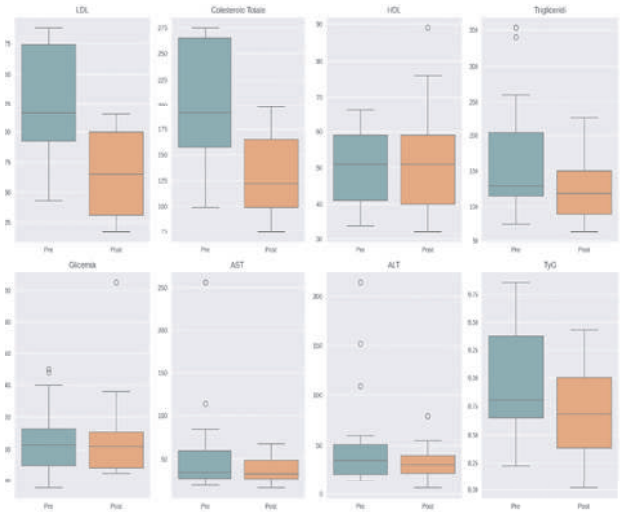
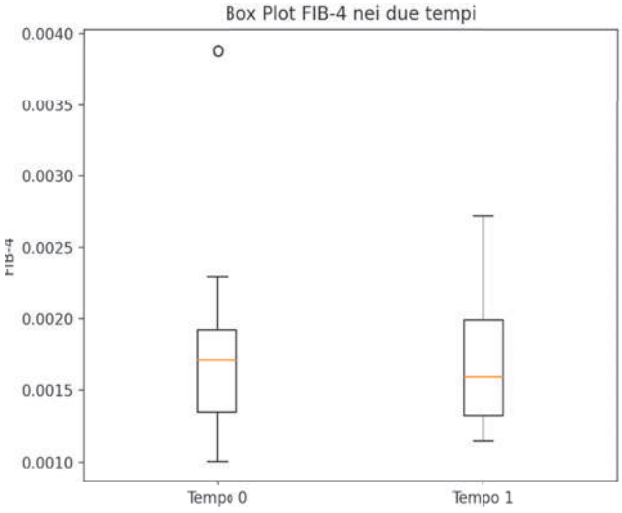
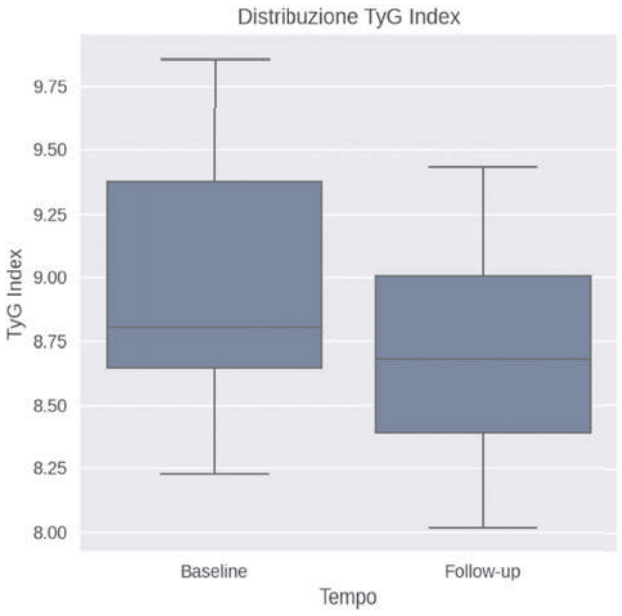
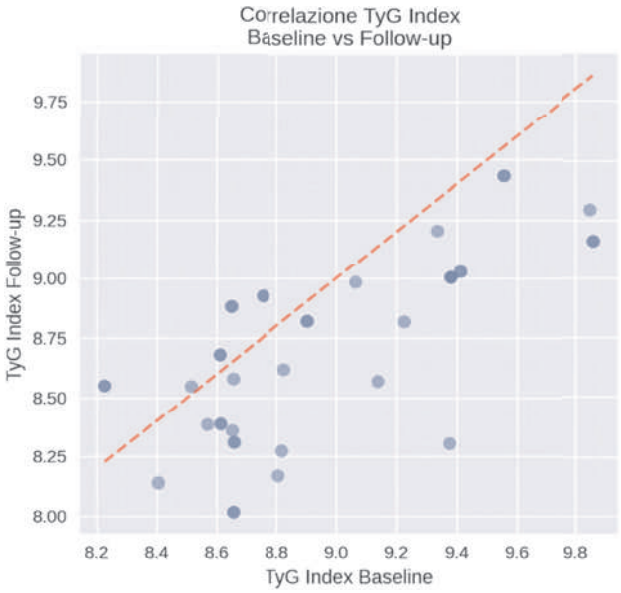
Introduction: Inclisiran is a novel drug available for several years for hypercholesterolemia. It is an siRNA that inhibits the production of PCSK9. Clinical studies have shown that inclisiran can significantly reduce LDL-c levels, thereby reducing the probability of major adverse cardiovascular events (MACE).
The management of cardiovascular risk (CVR) is now a crucial clinical challenge, especially in patients with high-risk profiles. The integrated evaluation of lipid and metabolic parameters therefore plays a fundamental role. An emerging indicator of insulin resistance and cardiometabolic risk is the triglyceride-glucose index (TyG): high TyG values have been associated with an increased risk of cardiovascular events. We conducted an observational clinical study that aims to evaluate the changes in lipid and metabolic parameters, with particular attention to the TyG index, in a group of high CVR patients followed at the Cardiovascular Risk Outpatient Clinic undergoing therapy with Inclisiran.
Materials and methods: This is a longitudinal observational study with two measurement time points (baseline time 0 and follow-up at 3 months) of a group of male and female patients with dyslipidemia and high cardiovascular risk undergoing therapy with Inclisiran, referred to the Cardiovascular Risk Outpatient Clinic of the Internal Medicine 1 Unit of the San Giuseppe Hospital in Empoli (FI). Clinical and anamnestic characteristics and the following biochemical data were evaluated before the start of Inclisiran therapy (time 0) and after 3 months of therapy: total cholesterol, HDL-c, LDL-c, triglycerides, TyG, AST, ALT.
Results: The study population consisted of 28 males and 11 females with a mean age of 65 years. 84.6% of the patients had hypertension. 33.3% of the patients had impaired glucose metabolism (diabetes or IGT). 30.8% of the patients had hyperuricemia. Approximately 56% of the patients were statin-intolerant. 66.7% of the patients (26 patients) were in secondary prevention; 33.3% of the patients were in primary prevention. Regarding the type of CV events: the majority (17 patients) had experienced cardiac events; 6 patients had experienced AOP/carotid stent events; 2 patients had a combination of all types of events (cerebrovascular, AOP, cardiac). Figure 1 shows the mean values of LDL-c, triglycerides, blood glucose, AST, and ALT at both baseline (before treatment) and follow-up (after 3 months of treatment). The mean LDL-c decreased from approximately 124 mg/dL to 64 mg/dL after treatment, with a percentage reduction of approximately -48% with a significant p-value; total cholesterol decreased after treatment by -34% with a significant p-value; triglycerides decreased by 24% ($p < 0.001$); conversely, HDL-c showed a slight but non-significant variation (+2%).
Mean blood glucose values remained more or less unchanged between baseline and follow-up, with a slight reduction in the median but without reaching statistical significance.
Transaminases (AST and ALT) decreased, with a significant reduction for ALT (-29%, $p = 0.045$). The TyG index, an indicator of insulin resistance, decreased by 2.7%, reaching statistical significance ($p < 0.001$), thus suggesting an improvement in the metabolic profile of the patients. The reduction in ALT suggests a positive impact on hepatic steatosis, but this data is purely speculative in this case, as patients were not evaluated for this parameter. In 46% of cases, it was possible to calculate the FIB4 (Fibrosis-4 Index for Liver Fibrosis) at time zero and time 1, observing a reduction of 1.42% (p-value 0.235) (Figure 2). Figure 3 compares the distribution of the TyG Index at baseline and follow-up. The analysis shows a statistically significant reduction in the TyG Index (p-value < 0.0001), with a mean decrease of 2.62% (Figure 4). This suggests a reduction in insulin resistance and improvement in the metabolic profile after treatment with Inclisiran.
Conclusions: This observational study in real clinical practice demonstrates the effectiveness of Inclisiran in determining a significant improvement in the lipid profile in high cardiovascular risk patients, often statin-intolerant. Of particular interest is the statistically significant reduction in the TyG index observed after only 3 months of therapy, thus suggesting a potential additional benefit of Inclisiran on the metabolic profile and insulin resistance in a

vulnerable population. Also interesting is the reduction (although not statistically significant) of FIB 4 only three months after the start of therapy. Further prospective studies with longer follow-ups are needed to confirm these promising results and evaluate their long-term clinical impact.









ATRIAL FLUTTER IN THE EMERGENCY DEPARTMENT: WHAT ROLE FOR TROPONIN?

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Introduzione e obiettivi: Il flutter atriale (FlA) è una delle tachiaritmie sopraventricolari più frequenti osservate in Pronto Soccorso (PS), insieme a fibrillazione atriale (FA) e tachicardia parossistica sopraventricolare (TPSV). Il FlA sembra associato a una maggiore incidenza di cardiopatia ischemica rispetto a FA e TPSV, e a un outcome clinico meno favorevole. La troponina viene spesso dosata nei pazienti con TPSV, ma il suo valore diagnostico e prognostico appare limitato. Mancano, tuttavia, dati analoghi per i pazienti con FlA.
Gli obiettivi del nostro studio sono stati quelli di:
Materiali e metodi: Studio osservazionale, retrospettivo, monocentrico, condotto presso il PS del Policlinico Universitario "A. Gemelli" di Roma, su pazienti con diagnosi di FlA tra gennaio 2014 e luglio 2023, di età compresa tra 18 e 85 anni. Criteri di esclusione: tachicardie sopraventricolari non-FlA e comorbidità gravi (neoplasie attive, insufficienze renale, epatica o cardiaca avanzate). Sono stati raccolti: dati anagrafici, fattori di rischio cardiovascolare, parametri vitali al triage, sintomi riferiti, caratteristiche ECG (frequenza e segni di ischemia), esami di laboratorio (troponina, NT-proBNP, creatinina, emoglobina), referti ecocardiografici e accertamenti ischemici (quando eseguiti). Follow-up a 6 mesi mediante consultazione dei registri informatizzati per valutare endpoint cardiovascolari maggiori e mortalità.
Risultati: Su 476 pazienti con diagnosi di FlA, 205 hanno soddisfatto i criteri di inclusione (età media 68.4 ± 11.9 anni; 63% uomini). La troponina è stata dosata in 124 pazienti (62,3%) ed è risultata elevata in 42 (33.8%). In analisi univariata, la richiesta della troponina era associata a sesso maschile, ipertensione, fumo, familiarità cardiovascolare, dislipidemia, dolore toracico e dispnea (p<0,05); in multivariata, l'unico fattore indipendentemente associato era il dolore toracico (OR 9.8; IC 95% 3.7–29.0; p=0.002). La positività della troponina era associata, in univariata, a età avanzata, pregressa coronaropatia, maggiore creatininemia, ipotensione, ipossiemia, sincope/presincope e anomalie della cinesi ventricolare. In multivariata, solo l'età risultava associata (OR 1.6; IC 95% 1.03–2.5; p=0.038). Solo 29 pazienti (14.1%) sono stati sottoposti ad accertamenti per ischemia, con esito positivo nel 44.8% dei casi. Tuttavia, non si è osservata una correlazione significativa tra troponina elevata e test positivi per ischemia (60.8% vs 46.2%, p=ns). L'endpoint combinato si è verificato in 32 pazienti (15.6%). Anche in questo caso, pur rilevando un maggior numero di eventi nei pazienti con troponina elevata (23.8% vs 14.1%), l'associazione non era statisticamente significativa (p=ns).
Conclusioni: Nei pazienti con FlA in PS la troponina viene frequentemente dosata, soprattutto in presenza di dolore toracico. L'elevazione della troponina

è associata solo all'età avanzata, senza chiara correlazione con cardiopatia ischemica documentata. Non emerge una significativa associazione tra troponina positiva e prognosi a 6 mesi. Sebbene la troponina venga spesso utilizzata nei pazienti con FlA, il suo valore diagnostico e prognostico resta incerto. Sono auspicabili studi prospettici su casistiche più ampie per chiarire il ruolo di questo biomarcatore in tale contesto clinico.

EFFECTIVENESS OF AN EARLY INTRODUCTION OF INTERLEUKIN (IL)-1 RECEPTOR ANTAGONIST ANAKINRA IN PATIENTS WITH RECURRENT PERICARDITIS

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Background: Recurrent pericarditis (RP) affects up to 30% of patients after a first episode of acute pericarditis. Therapeutic options in recurrent forms are based on the use of colchicine and non-steroidal anti-inflammatory drugs as first line treatment, and corticosteroids, immunosuppressants or intravenous immunoglobulin in refractory patients. Recently the effectiveness of anakinra, an IL-1 recombinant receptor antagonist (IL-1r), has been established in controlled and multicenter observational studies in corticosteroid-dependent and colchicine-resistant RP. However, guidance for addressing optimal timing of introduction and tapering strategies of biological treatment in RP is limited and anakinra is usually prescribed as a third-line option.
Methods: a single center retrospective study including patients from the cardio-immunology outpatient clinic of the Careggi University Hospital was designed to investigate the effectiveness and safety of starting anakinra 100 mg/day within 6 months from RP onset, compared to its introduction according to ESC guidelines. Differences in the rate of resolution of clinical, laboratory and echocardiographic IRP manifestations after 3, 6, and 12 months since anakinra introduction were analyzed.
Results: A total of 30 patients with a median of 3 prior recurrences (56.7% male, median age 60.3 years) treated with anakinra 100 mg/day were included in the study. At 3 months, patients starting anakinra within 6 months since RP onset showed a significantly more rapid regression of clinical symptoms (chest pain and fatigue, p = 0.048 and p = 0.031, respectively) and resolution of pericardial effusion (p = 0,046) than observed among patients starting anakinra according to ESC guidelines. Meanwhile, corticosteroid use decreased from 33% to 0% in patients who started anakinra earlier and from 57% to 19% in the other group. At 6- and 12-month, no significant differences were identified in anakinra effectiveness on clinical, laboratory and frequency of pericardial effusion. Moreover, we observed a significant reduction in the recurrence of flares after an early introduction of anti-IL-1r treatment from first pericarditis episode
Conclusion: Our findings suggest that an early introduction of anakinra within 6 months of RP onset allows a rapid improvement of clinical symptoms and pericardial effusion, and a tendency to reduce the number of recurrences as compared to a delayed treatment. Further studies are needed to corroborate these preliminary data.

PROBABLY CARDIAC SARCOIDOSIS IN A PATIENT WITH AN L-VAD DUE TO DILATED CARDIOMYOPATHY

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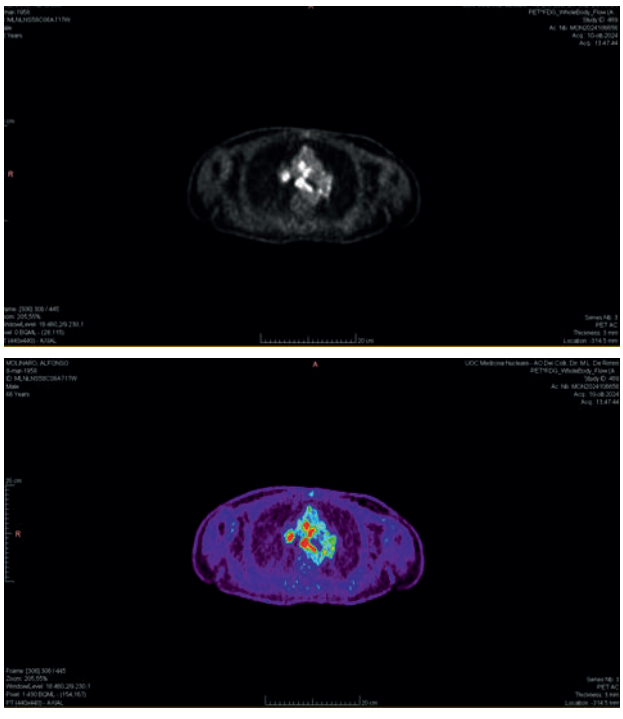
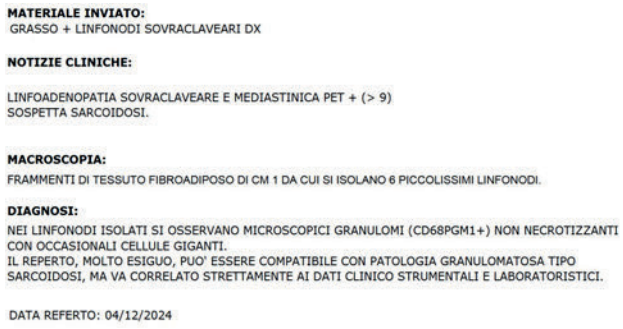
Si presenta il caso di M.A., di anni 66, ricoverato presso il nostro reparto per infezione della drive line di L-VAD, impiantato nel 2022 per scompenso cardiaco grave secondario a cardiomiopatia dilatativa post-ischemica, per cui aveva già impiantato CRT-D nel 2015. Il paziente veniva escluso da trapianto cardiaco per ipertensione polmonare di grado severo.
Durante il ricovero è stata eseguita una PET/TC per definire l'estensione dell'infezione della drive-line, da cui si evidenziavano multiple linfoadenopatie in sede toracica (SUV max 19.32 in sede pre e sotto carenale). Tali linfoadenopatie erano già state rilevate a una precedente PET/TC, ma con captazione minore. Si poneva il sospetto di origine neoplastica delle linfoadenopatie, per cui praticava TC torace, che osservava note disventilatorie del parenchima polmonare senza evidenti definite focalità, prelievo per markers neoplastici non suggestivi di neoplasia solida e striscio di sangue periferico senza evidenza di cloni neoplastici in circolo. Ulteriormente, per escludere causa di tipo infettivo, si effettuava il test Quantinferon, che risultava negativo. Successivamente, l'esame istologico praticato su linfonodo profondo in sede sovraclaveare dx, evidenziava la presenza di microscopici granulomi (cd68pgm1+) non necrotizzanti ed occasionali cellule giganti. Tale reperto è compatibile con patologia granulomatosa tipo sarcoidosico.
Alla luce di tale dato, si revisionava la biopsia eseguita all'apice del ventricolo destro nel 2022, che aveva mostrato presenza di tessuto cardiaco sede di estese aree di necrosi e d'infiltrato infiammatorio acuto e cronico con presenza di ricca quota di istiociti. Tali cellule sono alla base dei granulomi tipici della sarcoidosi, verosimilmente all'origine della patologia cardiaca del paziente in associazione al danno ischemico.
La sarcoidosi è un disordine granulomatoso multisistemico caratterizzato dall'accumulo di granulomi non necrotizzanti in diversi organi. La patologia può essere asintomatica con riscontro accidentale. Gli organi maggiormente interessati sono polmoni e cute con manifestazioni cliniche più comuni che includono: adenopatia ilare bilaterale, fibrosi polmonare o opacità nodulari e lesioni di cute, articolazioni e occhi.
Tra il 2 e il 20% dei pazienti con sarcoidosi presentano ipertensione polmonare, classificata nel 5 gruppo (ipertensione da causa multifattoriali) secondo la più recente classificazione. (1)
In circa il 5% dei casi di pazienti con sarcoidosi polmonare e/o sistemica, si associa coinvolgimento cardiaco, spesso misconosciuto a causa della clinica aspecifica (2). Le manifestazioni più comuni sono: scompenso cardiaco, anomalie di conduzione, aritmie ventricolari e morte improvvisa cardiaca. La diagnosi di sarcoidosi cardiaca è certa in caso di dato istologico su biopsia miocardica, oppure si ritiene probabile se, dopo aver escluso altre cause di patologia cardiaca, risultano esserci istologia positiva per sarcoidosi extra-cardiaca, manifestazioni cliniche suggestive o presenza di esami strumentali (come PET o RM cardiaca) con reperti caratteristici di sarcoidosi (3).
Bibliografia:
(1) Pulmonary hypertension in patients with sarcoidosis: A single-center experience (D. K. Özen, B. Mutlu, D. Kocakaya, B. Turan, S. S, Şekerci, B. Ceyhan) 2021 Jan;25(1):36-41.
(2) Cardiac Sarcoidosis (Birnie D, Ha AC, Gula LJ, Chakrabarti S, Beanlands RS, Nery P) Clin Chest Med. 2015;36(4):657. Epub 2015 Sep 11.
(3) HRS expert consensus statement on the diagnosis and management of arrhythmias associated with cardiac sarcoidosis
(D.H Birnie, W.H Sauer, F. Bogun, J. M Cooper, D. A Culver, C. S Duvernoy, M. A Judson, J. Kron, D. Mehta, J. Cosedis Nielsen, A. R Patel, T. Ohe, P. Raatikainen, K. Soejima) 2014 Jul;11(7):1305-23. doi: 10.1016/j.hrthm.2014.03.043. Epub 2014 May 9.





MATERIALE INVIATO:
GRASSO + LINFONODI SOVRACLAVEARI DX

NOTIZIE CLINICHE:

LINFOADENOPATIA SOVRACLAVEARE E MEDIASTINICA PET + (> 9)
SOSPETTA SARCOIDOSI.

MACROSCOPIA:
FRAMMENTI DI TESSUTO FIBROADIPOSO DI CM 1 DA CUI SI ISOLANO 6 PICCOLISSIMI LINFONODI.

DIAGNOSI:
NEI LINFONODI ISOLATI SI OSSERVANO MICROSCOPICI GRANULOMI (CD68PGM1+) NON NECROTIZZANTI CON OCCASIONALI CELLULE GIGANTI.
IL REPERTO, MOLTO ESIGUO, PUO' ESSERE COMPATIBILE CON PATOLOGIA GRANULOMATOSA TIPO SARCOIDOSI, MA VA CORRELATO STRETTAMENTE AI DATI CLINICO STRUMENTALI E LABORATORISTICI.

DATA REFERTO: 04/12/2024

RENAL VENOUS CONGESTION ASSESSED BY VEXUS I N HEART FAILURE WITH REDUCED EJECTION FRACTION INITIATING VERICIGUAT: A PILOT STUDY

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Background: Heart failure with reduced ejection fraction (HFrEF) is a clinical syndrome characterized by systemic congestion, which is a key target in therapeutic management. In HFrEF renal venous congestion due to backward heart failure leads to disturbance of renal function. Increased pressure in the right atrium and central veins is transmitted to the renal veins, causing congestion and decreased the glomerular filtration rate (GFR). Recent studies have shown that ultrasound can perform a complementary assessment to the clinic to better quantify the degree of congestion. The Venous Excess Ultrasound (VExUS) system is a novel ultrasound protocol that combines venous Doppler assessments of multiple districts, including the inferior vena cava, internal jugular vein, lungs, hepatic and kidneys veins.
Aim: The aim of this study is to assess renal venous congestion in outpatients with HFrEF, with particular focus on identifying subclinical congestion through the VExUS grading system and the correlation between clinical, ultrasound and laboratory findings.
Methods: We conducted a prospective observational study with the current enrollment of 35 outpatients (6 female) with HFrEF with a median age of 75 (56-89). The patients underwent multiple clinical diagnostic tests (NYHA class, edema, crackles), laboratory tests (including NT-proBNP, creatininemia with calculation of eGFR according to CKD-EPI), ultrasound tests such VExUS system [internal jugular vein diameter ratio (iJVD ratio) ,inferio vena cava(IVC), B lines, renal and hepatic venous flow). The iJVD ratio is given by the ratio between the diameter after the Valsalva maneuver and at rest, measured with the patient in a semi-supine position, with the head and neck elevated at approximately 45 degrees using high-frequency linear transducer. Hepatic and interlobar renal veins can be identifed by positioning a convex transducer to perform Doppler acquisition with the patient in supine position. A pathological renal flow is defined as biphasic or pulsatile, Lung congestion is defined by the presence of at least three B-lines (in a specific intercostal space) in at least two zones per hemithorax. Assessment of the IVC was performed using subcostal longitudinal views applying M-mode convex transducer. Pathological IVC values were defined as diameter ≥ 2.1 cm and a respiratory collapsibility index of less than 50%.Descriptive statistics, chi-square tests, ANOVA, and non-parametric correlation analyses (Spearman and Mann-Whitney U) were performed with Jamovi version 2.6.26.0.
Results: At the time of enrollment, all patients already on optimized heart failure therapy with SGLT2i, MRA, ARNI/ACEi, and beta-blocker underwent VExUS evaluation and had started therapy with Vericiguat.Median serum creatinine was 1,29 mg/dl (0,6-3,1), median eGFR 54 ml/min (18-98) and median NT-proBNP was 1542 pg/ml (97-8890). We found that 15 patients (42.9%) with a median age of 76 (62-87) had altered renal venous flow: 9 patients (60%) had a biphasic pattern and 6 patients (40%) had a pulsatile pattern. Clinically, 40% of patients had edema and 66% had crackles. The median creatinine value was 1.96 mg/dl (0.6-3,1), 11 patients (73%) had chronic kidney disease and the median NT-proBNP was 1824 pg/ml. All patients had a positive JVD Radio <4. Five patients had a dilated IVC ≥ 21 mm) and it was collapsible >50% in 4 patients. Pulmonary B-lines were present in 12 patients (80%) and 10 patients had altered hepatic venous flow. There is a significant correlation between renal venous congestion and NYHA functional class (p=0.013), as well as with creatinine values (p=0.027). Additionally, we found a significant correlation between renal venous congestion and the presence of crackles(p=0.036), but not with edema (p=0.383). The VExUS system also showed a significant correlation between renal venous congestion and altered hepatic venous flow (p=0.004) and pulmonary B-lines (p<0.001). Furthermore, we found a significant correlation between renal venous congestion and the diameter of the inferior vena cava (p<0.001), but not with its collapsibility.
Discussion: The high prevalence of altered renal venous flow in our study population indicates that renal venous congestion is a significant issue in patients with HFrEF. This congestion is associated with increased creatinine values and higher NYHA functional class. The correlation between renal venous congestion and creatinine values warrants further evaluation to determine if it represents a functional response to chronic diuretic therapy, a manifestation of cardiorenal syndrome, or an indicator of systemic worsening. Furthermore, the association between renal venous congestion and NYHA functional class implies that renal venous congestion is likely an important determinant of functional capacity in patients with HFrEF.
Conclusion: Renal venous congestion is a common finding in HFrEF, especially in patients with a significant degree of ultrasound congestion in other sites and it is associates with reduced renal function and poorer NYHA functional class.

LIVER STIFFNESS PREDICTS MUSCLE LOSS IN CIRRHOSIS: TOWARD A FIBROSCAN-BASED STRATEGY FOR SARCOPENIA PREVENTION

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Sarcopenia, the progressive loss of skeletal muscle mass and function, is a major determinant of poor prognosis in patients with liver cirrhosis. While computed tomography (CT)-based measurements such as psoas muscle area (PMA) and transverse psoas muscle thickness (TPMT) have been studying for the assessment of sarcopenia, the relationship between their temporal decline and liver stiffness measured by FibroScan remains unclear.
The aim of this study was to identify liver stiffness thresholds associated with the greatest loss of muscle mass over time, in order to determine a clinically meaningful FibroScan cut-off for starting sarcopenia surveillance and management.
We retrospectively analyzed 205 patients with liver cirrhosis who underwent baseline FibroScan assessment. Psoas muscle area (PMA) at the inferior margin of the L4 vertebral body and the transverse psoas muscle thickness (TPMT), the maximum transverse diameter of the psoas muscle were measured every six months over a two-year period. We observed a significant inverse correlation between liver stiffness and delta TPMT, indicating that patients with lower baseline stiffness experienced greater reductions in muscle mass over time.
Stratifying the population by FibroScan values, we found that patients with values between 20 and 25 kPa showed the highest rates of muscle delta changes (both delta PMA and TPMT). Conversely, those with higher stiffness values showed more stable muscle mass with smaller delta changes. These findings suggest that patients with FibroScan at baseline between 20 and 25 kPa have the greatest risk of delta TPMT and PMA changes, and therefore may be the subgroup for which preventive strategies may be most effective.
Our results support the integration of FibroScan into sarcopenia diagnosis algorithms, and propose the use of liver stiffness (cut-off values between 20 and 25 KPa) as a noninvasive criterion for starting screening, targeted nutritional and rehabilitative interventions in cirrhotic patients.

ENDOCRINE NIGHT FEVER: A MULTIFACTORIAL THYROTOXICOSIS IN A PATIENT HOSPITALIZED FOR SUSPECTED ENDOCARDITIS

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Background: Fever may be the presenting complaint of several endocrine disorders and requires differential diagnosis with infectious conditions. Here we describe an unusual case of thyrotoxicosis in patient admitted for possible infective endocarditis (IE).
Case description: A 75-year-old woman with a mechanical mitral valve prosthesis was admitted to our Unit for low-grade evening fever, palpitations and a suspected vegetation on the valve prosthesis on transthoracic echocardiography. She had a history of Hashimoto's thyroiditis with hypothyroidism on

substitution therapy, which was later discontinued due to thyroid functional recovery. Additionally, she underwent pharmacological cardioversion with amiodarone following recurrent episodes of atrial fibrillation.
Clinical hypothesis: The main alternative hypothesis were prosthetic valve IE or thyrotoxicosis.
Diagnostic pathway: IE was ruled out through serial negative blood cultures and a transesophageal echocardiography, which excluded vegetations. Laboratory tests revealed increased inflammatory markers, elevated free thyroxine levels, low thyroid-stimulating hormone levels and increased levels of thyroperoxidase and thyroid receptor antibodies, suggesting ongoing autoimmune thyrotoxicosis. A neck ultrasonography revealed, among a widespread thyroid inhomogeneity, some poorly vascularized hypocogenic areas in the right thyroid lobe, suggestive of subacute thyroiditis.
Discussion: and learning pointsFever remains a diagnostic challenge. In our case it is an unusual presentation of a thyrotoxicosis, likely triggered by unknown virus infection, on a background of autoimmune thyroiditis.Prednisone and methimazole was started bringing clinical benefit. At the three-month follow-up, patient was asymptomatic, and the thyroid profile was within normal range.

PREVALENCE AND CLINICAL OUTCOMES OF PATIENTS WITH EOSINOPHILIA IN INTERNAL MEDICINE WARD: A RETROSPECTIVE COHORT STUDY

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Background: Eosinophilia is not rare in hospitalized patients, and it seems to contribute to reduced survival and worse clinical outcomes. Additionally, when associated with specific signs and symptoms, eosinophilia can readily represent an important diagnostic indicator. Despite growing evidence on the role of increased eosinophil counts in the inflammatory response and organ damage, eosinophilia has been poorly investigated in hospitalized patients. For these reasons, we performed a retrospective analysis of patients admitted to Internal Medicine Ward to assess the prevalence of eosinophilia and its association with clinical outcomes.
Methods: Data were extracted from the MED-CLI registry using standardized procedures by trained data scientists, including demographic, clinical, and hospitalization data, including adverse events. Patients were stratified by admission eosinophil count into non-eosinophilic (≤500 cells/μL) and eosinophilic (>500 cells/μL) groups. The primary outcome was the occurrence of any adverse event during hospitalization; secondary outcomes included length of stay and number of adverse events per patient.
Results: Among 393 hospitalized patients, 10.7% had eosinophilia at admission. Baseline characteristics were similar between eosinophilic and non-eosinophilic groups. Patients with eosinophilia at admission had a significantly high risk of experiencing at least one in-hospital adverse event (71.4% vs 51.6%), with an adjusted odds ratio of 2.38 (p = 0.016). The unadjusted odds ratio for this composite outcome was 2.35 (95% CI: 1.16–4.74, p = 0.017), indicating a significantly higher risk of in-hospital complications among patients with elevated eosinophil counts at admission.In univariate logistic regression, age (OR = 1.02, 95% CI: 1.00–1.03, p = 0.042) and dementia (OR = 2.21, 95% CI: 1.03–4.75, p = 0.043) were also significantly associated with adverse events. Chronic kidney disease, solid tumors, and hypertension showed trends toward association but did not reach statistical significance. These variables were included in multivariate analysis. In the adjusted logistic regression model incorporating age and dementia, eosinophilia remained an independent predictor of adverse events (OR = 2.38, 95% CI: 1.18–4.80, p = 0.016). In this model, age (p = 0.123) and dementia (p = 0.066) showed borderline associations.Patients with eosinophilia at admission experienced a significantly higher number of adverse events (2.07 vs 1.63 per patient, p = 0.0016) and longer hospital stays (29.7 vs 20.4 days, p < 0.001) compared to those without eosinophilia. Multivariate analysis confirmed eosinophilia as an independent predictor of both outcomes, alongside age and chronic kidney disease for adverse events, and dementia for prolonged hospitalization. Exploratory analyses indicated non-significant trends toward increased incidence of neurological, hematologic, and other organ complications in the eosinophilic group.
Conclusion: Eosinophilia at hospital admission was independently associated with increased risk of adverse events and prolonged hospitalization. These findings suggest that peripheral eosinophil count may serve as a useful early marker for identifying patients at higher risk of in-hospital complications.

PROGNOSTIC ROLE OF THE ARTERIAL-VENOUS PCO_2 GAP ON PERIPHERAL VENOUS BLOOD IN PATIENTS ADMITTED TO THE EMERGENCY DEPARTMENT FOR SEPSIS

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Introduzione ed obiettivi: Il gap artero-venoso della pCO2 (A-VpCO2 gap) è considerato un indicatore di perfusione tissutale, che riflette l'output cardiaco (CO), considerato normale quando <6 mmHg, calcolato utilizzando sangue venoso centrale (o misto, se disponibile). Molti studi hanno mostrato che un A-VpCO2 gap <6 mmHg, calcolato su sangue venoso centrale, si associa a prognosi sfavorevole nel paziente settico. Studi preliminari suggerirebbero l'affidabilità del sangue venoso periferico, molto più facile da ottenere in un contesto rapido ed affollato come il Pronto Soccorso (PS), per valutare A-VpCO2 gap. Obiettivo del nostro studio è stato quello di valutare se A-VpCO2 gap, calcolato su sangue venoso periferico (A-PVpCO2 gap), è correlato alla mortalità a 7 giorni nei pazienti che giungono in Pronto Soccorso per sepsi.
Materiali e metodi: Si tratta di uno studio monocentrico, osservazionale, prospettico. Sono stati arruolati pazienti con età > 18 anni, di entrambi i sessi, giunti presso il PS del Policlinico universitario "Agostino Gemelli" di Roma, tra il maggio 2021 ed il maggio 2023, per sepsi di diversa origine e gravità. All'arrivo ogni paziente è stato sottoposto contemporaneamente ad un'emogasanalisi arterioso e venoso periferica. Di ogni paziente sono stati analizzati: i parametri vitali; gli esami di laboratorio, di routine e indici di flogosi. Sulla base del SOFA score e dell'APACHE-II score i pazienti sono stati suddivisi in 2 gruppi: rischio basso (<7 per il SOFA, <15 per l'APACHE-II), e medio-alto (i pazienti che non rientravano nel rischio basso). Le differenze tra i gruppi sono state considerate significative in caso di p value ≤ 0.05.
Risultati: Sono stati reclutati 121 pazienti, con età 72.6 ± 13.2, 71.5% uomini. La mortalità a 7 giorni risultava statisticamente associata ai seguenti fattori: pressione arteriosa sistolica (101.1 ± 24.0 vs 118.5 ± 24.6) e diastolica (59.9 ± 13. vs 70.1 ± 14.1) più basse (p=0.02); PCR inferiore (93.8 ± 50 vs 185.3 ± 119.1; p < 0.001); lattati più alti (5.9 ± 3.3 vs 2.3 ± 4.4, p=0.02); score APACHE-II e SOFA più alti (rispettivamente 93% vs 51% e 71.4% vs 30.5%, p=0.003). A-PVpCO2 gap risultava più elevato nei pazienti ad outcome peggiore (10.3 ± 4.7 vs 7.8 ± 5.7, pur in assenza di una significatività statistica (p=0.08). Dall'analisi delle coordinate della curva ROC (AUC=0.65 quindi accuratezza scarsa) è emerso che il valore di A-PVpCO2 gap più accurato, da usare come cut off quale marcatore prognostico di mortalità a 7 giorni, era 6.75 mmHg (sensibilità 92.9%, specificità 50.5%). Infine, l'analisi di correlazione di Pearson tra la ΔA-VpCO2 e le altre variabili incluse nello studio ha evidenziato una significativa associazione unicamente tra ΔA-VpCO2 e lattati (R 0.235, p=0.01).
Conclusioni: Dal nostro studio emerge che A-PVpCO2 gap risulta mediamente più elevato nei pazienti ad outcome peggiore, pur in assenza di una significatività statistica, mentre un valore di cut off < 6.75 identifica i pazienti con outcome migliore. Il cut off da noi trovato è molto vicino a quello indicato in letteratura (< 6 mmHg) quando A-VpCO2 gap è calcolato sangue venoso centrale, e a quello descritto da Wei Gao et al (2018), il cui A-PVpCO2 gap è risultato significativamente associato alla mortalità a 28 giorni quando superiore a 7.1 mmHg. I principali limiti dello studio sono stati: bassa numerosità del campione, assenza della contemporanea misurazione di A-VpCO2 gap su sangue venoso centrale, ed eterogeneità dei pazienti settici in PS.

EXTRASKELETAL EFFECTS OF SCLEROSTIN INHIBITION: ROMOSOZUMAB IMPROVES SARCOPENIA IN POST-MENOPAUSAL OSTEOPOROSIS

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The Wnt signalling pathway is a key regulator of skeletal homeostasis through promotion of osteogenic differentiation of mesenchymal stem cells (MSCs) and their maturation into osteoblasts, therefore stimulating bone formation and inhibiting osteoclastic bone resorption. In addition, canonical Wnt signaling promotes MSCs differentiation into myoblasts, chondrocytes, and fibroblasts and suppresses adipogenesis. Several inhibitors of the Wnt pathway, including sclerostin (SOST), DKK1, WIF1 and secreted frizzled-related proteins (sFRPs), have been identified. Overexpression of SOST, in particular, is increasingly recognized as a potential central mechanism underlying the development of osteoporosis, sarcopenia, and ectopic adipose tissue accumulation, resulting in

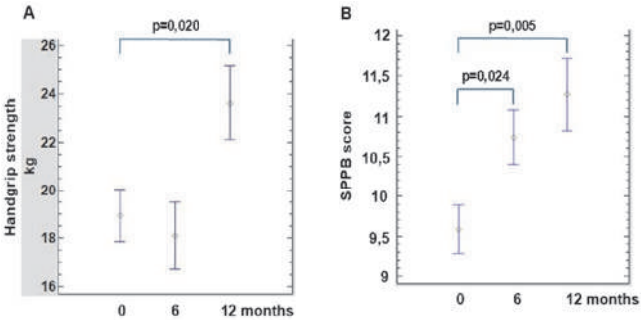
the onset of osteosarcopenia[1].
Sarcopenia is an heterogeneous condition, recognized as an independent risk factor for fracture[2], actually defined by the integrated sum of low muscle mass, compromised muscle strength and poor physical performance, the last assessed respectively with handgrip strength and the Short Physical Performance Battery (SPPB)[3]. Inhibition of SOST with Romosozumab, an anti-SOST monoclonal antibody, induces a rapid and significant increase in bone mass and a reduction in fracture risk. A recent meta-analysis suggested a decreased risk of falls in patients treated with Romosozumab[4].
The rationale for this study is to investigate the potential extra skeletal effects of Romosozumab treatment on body composition, sarcopenia and haematopoiesis in a real-world prospective study.
The preliminary data shown here are focused on sarcopenia in women affected by postmenopausal osteoporosis.
This prospective 12 months open label case-control real world study included 45 postmenopausal osteoporosis women treated with oral bisphosphonates (2 years±6 months): 24 patients were switched to Romosozumab 210mg/month (ROMO) and 21 patients maintained bisphosphonates treatment (CON). Patients with mobility limitations, moderate-severe chronic kidney disease (eGFR<30mL/min), type 2 diabetes mellitus, chronic (≥3 months) corticosteroid treatment, autoimmune diseases, active solid or haematologic malignancies and liver cirrhosis were excluded. After obtaining informed consent, each patient underwent at 0, 6 and 12 months DEXA scan for spine BMD,total hip BMD and body composition assessment (Hologic Horizon A), Short Physical Performance Battery (SPPB) test as previously reported[3], handgrip strength test (HG) as previously reported[5]. Appendicular lean mass/height^2 (ASM, Kg/m^2) was obtained by DEXA Body composition assessment. According to EWGSOP2 consensus, the diagnostic criteria for identifying sarcopenia in females are the presence of HG<16 kg and ASM<5.5 kg/m^2; severe sarcopenia is defined in presence of SPPB≤8 points[3].
ROMO and CON groups were comparable for age, BMI, prevalence of sarcopenia (37%, 9/24 in ROMO and 33%, 7/21 in CON, χ-square p=0.928) and severe sarcopenia (14.2%, 3/24 in ROMO and 12.5%, 3/21 in CON group, χ-square p=0.234). In the ROMO group lumbar spine BMD, total hip BMD, HG and SPPB were significantly lower compared with CON (Tab. 1).
Preliminary data showed a significative increment in HG at 12 months compared with baseline in ROMO (+21.5%, p=0.020) (Fig.1A). Furthermore, in ROMO SPPB score improved significantly at 6 and 12 months compared with baseline (+12.10%, p=0,024, and +17.64%, p=0.005 respectively) (Fig.1B). We didn't observe significant changes regarding HG and SPPB score in CON. No significant changes in ASM were observed in both groups. The increase in HG and SPPB at 12 months in ROMO reduced the prevalence of sarcopenia from 37% to 16.6% (4/24), with no patient with severe sarcopenia (from 14.2% to 0%)
For the first time to our knowledge, these preliminary data suggest a rapid extra-skeletal effect of Romosozumab, specifically on sarcopenia and severe sarcopenia, independently from changes in appendicular muscle mass. These findings are consistent with the effect of Romosozumab on falls observed in RCTs.

Bibliography:

1. Moretti A, et al. Sclerostin: clinical insights in muscle–bone crosstalk. J Int Med Res. 2023;51(8):03000605231193293.
2. Chen H, et al. The association between sarcopenia and fracture in middle-aged and elderly people: A systematic review and meta-analysis of cohort studies. Injury. 2020;51(4):804-811.
3. Cruz-Jentoft AJ, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age and Ageing. 2019;48(1):16-31.
4. Kobayashi T, et al. Efficacy and safety of romosozumab: a meta-analysis of placebo-controlled trials. J Bone Miner Metab. 2024;42(5):492-502.
5. Dodds RM, et al. Grip Strength across the Life Course: Normative Data from Twelve British Studies. Vina J, ed. PLoS ONE.2014;9(12):e113637.

	CON	ROMO	p
AGE (years)	73,86 ± 6,19	73,96 ± 7,21	0,960*
BMI (Kg/m^2)	26,34 ± 4,50	24,14 ± 3,45	0,071*
Lumbar spine T-Score	-2,07 ± 0,72	-2,91 ± 1,03	**0,002***
Total hip T-Score	-1,68 ± 0,79	-2,40 ± 0,58	**0,048***
Appendicular lean mass/ Heigth^2 (Kg/m^2)	36,63 ± 9,70	42,77 ± 8,78	0,115*
Handgrip strength (Kg)	21,67 ± 3,86	18,93 ± 4,54	**0,042***
Short Physical Performance Battery (SPPB) test (point score)	10,24 ± 1,97	9,58 ± 1,89	**0,023***
Subjects with Sarcopenia (%)	33 (7/21)	37 (9/24)	0,928**
Subjects with severe Sarcopenia (%)	14,2 (3/21)	12,5 (3/24)	0,234**

*ANOVA test;
χ-square test



THE TIP OF THE ICEBERG: UNCOVERING HIDDEN IMMUNODEFICIENCY IN AN ADULT WITH INVASIVE ASPERGILLOSIS

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Background: The occurrence of opportunistic infections in an apparently immunocompetent host should prompt investigations for less common forms of adult-onset immunodeficiencies.
Case description: A 35-year-old man with a recent history of bilateral pneumonia due to *Aspergillus fumigatus*, treated with Voriconazole, was admitted to our Unit because of fever associated with headache. No other relevant comorbidities were present and physical and neurological examination were unremarkable.
Clinical hypothesis: A suspicion of central nervous system (CNS) invasive aspergillosis was raised. Moreover, the patient underwent screening tests for both secondary and primary immunodeficiencies.
Diagnostic pathway: Laboratory tests revelead increased inflammatory markers and moderate normocytic anemia; both IgA and IgE levels were elevated without eosinophilia. The Human Immunodeficiency Virus serology was negative while Interferon-gamma release assay resulted positive.
A whole-body CT scan demostrated reduced pulmunary consolidations and an oval fluid-corpuscolar lesion in the right frontal cerebral cortex lobe, whose characteristics were suggestive of a cerebral aspergillosis on a subsequent brain MRI.
Lumbar puncture only revealed the presence of a high viral load of HHV-6, which was also confirmed in peripheral blood. CNS invasive aspergillosis raised suspicion for Chronic Granulomatous Disease (CGD), that was confirmed on nitroblue tetrazolium (NBT) and dihydrorhodamin tests.
The patient underwent allogenic bone marrow transplantation presenting excellent clinical response to long-term antifungal therapy.
Discussion and learning points: Adult-onset CGD is rare condition that must be considered in differential diagnosis of patients with multiple concomitant opportunistic infections, especially CNS invasive aspergillosis.
The occurrence of invasive aspergillosis in a child or adult without a known

predisposing risk should prompt an evaluation for CGD.

MACHINE LEARNING APPROACH FOR PREDICTING NON-BENEFICIAL TREATMENTS IN INTERNAL MEDICINE: REAL-WORLD EVIDENCE FROM THE MED-CLI STUDY

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Background: The evolving phenotype of internal medicine patients, characterized by increasing age, multimorbidity, and complex care needs, presents significant challenges to healthcare in allocation and treatment decision-making. Despite this, limited real-world evidence exists to guide internists in identifying patients at risk for adverse outcomes or likely to receive non-beneficial treatments. The MED-Cli study represents an ongoing institutional effort to collect comprehensive clinical data from patients admitted to internal medicine wards, creating an opportunity to develop evidence-based predictive tools derived from real-world data (RWD).
Aim: This study aims to develop and prospectively validate a machine learning (ML) model using MED-Cli data to predict a composite adverse outcome (prolonged length of stay >22 days, in-hospital mortality, or discharge to palliative care) in internal medicine patients. The primary objective is to create a stratification tool that identifies patients at high risk of adverse outcomes at admission despite optimal therapy, thereby enabling clinicians to avoid non-beneficial treatments, optimize resource allocation, and improve the appropriateness of care based on RWE of current medical practices.
Methods: The study employs a two-phase design. In phase one, we analysed RWD collected from February 2024 to January 2025 and trained an XGBoost ML algorithm incorporating 20 among demographic, clinical, functional, and laboratory features. Feature selection followed up-to-date ML standards: variables with > 40% missingness and highly collinear variables were excluded from the final dataset. Model training was achieved with a 5-fold cross validation with grid search for hyperparameter tuning. The model was informed of the class balance of the target variable. Test set size was set at 20%. Shapley Additive Explanations (SHAP) approach was used to measure the features' contributions to model's prediction. In phase two, we prospectively validate the best-performing model on patients admitted between February 2025 and July 2025. Performance metrics include sensitivity, specificity, AUC-ROC, F1 score and the Matthews correlation coefficient (MCC).
Results: A total of 410 admission episodes for 395 patients were included, covering ~81% of ward admissions (mean 34.1/month). The composite outcome occurred in 181 episodes (44%): 27 deaths (7%), 37 discharges to palliative care (9%), and 147 long stays (36%). Characteristics for the overall study population and for the subgroups with and without the outcome are reported in Table 1. XGBoost achieved the following metrics: accuracy 0.67, ROC AUC 0.75, sensitivity 0.54, specificity 0.78, F1 Score: 0.60, MCC: 0.33. Figure 1 shows the SHAP summary plot to explain model's predictions.
Discussion: Patients with adverse outcomes showed lower functional scores and more interventions, but similar comorbidity counts—highlighting functional status over diagnostic count as a predictor of vulnerability. The model's moderate sensitivity (0.54) compared to specificity (0.78) may reflect suboptimal calibration, given the 44% event rate. SHAP analysis revealed alignment with literature: low Barthel and Braden scores, and hyponatremia, were key drivers of poor outcomes.
To improve sensitivity, further steps are planned: adjusting the decision threshold; implementing cost-sensitive learning to penalize false negatives; applying post-hoc calibration (e.g., Platt scaling); and exploring ensemble techniques. As the model is intended to inform clinical choices and reduce overtreatment, maximizing sensitivity is crucial to identify at-risk patients without under-triage.
Conclusion: This study shows that RWD from internal medicine wards can support the development of ML models to predict adverse outcomes. The model's promising discriminative ability (AUC 0.75) and the prominence of functional status over comorbidities offer actionable insights for clinical practice. Future calibration and validation work—through a multidisciplinary approach involving clinicians and data scientists—will be critical for real-world adoption. With further optimization, the model could aid in personalizing care intensity, avoiding non-beneficial interventions, and improving outcomes in complex internal medicine patients.

Characteristic	All	No outcome	Outcome	p-Value
GENERAL				
Age	**75.50 (19.00)**	**73.00 (19.00)**	**78.00 (18.00)**	**0.00**
Female sex	**46%**	**61%**	**39%**	**0.04**
Years of Education	10.00 (7.25)	10.00 (5.50)	10.00 (8.00)	0.46
Charlson Comorbity Score	**6.00 (4.00)**	**5.00 (3.00)**	**7.00 (4.00)**	**0.00**
Count of Chronic Diseases	7.00 (5.00)	7.00 (5.00)	7.00 (5.00)	0.15
Count of Therapies	**11.00 (6.00)**	**10.50 (6.00)**	**12.00 (6.00)**	**0.01**
Count of Reasons for Admission	**1.00 (1.00)**	**1.00 (1.00)**	**1.00 (1.00)**	**0.00**
Days in the ER	**4.00 (3.00)**	**4.00 (2.00)**	**5.00 (3.00)**	**0.01**
Number of Admissions in the last 12 months	1.00 (1.00)	1.00 (1.00)	1.00 (2.00)	0.15
Number of Admissions in the last 6 months	1.00 (1.00)	1.00 (1.00)	1.00 (1.00)	0.09
Number of Admissions in the last month	0.00 (0.00)	0.00 (1.00)	0.00 (0.00)	0.30
Home dependency: None	**72%**	**63%**	**37%**	**0.00**
Home dependency: Partial	**19%**	**42%**	**58%**	**0.00**
Home dependency: Total	**9%**	**29%**	**71%**	**0.00**
Origin: Home (acute) or Emergency Room	**88%**	**53%**	**47%**	**0.03**
Origin: Other lower intensity wards	**4%**	**69%**	**31%**	**0.03**
Origin: Other higher intensity wards	**1%**	**50%**	**50%**	**0.03**
Origin: Home (elective)	**7%**	**81%**	**19%**	**0.03**
LIFESTYLE				
Smoking: Current	15%	63%	37%	0.20
Smoking: Ex	43%	50%	50%	0.20
Smoking: NA	1%	33%	67%	0.20
Smoking: Never	39%	59%	41%	0.20
Smoking: Passive	1%	80%	20%	0.20
Packs of cigarettes smoked per day	**1.00 (0.50)**	**1.00 (0.88)**	**1.00 (0.50)**	**0.02**
Pack years	0.00 (30.00)	0.00 (37.00)	0.00 (25.00)	0.64
Alcohol: Daily	20%	57%	43%	0.16
Alcohol: Weekly	12%	57%	43%	0.16
Alcohol: Monthly	10%	65%	35%	0.16
Alcohol: Ex	7%	38%	62%	0.16
Alcohol: NA	1%	20%	80%	0.16
Alcohol: Never	48%	57%	43%	0.16
Alcohol Units per week	7.00 (13.00)	5.00 (13.00)	7.00 (12.00)	0.81
VITALS AT ADMISSION				
BMI	24.44 (6.20)	24.49 (6.37)	24.22 (6.32)	0.27
Systolic Blood Pressure	126.58 (23.58)	127.55 (22.86)	125.30 (24.49)	0.34
Diastolic Blood Pressure	70.50 (16.00)	75.00 (15.00)	70.00 (20.00)	0.14
Heart Rate	85.00 (24.00)	85.50 (23.00)	85.00 (25.00)	0.58
Respiratory Rate	18.00 (7.00)	18.00 (7.00)	18.00 (7.00)	0.70
Body Temperature	36.45 (1.00)	36.45 (1.00)	36.45 (1.00)	0.85
Blood Saturation of Oxygen	96.00 (3.80)	97.00 (3.00)	96.00 (4.00)	0.23
FUNCTIONAL SCALES				
Barthel Score before Admission	**90.00 (55.00)**	**100.00 (45.00)**	**55.00 (80.00)**	**0.00**
Barthel Score at Admission	**55.00 (75.00)**	**90.00 (50.00)**	**45.00 (55.00)**	**0.00**
Braden Score at Admission	**18.00 (8.00)**	**20.00 (6.00)**	**15.00 (6.00)**	**0.00**
Glasgow Coma Scale at Admission	**15.00 (0.00)**	**15.00 (0.00)**	**15.00 (0.00)**	**0.02**
Cumulative Index Rating Scale	**5.00 (9.00)**	**4.00 (8.00)**	**6.00 (10.00)**	**0.01**
Barthel Score at Discharge	**75.00 (75.00)**	**90.00 (55.00)**	**45.00 (70.00)**	**0.00**
Frailty Index at Admission	**0.29 (0.41)**	**0.21 (0.34)**	**0.50 (0.37)**	**1E-11**
BLOOD PANEL AT ADMISSION				
Haemoglobin (g/dL)	11.45 (2.50)	11.60 (2.49)	11.26 (2.51)	0.18
White Blood Cells (10^9/L)	**9.90 (6.05)**	**9.40 (5.90)**	**10.50 (7.40)**	**0.04**
Platelets(10^9/L)	213.00 (157.50)	213.00 (141.00)	209.00 (169.50)	0.77
C-reactive protein (mg/L)	**47.00 (118.85)**	**38.50 (116.80)**	**65.10 (122.70)**	**0.05**
Sodium (mmol/L)	**137.90 (6.07)**	**138.20 (5.70)**	**137.20 (7.00)**	**0.02**
Potassium (mmol/L)	4.30 (0.81)	4.24 (0.76)	4.39 (0.87)	0.10

Table 1.

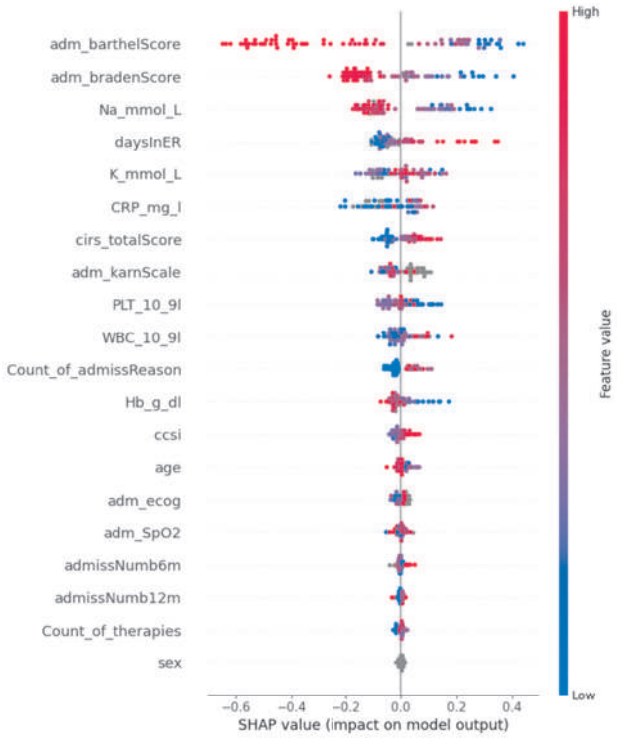

Figure 1

RECURRENT MDR UTIS DURING CANCER IMMUNOTHERAPY: WHEN THE HOST BECOMES THE BARRIER TO CURE

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Urinary tract infections (UTIs) are a frequent and often underestimated complication in oncologic patients, particularly those receiving targeted immunotherapy. In these high-complexity clinical settings, it is essential to consider multiple host- and drug-related factors. The presence of infection cannot be interpreted linearly: the altered immunological microenvironment, compromised anatomical barriers, and the host's ability to respond must all be assessed. This clinical case, emblematic in its course, demonstrates that therapeutic failure does not result solely from antibiotic choice, but from the host's actual ability to mount an effective antimicrobial response.
Case report: A 63-year-old woman with metastatic endometrial carcinoma receiving pembrolizumab and lenvatinib, and with bilateral nephrostomies due to malignant ureteral obstruction, developed recurrent UTIs caused by multidrug-resistant pathogens (Klebsiella KPC, VRE, E. coli, P. aeruginosa, Candida glabrata). Previous antibiotic therapies, including next-generation agents like meropenem, ceftazidime/avibactam, led to temporary microbiological clearance followed by rapid relapses. The patient presented with chronic inflammatory anemia, persistent selective lymphopenia (<500/mm^3), fluctuating creatinine (1.2–2.4 mg/dL), CRP 63–180 mg/L, procalcitonin 1.2–2.96 ng/mL, and hemoglobin 7.9–8.9 g/dL. Anemia consistently dropped 24–48 hours before fever onset and the rise of inflammatory markers. Initially attributed to device colonization, infections were later reinterpreted as manifestations of selective immune dysfunction induced by the immunotherapeutic combination.The regimen with fosfomycin, amikacin, colistin, and N-acetylcysteine was initiated during yet another recurrence caused by Klebsiella KPC, which showed an extended resistance profile and previous therapeutic failures. Nephrostomy replacement was carefully timed to coincide with the peak of antimicrobial activity, reducing the risk of recolonization. The antibiotic regimen—fosfomycin, amikacin, colistin, and NAC, was selected not only for microbiological coverage but also for its synergistic potential against biofilm-producing strains. This approach led to a shift in KPC susceptibility from resistant to sensitive to amikacin, highlighting the importance of modulating ecological pressure in the management of multidrug-resistant infections.
Discussion: Pembrolizumab is an anti–PD-1 monoclonal antibody that reactivates T-cell function; lenvatinib is a multikinase inhibitor (VEGFR, FGFR, PDGFR) that acts on tumor angiogenesis but can also compromise tissue perfusion, vascular integrity, and epithelial barriers. In some patients, this combination can induce a paradoxical immune state: ineffective systemic activation, T-cell dysfunction, and impaired mucosal defenses. Immune checkpoint inhibitors may alter the regulation of innate immunity, predisposing to severe infections even in non-neutropenic patients, as described in a case of nivolumab-associated sepsis (Am J Case Rep 2022; ID 941835). Recognizing these atypical infection patterns is crucial for implementing effective therapeutic strategies.In the selected therapeutic regimen, fosfomycin was used for its excellent tissue penetration and inhibition of bacterial cell wall synthesis; amikacin for its rapid bactericidal activity on Gram-negative organisms through inhibition of protein synthesis; colistin for its ability to disrupt the cytoplasmic membrane of multidrug-resistant pathogens; and NAC for its mucolytic and anti-biofilm action, aiding in the degradation of the extracellular matrix and enhancing antibiotic efficacy.In this case, simple antibiotic escalation proved ineffective. A synergistic pharmacological strategy was adopted, based on complementary mechanisms of action and aimed at biofilm disruption. Fosfomycin, amikacin, colistin, and N-acetylcysteine were combined to improve tissue penetration and overcome biofilm defenses, enhancing therapeutic synergy over additive effects. The Klebsiella KPC strain shifted from resistant to sensitive to amikacin, suggesting ecological changes induced by biofilm removal and reduced selective pressure. Nephrostomies were replaced at the peak of antibiotic efficacy to reduce the risk of recolonization. Subsequent isolation of Candida glabrata was successfully treated with IV caspofungin.
Conclusions: In an oncologic patient with selective immune dysfunction induced by an immuno–target combination, infection was controlled not by antibiotic escalation, but through a synergistic strategy: combining antibiotics with complementary mechanisms, disrupting biofilm, and timely nephrostomy replacement. This case highlights the role of internal medicine in managing complex infections in immunocompromised hosts. Beyond following guidelines, a dynamic, pathophysiology-based approach proved essential. Infections must be interpreted not only by resistance profiles, but also considering immune status, drug interactions, and clinical timing. A multidisciplinary, immune-aware strategy can overcome major therapeutic barriers. Integrating infectious disease expertise into oncologic care is key to improving outcomes.

652. CHALLENGING THE ALGORITHM: THE IMPACT OF BRCA1 TESTING BEYOND STANDARD CRITERIA IN BREAST CANCER CARE

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Background: Women carrying a pathogenic BRCA1 variant face a 55–72% lifetime risk of breast cancer and a 39–44% risk of ovarian cancer. BRCA1-associated breast cancers typically present at a younger age, are more frequently triple-negative, and are characterized by a higher grade and increased proliferation index. Current therapeutic approaches include standard chemotherapy regimens and the use of PARP inhibitors. Prophylactic surgeries in BRCA-carriers, including bilateral mastectomy and salpingo-oophorectomy, are considered effective strategies to reduce the incidence of primary and contralateral tumors in high-risk individuals.
Case presentation: A 62-year-old postmenopausal woman with no significant family history of cancer underwent screening mammography in February 2023, which revealed a suspicious lesion in the left breast, confirmed as invasive breast cancer at the breast biopsy. Histology following sectorial resection and sentinel node biopsy confirmed a poorly differentiated invasive ductal carcinoma classified as luminal B-like, with low hormone receptor expression, high grade, and high proliferation index (estrogen receptor - ER 10%, progesterone receptor - PR <5%, HER2 negative, G3, Ki67 70%), limited to the breast (pT1cN0). Adjuvant treatment was subsequently initiated, including chemotherapy with epirubicin-cyclophosphamide followed by paclitaxel and endocrine therapy with letrozole. During the adjuvant treatment, the patient was found to carry a pathogenic BRCA1 mutation. Following multidisciplinary discussion, she elected to undergo prophylactic bilateral mastectomy and bilateral salpingo-oophorectomy in December 2023. Histology of the right breast revealed a multicentric invasive lobular carcinoma of triple-negative phenotype with nodal involvement (ER <1%, PR negative, Ki67 5%, HER2 score 1+, pT2N1mic).Given the diagnosis of a second, contralateral, triple-negative BRCA1-related breast cancer after-chemotherapy, the patient was started on adjuvant olaparib (300 mg BID) for 12 months, in line with OlympiA trial recommendations. Radiotherapy was also administered to the right chest wall and locoregional nodes, concurrently with a temporary suspension of olaparib. The patient experienced mild radiodermatitis and asthenia but no severe toxicities. Olaparib

was resumed and continued with periodic adjustments based on hematologic tolerance. The patient is currently under follow-up with no evidence of disease. **Conclusions:** This case illustrates the importance of genetic testing in breast cancer patients, even in the absence of a clear family history or young age, when diagnosed with aggressive or triple-negative like tumors. Notably, the identification of an occult contralateral cancer during risk-reducing mastectomy emphasizes the relevance of bilateral surgical approaches in BRCA mutation carriers. Comprehensive management, including systemic, surgical, and radiotherapeutic strategies, tailored to the molecular profile of the tumor and the patient's genetic background, can significantly improve outcomes in this high-risk population.

ATRIAL FIBRILLATION AND CANCER: A SUBANALYSIS OF THE NATIONWIDE ITALIAN START REGISTRY ABOUT THE USE OF DIRECT ORAL ANTICOAGULANTS

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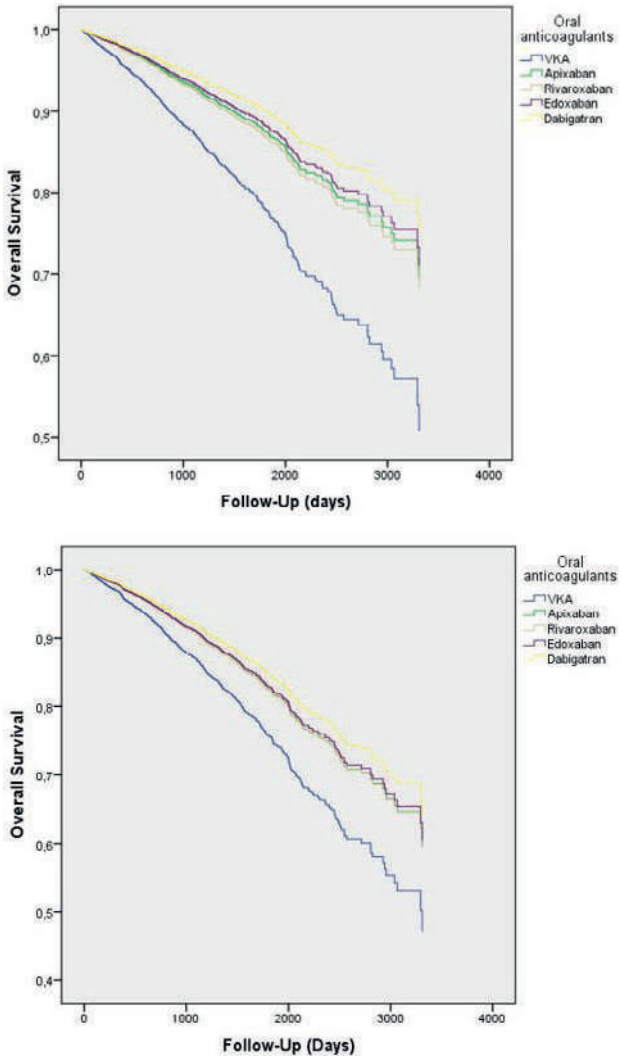
Background: The management of atrial fibrillation (AF) in cancer patients remains an ongoing clinical challenge due to a higher risk for thromboembolic events. For this reason, these patients are often left untreated or prescribed on heparin. Aims of our study were: to investigate the all-cause mortality and cardiovascular events (CVEs) risk in AF patients with cancer comparing the use of direct oral anticoagulants (DOACs) and warfarin.Methods: We performed a sub-analysis of the nationwide Italian START registry including only AF patients with cancer on treatment anticoagulants. Patients were grouped into 1) no cancer, 2) previous cancer and 3) active cancer. Results of the multivariable Cox stepwise regression analysis were expressed as hazard ratio (HR) and its 95% confidence interval (95%CI)Results: 1,605 patients with AF and either active or previous cancer were included in the analysis. Overall, 292 (18.2%) had active cancer with the most prevalent being haematological (27.4%) and genitourinary (22.6%). Mean age was 77.7±8.0 years and 45.3% were women. During a median follow-up of 729.8 days±597.4 days 153 deaths and 177 CVEs occurred. At multivariable stepwise Cox analysis patients with active cancer had an increased risk of death (HR 1.825, 95%CI 1.269–2.623, p< 0.001) and CVEs (HR 1.734, 95%CI 1.229–2.447, p= 0.002) compared to ones with previous cancer. In addition, we found that DOACs were associated with lower all-cause mortality (HR: 0.470, 95%CI: 0.327–0.675, p< 0.001) and CVEs (HR 0.657, 95%CI 0.482-0.895, p= 0.008) compared to warfarin.At univariable Cox regression analysis, we found that Apixaban (HR: 0.535, 95% CI: 0.421–0.679, p < 0.001), Rivaroxaban (HR: 0.564, 95% CI: 0.436–0.729, p < 0.001), Edoxaban (HR: 0.502, 95% CI: 0.346–0.730, p < 0.001), and Dabigatran (HR: 0.421, 95% CI: 0.315–0.562, p < 0.001) were associated with a lower all-cause mortality risk compared to warfarin.Similar results were found about CVEs, showing a risk reduction in patients treated with Apixaban (HR 0.689, 95%CI 0.559-0.850, p<0.001), Rivaroxaban (HR 0.691, 95%CI 0.550-0.870, p<0.001), Edoxaban (HR 0.671, 95%CI 0.486-0.928, p=0.016) and Dabigatran (HR 0.595, 95%CI 0.467-0.757, p<0.001).Conclusion: In conclusions, DOACs seem to be associated with a lower mortality and CVEs compared to VKAs in patients with AF and cancer, independently from the DOAC prescribed. DOACs may represent an optimal choice in AF patients with cancer.



SYSTEMIC LUPUS ERYTHEMATOSUS AND PNEUMONIA: A CASE COMPLICATED BY LUPUS NEPHRITIS

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Università degli studi della Campania Luigi Vanvitelli

A 47-year-old woman came to the emergency department with reported asthenia, mental confusion, diarrhoea, vomiting and a syncopal episode. In remote pathological history she had systemic lupus erythematosus under therapy with prednisone and isoniazid for suspected tuberculosis. On admission she presented as alert, oriented in time and space, collaborating, hypotensive with BP 70/50 mmHg, SpO2 88% in room air, HR 70 bpm and apiretic. On thoracic examination the vesicular murmur was significantly reduced over the entire lung area. The cardiological, abdominal and neurological objective examination was normal. The haemogas analysis showed a picture of lactic acidosis with acute hypoxaemic hypokapnic type I respiratory failure requiring oxygen therapy. Initially she was placed in a Venturi mask, but due to the failure to improve parameters and worsening respiratory distress, it was necessary to start a non-invasive ventilation cycle. The haematochemical examinations showed a picture of severe sepsis with hydro-electrolyte imbalance. She then underwent a CT scan of the chest, which revealed a large and extensive area of parenchymal consolidation occupying almost the entire right lower lobe, with a thin apico-parietal-basal pleural fluid film, and an area of parenchymal thickening in the middle and left lower lobes with a slight pericardial effusion. Reasoned empirical antibiotic therapy was therefore imposed. During her stay in the Internal Medicine ward, when proteinuria >300 mg/dl was found, targeted 24-hour urine tests were carried out, resulting in elevated proteinuria values, as in the case of lupus nephritis; treatment was therefore initially imposed with boluses of Methylprednisolone 500 mg in SF

500 cc to be infused in 3 hours for 3 days and subsequently replaced with Prednisone 0.5 mg/kg with progressive improvement. A control chest CT scan showed a marked improvement in parenchymal thickening but, at the same time, interstitial phenomena as per CTD-ILD.
Discussion: Pulmonary complications are frequently encountered in patients with SLE. Infections can increase immune activity and inflammation, stimulating the activation of autoreactive lymphocytes and leading to worsening of SLE symptoms, including lupus nephritis. Viral infections represent one of the most common triggers of SLE and lupus nephritis. Lupus nephritis represents one of the most severe manifestations of SLE. Clinically it can present with extremely variable pictures, ranging from isolated urinary abnormalities to rapidly progressive glomerulonephritis. Renal biopsy remains the gold standard for diagnosis, as the clinical-laboratory presentation does not always correlate with the histological finding. The clinical criterion for renal involvement is 24-hour proteinuria > 500 mg/day (or proteinuria/creatininuria ratio > 500 mg/g on an extemporaneous sample) and/or the presence of blood cylinders in the urine sediment. In severe forms, initial therapy lasts 3-6 months, aims to achieve remission of the acute inflammatory renal disease and is based on the use of corticosteroids in combination with immunosuppressive drugs. In order to reduce the cumulative dose of the steroid and related side effects, high-dose ev steroid administration is recommended (methylprednisolone boluses with a cumulative dose between 500 and 2500 mg, divided into 3 boluses on 3 consecutive days) followed by oral therapy (prednisone 0.3-0.5 mg/kg/day), to be reduced to ≤ 7.5 mg/day in 3-6 months. The immunosuppressive drugs recommended as first-line therapy remain low-dose cyclophosphamide (500 mg every 2 weeks for a total of 6 doses) or mycophenolate mofetil (target dose 2-3 g/day or mycophenolic acid at the same dose for 6 months). On the other hand, fibrosing interstitial lung diseases (ILDs) comprise a large group of more than 200 diseases, including fibrosing ILDs associated with autoimmune diseases that carry the risk of pulmonary fibrosis, i.e. the irreversible formation of scar tissue in the lungs, which impairs lung function.

ADULT-ONSET STILL'S DISEASE: A COMPLEX PATHOLOGY, A DIAGNOSTIC CHALLENGE

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Introduction: Adult-onset Still's disease (AoSD) is a rare systemic autoinflammatory syndrome with a complex and multifactorial etiology. It is likely caused by hyperactivation of the innate immune system and overexpression of pro-inflammatory cytokines (such as IL-1, IL-6, and IL-18), coming together along with environmental influences, for example viral and bacterial infections. The triad of fever, arthritis, and skin rash represents the typical scenario for the AoSD. Less frequently described symptoms comprise pharyngitis, lymphadenopathy, hepatosplenomegaly, myalgia, serositis, pericarditis, and pleurisy. Based on the Yamaguchi and Fautrel criteria, a diagnosis of exclusion is made by ruling out another inflammatory, infective, or neoplastic disease. Therefore, we report a rare case of AoSD in a young female patient admitted to our department for a fever of unknown origin (FUO).
Case presentation: A 33-year-old female patient was admitted to our hospital with a 1-month intermittent high-grade FUO (39 degrees Celsius), following a quotidian pattern, associated with chills, asthenia, pharyngodynia, skin rash, and widespread arthralgia, predominantly involving the knees, ankles, left shoulder and wrists. Prior medical history included dysthyroidism, treated with L-thyroxine, and SARS-CoV-2 infection, tested positive in January 2023; no allergies to food or drugs were reported. The fever was partially relieved by antipyretics and antibiotic therapy, but it was persistent. The patient presented to the hospital with a complaint of fever and polyarthralgia, therefore she was admitted in the medical ward . Skin examination showed a diffuse maculopapular and salmon-colored rash, nonpruritic, extending from the face to the neck and involving knees and metacarpophalangeal joints (MCP); skin lesions were evanescent and occurred concomitantly with fever spikes. The patient complained of tumefactive and painful wrists and MCP. Laboratory studies were significant for a markedly raised WBC count of 30.000/mm 3 (neutrophilia), platelets 600000 /mm 3, and mild anemia with hemoglobin of 10.5 mg/dL. Erythrocyte sedimentation rate, c-reactive protein (CRP) and serum ferritin were sent. Interestingly, all of which came high (~ 85 mm/h, ~ 15 mg/dL, >11.000 ng/dL), respectively. Liver function tests were deranged (aspartate aminotransferase (AST), alanine transaminase (ALT)). Only afterwards Rheumatology consultation we started to think of AOSD. Other autoimmune pathologies (SLE, polymyositis, dermatomyositis, rheumatoid arthritis, polyarteritis nodosa) were rolled out and ANA, ANCA, AMA and ENA antibodies (subtype: SS-A, SS-B, SM-RNP, SM, nDNA, anti-JO1) were negative. The only abnormalities were rheumatoid factor levels of 17,1 IU/mL (reference range: 0 - 17 IU/mL). Infection was excluded from drawing laboratory tests, including urine routine examination, urine and blood cultures, HIV, HBV, HCV, HAV and CMV tests, Brucellosis, Borrelia and Toxoplasma antibodies, Widal and quantiferon test. The test for EBV (Epstein-Barr Virus) antibodies IgG returned a positive result. Abdominal ultrasound revealed splenomegaly and swollen lymph nodes in the groin and neck. A whole-body F-fluorodeoxyglucose positron emission tomography (FDG-PET) detected pronounced FDG uptake in the spleen and in multiple reactive lymph nodes at cervical, axillary, mediastinal, abdominopelvic and inguinal locations; another hypermetabolic site was pericardium due to a slight inflammatory effusion. According to clinical and laboratory scenarios, the diagnosis of AsoD was achieved, meeting four major and five minor Yamaguchi criteria, and five major and two minor Fautrel criteria. The patient was started with steroids (prednisone 75 mg daily), which were associated with a reduction in symptoms. Due to persistent arthralgia the treatment regimen included methotrexate 15 mg weekly, steroids were tapered over (prednisone 25 mg daily). The patient is discharged from the hospita; she received appropriate medical follow-up in a specialised environment.
Conclusion: Adult-onset Still's disease (AoSD) is an uncommon disorder, which require monitoring and correct treatment in according to evolution of disease. Until a few years ago the treatment regimen included corticosteroids as first line and immunosuppressive (e.g. MTX) or immunostimulatory drugs were reserved as second-line therapy for patients who fail to achieve complete remission with corticosteroids. Lately the IL-1 receptor antagonist is approved for treating AoSD; other agents are also used to treat this disease such as anti-IL-6 and anti-IL-18 receptor monoclonal antibodies. Some clinical studies have demonstrated the effectiveness of these treatments. Further research into AoSD is needed to better understand the pathogenic mechanism, the optimal medical therapy and how to prevent risk of complications.

USE OF LIPID LOWERING DRUGS IN CLINICAL PRACTICE: A RETROSPECTIVE SURVEY AT A METABOLIC DISEASE OUTPATIENT CLINIC

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Background: Dyslipidemias, characterized by abnormal levels of lipids in the blood, are a significant contributor to the development of cardiovascular diseases, which remain among the leading causes of morbidity and mortality worldwide. Pharmacological management plays a pivotal role in the prevention of cardiovascular events associated with dyslipidemia, and statins are widely regarded as the cornerstone of lipid-lowering therapy. These drugs function by inhibiting HMG-CoA reductase, a key enzyme in cholesterol synthesis, thereby reducing low-density lipoprotein (LDL) cholesterol levels and mitigating cardiovascular risk.
Despite their efficacy, a notable portion of patients experience difficulty tolerating statins due to adverse effects. The most frequently reported issues include muscular symptoms such as myalgia and cramps, as well as hepatic dysfunction, which can lead to treatment discontinuation. These side effects pose a challenge to achieving long-term therapeutic goals, as reduced compliance diminishes the overall effectiveness of statin therapy.
For patients who are unable to tolerate statins, those with high cardiovascular risk, or those failing to reach target lipid levels despite treatment, alternative therapies are essential. Two significant options are:
Bempedoic acid: This oral therapy inhibits ATP citrate lyase, reducing hepatic cholesterol synthesis.PCSK9 inhibitors: These monoclonal antibodies lower LDL cholesterol levels by increasing the recycling of LDL receptors on hepatocytes.
Objective of the Study: This study aims to analyze, in a real clinical setting, the use of these drugs, with a particular focus on statin intolerance and the use of second-line treatments. As a secondary objective, it explores the potential correlation between age, sex, and the likelihood of developing statin intolerance in patients undergoing follow-up for dyslipidemia at our metabolic diseases clinic.
Materials and methods: We conducted a two-month retrospective analysis on a total sample of 286 consecutive patients with dyslipidemia (48.6% men and 51.4% women, with a mean age of 64.2 ± 13.8 years).
Among them, 65% were undergoing statin therapy, while 30% had discontinued it due to intolerance Statin-intolerant patients had a mean age of 65.5 ± 12.8 years, with a higher prevalence among women (58.3%) than men (41.7%) (p = n.s.). Non-intolerant patients had a mean age of 63 ± 13.4 years, with a balanced distribution between women (85) and men (93). Among second-line treatments, bempedoic acid wasincreasingly used in statin-intolerant patients, serving as an alternative therapy in 20% of the total patient cohort. However, 5% of patients reported intolerance to this treatment as well. A total of 12% of patients were on alirocumab, with 15 of these having a history of statin

intolerance. Age group analysis revealed that statin intolerance was more frequent among patients younger than 60 and older than 70. Specifically, 14 women and 9 men under 60 years (mean age 48.2) (p = 0.9) reported intolerance, while 19 women and 12 men over 70 years (mean age 74.9) reported intolerance (p = n.s.).
A correlation analysis between sex, age, and statin intolerance suggested a higher risk of intolerance in female patients and older individuals.
Conclusions: The study highlights the relevance of alternative lipid-lowering therapies for patients intolerant to statins, particularly those at higher cardiovascular risk. It also suggests a potential link between statin intolerance, female sex, and advanced age, warranting further investigation. These findings underline the importance of individualized therapeutic strategies to optimize treatment adherence and effectiveness in dyslipidemic patients.

ASSESSMENT OF ADAPTED PHYSICAL ACTIVITY IN PATIENTS WITH ANDERSON-FABRY DISEASE

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Background and Aim: Fabry disease (FD) is a rare X-linked lysosomal storage disorder caused by mutations in the GLA gene, which encodes the enzyme α-galactosidase. The accumulation of globotriaosylceramide (Gb3) in various tissues and organs underlies the clinical manifestations of the disease, which range from muscular involvement to renal, peripheral nervous system, and cardiac complications. Due to its X-linked inheritance, disease manifestations are typically more pronounced in males, whereas females, owing to the phenomenon of X-chromosome lyonization, usually present with milder forms. FD patients experience a wide array of symptoms resulting from Gb3 accumulation in different organs and tissues, with fatigue and asthenia among the most commonly reported. In this study, we aimed to analyze the effects of adapted physical activity in FD patients, by means of bicycle ergometer stress test.
Methods: FD patients who had undergone at least two stress tests at our outpatient clinic, with a minimum interval of three months between tests, were included in the analysis.
Results: From February 2021 to September 2022, we enrolled 59 patients. Table 1 summarizes the main characteristics of the study population.

Table 1. General demographic characteristics of the study population.

We then compared the ergometer stress test parameters within our study population, as shown in Table 2.

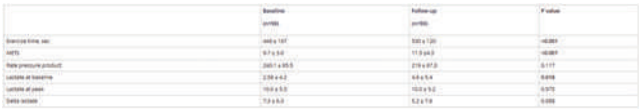

Table 2. Stress test variables at baseline and follow-up

As shown in Table 2, in our population, after a mean follow-up period of 13.3 ± 5.6 months, we observed an increase in exercise duration of approximately 60 seconds (from 446 ± 167 seconds at baseline to 530 ± 120 seconds at the final follow-up; p < 0.001), accompanied by an increase in METs from 9.7 ± 3.6 at baseline to 11.5 ± 4.3 at follow-up.

Conclusions: The prescription of regular physical activity in patients with FD appears to improve cardiovascular performance parameters, in terms of both exercise duration and METs, as assessed bicycle ergometer stress test. These results suggest that FD patients may benefit from exercise programs tailored to their specific clinical characteristics. Additionally, in our study we observed a reduction in the difference between baseline and peak lactate levels, indicating that regular physical activity may reduce the metabolic stress load in these patients.

COMMON SYMPTOMS, RARE DIAGNOSIS: PULMONARY EPITHELIOID ANGIOSARCOMA PRESENTING AS ASTHENIA, COUGH, DYSPNEA, AND FEVER

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Introduction: Epithelioid angiosarcoma is a rare, aggressive vascular tumor derived from endothelial cells, characterized by its epithelioid morphology. Primary pulmonary epithelioid angiosarcoma (PPEA) is an exceptionally rare malignancy, with fewer than 30 cases reported in the literature. Due to its rarity, PPEA is often misdiagnosed as common pulmonary conditions, such as infections, tuberculosis, or diffuse alveolar hemorrhage, especially when imaging reveals ground-glass opacities or nodular consolidations. The clinical presentation is typically nonspecific, including chronic cough, blood-streaked sputum, or massive hemoptysis. Radiological findings can closely mimic other pulmonary neoplasms, making histopathology and immunohistochemistry essential for a definitive diagnosis. This case report illustrates the significant diagnostic challenges in identifying PPEA.
Clinical Case: A.R., a 58-year-old woman, presented to the emergency department with hemoptysis. For the past four months, she had been experiencing asthenia and dyspnea on moderate exertion, which had worsened over the last ten days with the onset of low-grade fever and cough. She was a non-smoker, led an active lifestyle, and had undergone bilateral breast implant replacement 20 years post-aesthetic breast augmentation. Initial chest CT revealed multiple areas of inhomogeneous parenchymal thickening, most extensive in the left antero-lateral base, along with ground-glass opacities and consolidation in both lower lobes. Thickening of the central interlobular interstitium and a modest right pleural effusion were also noted. Due to the D-dimers elevation, thoracic CT angiography was performed a few days later to rule out pulmonary embolism, which showed no thromboembolic phenomena but documented a bilateral pleural effusion. Laboratory tests indicated a hemoglobin level of 9.3 g/dL (down from a prior 12 g/dL), without significant inflammatory markers. Autoimmunity panels, tuberculosis, respiratory atypicals, and viral tests (including TORCH and EBV DNA) were negative. Bronchoscopy revealed hyperemic mucosa with diffuse blood traces in the lower lobe bronchi, but cytological examination of the bronchoalveolar lavage (BAL) was negative for neoplastic cells. Fourteen days later, the patient's condition deteriorated rapidly, with acute respiratory failure, severe anemia, and worsening hemoptysis. A second bronchoscopy with biopsy was non-diagnostic. Follow-up CT demonstrated near-complete atelectasis of the right lower lobe and part of the middle lobe, with a marked increase in pleural effusion. Pleural drainage yielded hemorrhagic fluid, and the patient was transferred to intensive care. A PET scan revealed multiple hypermetabolic nodules in both lower hemithoraxes, with active lymph nodes in the mediastinum and left axillary region. Subsequent lymphadenectomy revealed an undifferentiated malignant neoplasm with a solid and cystic pattern, composed of pleomorphic epithelioid cells. Immunohistochemistry confirmed a high-grade epithelioid angiosarcoma (G3), positive for CD31, ERG, and WT1, with focal positivity for CKAE1-AE3. The patient unfortunately died two weeks after diagnosis.
Conclusions: Primary pulmonary epithelioid angiosarcoma is an exceedingly rare and aggressive malignancy that presents significant diagnostic challenges due to its nonspecific clinical and radiologic features. The case presented highlights the importance of considering rare pulmonary tumors in the differential diagnosis when more common causes have been excluded. Despite advances in molecular profiling, standardized treatment protocols remain lacking, with conventional therapies such as chemotherapy and radiotherapy demonstrating limited efficacy. Early and accurate tissue diagnosis is crucial, although often insufficient to significantly alter the typically fatal disease course. In this context, comprehensive immunohistochemical analysis, including markers like CD31, ERG, and WT1, remains essential for establishing a definitive diagnosis.

ADVANCED YOLK SAC TUMOR WITH LIVER METASTASES IN A 58-YEAR-OLD MALE: A RARE AND AGGRESSIVE PRESENTATION OF TESTICULAR GERM CELL TUMOR

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A 58-year-old male ultramarathon runner was admitted for constipation and right upper quadrant abdominal pain. Physical exam revealed firm hepatomegaly extending 5 cm below the costal margin. Abdominal ultrasound showed

multiple hyperechoic liver lesions and perihepatic effusion. Past medical history included multiple orthopedic surgeries, childhood appendectomy with adhesiolysis, blood donation, and active smoking. Laboratory tests revealed elevated liver enzymes, LDH (397 U/L), and markedly increased AFP (>20,000 ng/mL), with negative beta-hCG, hepatitis serologies, HIV, and autoimmune markers.
Chest-abdominal CT identified esophageal thickening, gastric wall irregularity, mediastinal lymphadenopathy, hepatomegaly with multiple lesions, thrombosis of intrahepatic portal veins and splenic vein, perisplenic collaterals, and pelvic effusion. Upper and lower endoscopies were negative for malignancy. Due to elevated AFP, testicular or hepatic origin was suspected. Testicular ultrasound was normal. Liver biopsy showed SALL4 and glypican-3 positivity, consistent with a yolk sac tumor (YST), likely of testicular origin.
Whole-body PET-CT confirmed no further disease and suggested regression of the testicular primary. Brain CT was negative. The patient was diagnosed with stage IV testicular YST with liver metastases and was started on chemotherapy with 4 cycles of PEB (cisplatin, etoposide, bleomycin), with cisplatin and etoposide at 75%. The first cycle was well tolerated. Supportive care included analgesics, anticoagulants, tumor lysis and neutropenia prophylaxis.
After one cycle, the patient developed grade 2 nausea, dysphagia, leg edema, and persistent asthenia. He required transfusions and potassium replacement; liver function worsened. Given the poor response and side effects, active treatment was discontinued in favor of best supportive care. The patient died within three months of diagnosis.
Germ cell tumors (GCTs) mostly affect males aged 15–40. About 95% are testicular; 5% arise along midline structures. Risk factors include cryptorchidism, prior GCT, subfertility, and environmental exposures. Genetic susceptibility is linked to chromosome 12p gain. YST is a subtype of non-seminomatous GCT (NSGCT), which accounts for 40–45% of GCTs. NSGCTs are less radiosensitive and require chemotherapy.
GCTs often present with a testicular mass, pain, gynecomastia, or metastatic symptoms. Serum tumor markers (AFP, beta-hCG, LDH) are crucial for diagnosis, staging, and monitoring. AFP is produced by YSTs; beta-hCG may be elevated in choriocarcinoma. However, only 50% of GCTs express any marker. Testicular ultrasound is highly accurate, but histology confirms diagnosis. Staging involves contrast CT, and in select cases, brain MRI or bone scan.
Recurrence risk after orchiectomy is tied to tumor size, vascular/rete testis invasion, and embryonal carcinoma component. Absence of YST may indicate higher relapse risk due to lack of AFP secretion. IGCCCG criteria stratify metastatic GCTs into good, intermediate, and poor prognosis using markers, metastatic sites, LDH, and age. This guides treatment intensity and regimen.
Localized disease is managed with orchiectomy, followed by surveillance or adjuvant therapy based on histology and risk factors. Orchiectomy alone cures 70% of NSGCTs. In advanced cases, systemic chemotherapy with PEB is standard. In life-threatening disease, dose-reduced chemotherapy may precede orchiectomy. Residual masses >1 cm should be surgically removed post-chemotherapy.
About two-thirds of patients with advanced NSGCT achieve complete response to first-line therapy. Those who relapse may undergo salvage regimens (e.g., TIP) or high-dose chemotherapy with stem cell support in expert centers. Tumor marker decline after initial therapy may guide further treatment. Promising biomarkers like miR-371a-3p show better sensitivity/specificity than classical markers.
Follow-up lasts at least five years, aiming to detect relapses early, monitor late toxicities, and prevent second malignancies. Most relapses occur in the first two years, often with marker elevation and imaging findings. Long-term issues include cardiovascular disease, secondary cancers, infertility, neurotoxicity, pulmonary and metabolic complications, and psychological distress.
Despite high survival rates, individualized care, survivorship support, and future research into early detection and molecularly targeted treatments remain essential to improve outcomes and quality of life.

GENDER DIFFERENCES IN INFLAMMATORY ACTIVATION AND LUNG INJURY DURING SARS-COV-2 INFECTION: FOCUS ON ALPHA-1-ANTITRYPSIN

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Introduction: COVID-19 is a highly contagious infectious disease caused by the SARS-COV-2 virus. It presents with a wide range of symptoms, including fever, dry cough, fatigue and pulmonary involvement. In severe cases, it can be complicated by excessive systemic inflammation and a "cytokine storm", i.e. the release of large amounts of pro-inflammatory cytokines, that contribute to inducing severe lung injury. This can lead to impaired respiratory function and increased mortality.
Alpha-1-Antitrypsin (AT-1) is a serine-protease inhibitor synthetized in the liver, which acts by preventing tissue damage induced by enzymes released during inflammation, in particular neutrophil elastase, thus playing a central role in maintaining the balance between proteases and anti-proteases.
Epidemiological data suggest the existence of marked gender differences in COVID-19, with men showing greater severity and higher mortality than women. Although some key molecules involved in SARS-COV-2 infection, including AT-1 and the viral receptor ACE2, have been implicated, the physiopathology underlying this phenomenon has not yet been really elucidated. Therefore, our aim was to investigate how the inflammatory response and lung tissue involvement during COVID-19 are influenced by gender.
Materials and methods: Subjects were recruited between 6 March and 25 April 2020 among all patients admitted to the "Covid Hospital 2" unit of the University Hospital of Parma, with a diagnosis of respiratory failure secondary to interstitial pneumonia due to SARS-COV-2 infection. Of the 549 patients hospitalized during this period, 143 underwent biological tests relevant to the study. Finally, 80 patients (40 men and 40 women) were included by retrospective data analysis. To evaluate the possible role of estrogens in the gender differences, analyses were performed by dividing the women into two groups according to age (above and below 50 years, n=33 and n=7, respectively). C-reactive protein (CRP), a known marker of inflammatory response activation, and AT-1 were assessed and correlated with respiratory functional parameters, namely PaO2/FiO2 ratio, and imaging findings (CT score) to evaluate their association with the severity of lung involvement.
Results: Women below 50 years of age had higher circulating AT-1 levels than both men and women above 50 years of age ($p<0.05$), even after correction for CRP levels. Regarding lung involvement, premenopausal women also had higher PaO2/FiO2 ratios and lower CT scores ($p<0.05$ for both), indicating less severe parenchymal damage. In addition, a significant negative correlation was found between AT-1/CRP ratio and both CT score ($p<0.01$) and PaO2/FiO2 ratio ($p<0.05$), especially in women, further supporting the protective role of AT-1 against lung tissue damage.
Conclusions: Our data, although preliminary and retrospectively obtained, indicate significant gender differences in circulating AT-1, with higher levels in women younger than 50 years being associated with better outcome of SARS-CoV-2 infection. Thus, estrogens can be suggested to play a protective role against SARS-CoV-2-induced lung injury by increasing AT-1 levels and consequently enhancing its antiprotease activity.

DENTAL CARE AND ORAL MICROBIAL BALANCE IN HOMELESS PATIENTS WITH ALCOHOL USE DISORDER

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Introduction: Alcohol Use Disorder (AUD) is linked to severe oral health deterioration and microbiota imbalance. Among homeless individuals, these conditions are worsened by poor hygiene and limited access to care. In this context, structured dental care plays a critical role in managing both clinical symptoms and microbial stabilization.
Study Objective: To assess the clinical and microbiological effects of dental care intervention in homeless patients with AUD, focusing on oral health indicators and microbial composition before and after treatment.
Methods: In this prospective cohort study, 32 homeless patients with AUD received structured dental interventions within the Internal Medicine and Alcohol-Related Disorders Unit. Treatments included professional hygiene, non-surgical periodontal therapy, conservative procedures, extractions, endodontic treatments, and prosthetic work. Oral microbiota was analyzed at baseline and follow-up using 16S rRNA sequencing, and potential associations with psychological status (SF-36, Zung, STAIY, SCL-90) were examined.
Results: Non-surgical periodontal therapy was performed in 30.3% of patients; 21.2% underwent extractions, 9.1% received restorative treatments, and 6.1% needed endodontic therapy. Prosthetic interventions involved 6.1% for rehabilitation and 9.1% for adjustments. Post-treatment, microbial analysis showed significant changes: Proteobacteria rose from 10% to 12%, and Bacteroidetes dropped from 35% to 32% (both $p < 0.05$). Prevotellaceae and Fusobacteriaceae decreased, while Neisseriaceae increased from 5% to 8%. Pathogens such as *Streptococcus mutans* and *Porphyromonas gingivalisdeclined*; Neisseria subflava, a commensal species, increased. Alpha diversity remained stable, while beta diversity indicated microbial reorganization.
Psychobiological correlations were explored. Although most were not statistically

significant, trends suggested that higher baseline levels of Archaea and Verrucomicrobia aligned with better oral and emotional health. Post-treatment increases in Proteobacteria and Fusobacteria trended with higher anxiety and reduced physical function. Bacteroidetes and Spirochaetes appeared linked to higher depression scores, hinting at possible microbiome–mental health interactions.
Conclusion: This study highlights the broader impact of dental care in managing complex patients. Targeted oral interventions improved periodontal health and modulated microbial profiles, with emerging evidence suggesting links between microbiota and emotional wellbeing. These findings support integrated oral care as a valuable component in managing vulnerable populations with AUD.

WHEN THE ESSENTIAL IS INVISIBLE TO THE EYE: THE CASTELMAN'S DISEASE

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Introduction: Haematological and inflammatory disorders are commonly encountered in Internal Medicine Units. Their co-presence in an adult or elderly male deserves particular attention. It could underlie a rare condition that was only recently discovered and probably underdiagnosed.
Case presentation: In March 2025 a 70-year-old Caucasian man presented with asthenia, worsening dyspnoea, oedema of the lower limbs and anaemia recently discovered to the Internal Medicine clinic visit of the University Hospital of Verona. The patient's medical history was notable, since the young age, for recurrent basal cell carcinomas spread throughout the body (especially on the face, chest and lower limbs). They are surgically removed at the Plastic Surgery Department of the University Hospital of Verona. Furthermore, since 2021 he has been suffering from Diabetes Mellitus type 2 treated with Biguanides with good metabolic control. The clinical history starts in December 2024 when the patient complained of easy fatigue during effort, polyuria and uncontrolled episodes of hyperglycemia by the antidiabetic drug. Thanks to his General Practitioner (GP) he performed some blood tests that revealed a new microcytic anaemia (Hb 10.1 g/dL, MCV 75 fL) with mild thrombocytosis (PLTs 535'000/mm3), iron deficiency (iron 26 mcg/L, ferritin 182 ng/mL, transferrin saturation 8%) and an increase in inflammation markers (PCR 66 mg/L, ESR 116 mm/h). Six months earlier, in June 2024, the blood count and the body iron stores were normal (Hb 14 g/dL, PLTs 231'000/mm3, transferrin saturation 19.7%). In March 2025, during the Internal Medicine clinic visit, the patient reported a weight loss of about 20 kg in the last 3 months without hyporexia, episodes of diarrhea, hands' arthralgia with morning stiffness. The patient denieed fever and night sweats. During the objective examination, enlarged lymphonodes were found in the axillary and inguinal areas, while hepatomegaly and splenomegaly were not evident. Therefore, the clinical suspicion was anaemia secondary to a systemic inflammatory disease, so the Internal Medicine Doctor decided to admit the patient to the Internal Medicine Department of the University Hospital of Verona for further investigations. Extra blood tests were performed, which revealed hypergammaglobulinemia with a monoclonal protein IgG lambda (2 g/L), creatinine 1.25 mg/dL (eGFR 54 mL/min/1.73^2). A total-body CT scan with contrast agent was performed which revealed multiple enlarged lymphonodes at the supraclavicular, axillary, mediastinal, right pulmonary hilum, retroperitoneal and inguinal region; furthermore, an enlargement of the liver and spleen was highlighted. So, a biopsy of the largest left inguinal lymphonode (3x2x1 cm) was performed, which showed at the histological study a marked plasmacytosis, with small germinal centers, penetrating blood vessels, small granulomas, and thickening of the blood vessel wall. The research for HHV-8 was negative.
The association between the multiple lymphoadenopathy and the histological finding leaded to the diagnosis of Multicentric Castelman Disease. Nowadays, the patient is about to start the treatment for Castelman's Disease. Before that, because of the paresthesia in the lower limbs, he is going to perform an electromyography to define which specific form of the Disease it is.
Discussion and conclusion: Castelman's Disease is a heterogeneous group of rare lymphoproliferative disorders. It is characterized by an angiofollicular lymphonode hyperplasia and two forms are observed: Unicentric (UCD) and Multicentric (MCD). The Unicentric involves one or more enlarged lymphonodes in a single region of the body; instead, the Multicentric involves multiple regions of lymphoadenopathy and also have systemic inflammatory symptoms, hepatosplenonomegaly, cytopenias and organ disfunction due to excessive pro-inflammatory hypercytokinemia, often including interleukin (IL)-6. In half of the cases, both forms can be HHV-8-associated. The etiology of this pathology is unknown: chronic inflammation, immunodeficiency, autoimmunity and infection have been incriminated. The role of interleukin 6 (IL-6) has been reported in the genesis of Castelman's Disease. Surgical resection is the gold standard treatment for UCD. Multicentric form is more aggressive and has poor prognosis. It is further categorized based on the presence/absence of co-occurring POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, skin changes) or TAFRO syndrome (thrombocytopenia, anasarca, myelofibrosis, renal dysfunction and organomegaly). It is important because the POEMS associated MCD is treated with radiotherapy or chemotherapy, while the other forms are treated with an IL-6 inhibitor-based therapy with or without glucocorticoids plus cytotoxic chemotherapy. The Internist has a key role in detecting and managing rare, underdiagnosed and multisystemic disorders. In the case of Castelman's disease, the Internist's holistic approach can make a difference by helping to reduce diagnostic delay and avoid consulting multiple specialist and unnecessary investigations.

INFLAMMATORY ACTIVATION DURING SARS-COV-2 LUNG INFECTION: ASSOCIATION WITH RESPIRATORY FUNCTIONAL PARAMETERS AND DIAGNOSTIC IMAGING

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Introduction: The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has spread rapidly around the world with a high morbidity and mortality since its emergency in 2019. Severe forms are characterized by extensive interstitial pneumonia and a significant systemic inflammatory response, potentially leading to acute respiratory distress syndrome (ARDS), coagulopathy and multi-organ dysfunction. In this context, alpha-1-antitrypsin (AAT), an acute-phase protein with anti-inflammatory and antiviral functions, has gained increasing interest because of its potential protective role against lung injury. The aim of our study was thus to evaluate the association between COVID-19 mortality and plasma levels of AAT, inflammatory and coagulation parameters, respiratory function and the extent of lung damage assessed by imaging.
Materials and Methods: The study population was recruited among patients hospitalized at the "Covid Hospital 2" Unit of the University Hospital of Parma between 6 March and 25 April 2020 with a diagnosis of respiratory failure due to interstitial pneumonia caused by SARS-CoV-2 infection. Clinical data were collected together with blood gas analysis and laboratory parameters, including blood count, C-reactive protein (CRP), fibrinogen, interleukin-6 (IL-6), D-dimer and AAT. Respiratory function was estimated by the PaO2/FiO2 ratio, while the entity of lung involvement was expressed as the CT score, indicating the percentage of interested lung assessed by computed tomography (CT). After retrospective analysis of the data, 25 patients, 10 women and 15 men, for whom complete results were available for most of the longitudinally studied parameters, were included. Exclusion criteria were a positive history of chronic obstructive pulmonary disease (COPD), bronchial asthma or pulmonary emphysema, and/or chronic treatment with glucocorticoids.
Results: Of the patients included, 17 survived and 8 died. The deceased were older and more likely to be men (6 out of 8). There were no significant differences in blood pressure, heart rate, PaO2, FiO2 and coagulation profile between the groups. However, compared to survivors, the deceased had significantly higher levels of D-dimer at baseline ($p<0.01$) and showed an increasing trend in plasma levels of CRP, AAT, IL-6 and fibrinogen during hospitalization. In addition, contrary to what was expected, survivors tended to have a lower PaO2/FiO2 ratio and a higher CT score throughout the hospital stay than deceased subjects, indicating a worse respiratory functional capacity.
Discussion: Due to the small sample size and the high variability of the data, our results should be considered as purely qualitative data, which may be a source of new hypotheses to be confirmed in larger prospective studies. However, from our preliminary data, systemic inflammation, as well as circulating levels of D-dimer and AAT, emerge as a central pathophysiological element in the natural history of COVID-19, probably more weighty than lung damage itself in determining short-term outcome. This insight may inform more comprehensive clinical evaluations and tailored therapeutic strategies to improve patient care and survival.

PROGNOSTIC ROLE OF THE ALVEOLAR–ARTERIAL OXYGEN GRADIENT IN PATIENTS ADMITTED TO THE EMERGENCY DEPARTMENT FOR COVID-19

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Introduzione e obiettivi: La polmonite da SARS-CoV-2 può evolvere rapidamente verso un'insufficienza respiratoria acuta di tipo 1. In fase precoce, il mismatch ventilazione/perfusione sembra predominare rispetto al collasso alveolare. L'emogasanalisi (EGA) è essenziale per classificare il tipo e la severità dell'insufficienza respiratoria. Il rapporto PaO2/FiO2 (P/F) è ampiamente utilizzato per diagnosticare e stratificare l'ARDS. Un altro indice, il gradiente alveolo-arterioso dell'ossigeno (AaDO2), esprime il danno parenchimale polmonare ed è proporzionale alla sua gravità. Tuttavia, il valore prognostico dell'AaDO2 in pazienti con COVID-19 sintomatico al momento dell'accesso in PS è ancora poco definito. Obiettivo dello studio è valutare se l'AaDO2 possa essere utile nella stratificazione prognostica per identificare i pazienti a rischio di evoluzione verso COVID-19 critico.
Materiali e metodi: Si tratta di uno studio retrospettivo condotto presso il PS della Fondazione Policlinico Gemelli su pazienti ricoverati per COVID-19 sintomatico tra marzo 2020 e gennaio 2022. Criteri di inclusione: età >18 anni, presenza di febbre ≥38°C, tosse o dispnea, tampone molecolare positivo all'arrivo, disponibilità di anamnesi, EGA, dati clinici e outcome. Sulla base dei dati dell'EGA è stato calcolato il AaDO2 e a partire da esso la differenza alveolo-arteriosa dell'ossigeno (gradiente misurato - atteso), che permette di correggere per il fattore età. Il gradiente A-a O2 atteso era derivato dalla formula: (età in anni + 10) / 4. Nei risultati vengono esposti i dati relativi alla differenza e non al gradiente, per i motivi spiegati sopra, quindi l'abbreviazione AaDO2 si riferisce alla differenza. Sono stati esclusi pazienti con interstiziopatie pregresse. L'outcome composito comprendeva: 1) ricovero/trasferimento in Terapia Intensiva (TI); 2) utilizzo di C-PAP, NIV, intubazione o ventilazione meccanica; 3) decesso intra-ospedaliero per complicanze COVID-19.
Risultati: Dei 634 pazienti valutati, 322 sono stati inclusi (età media 78.5 ± 5 anni, 56.2% maschi). Il 92.2% è stato ricoverato, 17.7% trasferito in TI, 21.7% è deceduto durante il ricovero. L'outcome composito si è verificato nel 31.1% dei casi. All'analisi univariata, l'outcome critico è risultato associato a età (p=0.024), neoplasie pregresse (p=0.031), P/F e AaDO2 (entrambi p<0.001), mentre la vaccinazione ha mostrato effetto protettivo (p=0.048). All'analisi multivariata, sia P/F che AaDO2 erano indipendentemente associati all'outcome. I modelli di regressione hanno confermato che entrambi gli indici derivati dall'EGA forniscono valore prognostico simile nei pazienti COVID-19 (P/F OR 0.98, 95% IC 0.97-0.99 e AaDO2 OR 1.05, 95% IC 1.02-1.07).
Conclusioni: L'AaDO2 calcolato all'arrivo in PS è risultato utile per identificare i pazienti a rischio di evoluzione critica mostrando valore comparabile al P/F. Entrambi gli indici, se calcolati correttamente, possono contribuire alla stratificazione prognostica iniziale. L'utilità di AaDO2 è ben nota nelle insufficienze respiratorie tipo 2, per distinguere tra pump e lung failure. Tuttavia, nel COVID-19, solitamente normo- o ipocapnico, questo vantaggio si riduce, e, vista anche la simile performance dei due indici conviene utilizzare il P/F in quanto più semplice da ottenere.

A RARE CASE OF UNILATERAL ISOLATED PAROTID GLAND SARCOIDOSIS IN A CAUCASIAN PATIENT.

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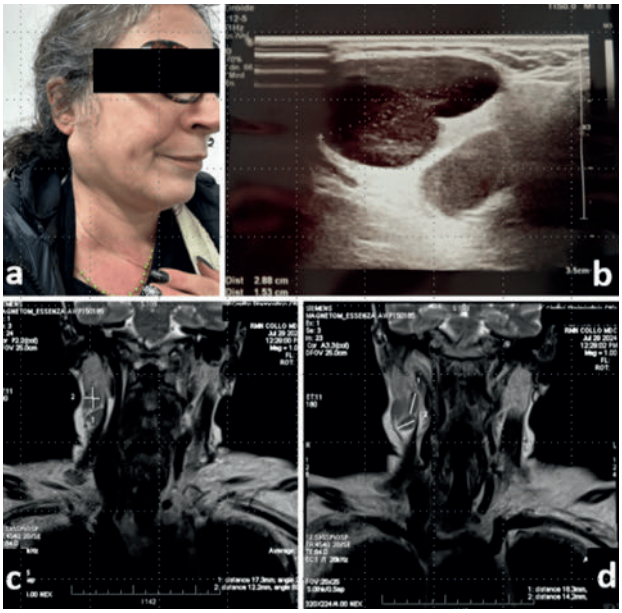
Sarcoidosis is a multisystem disease of unknown aetiology, causing bilateral hilar lymphadenopathy and granulomatous lesions of the lungs, eyes, or skin. Involvement of the parotid gland is a well-known extra-thoracic feature of sarcoidosis, rarely as a primary manifestation. Ungprasert in an Americanseries of 345 cases of sarcoidosis identified only one case of isolated parotid sarcoidosis. No cases of isolated unilateral parotid sarcoidosis in the Caucasian population have been reported in the English-language literature.
Case presentation: A 52-year-old Caucasian woman with no significant comorbidities presentedwith a 2-month history of persistent right parotid enlargement. She reported no xerostomia, dysphagia, dyspnea, skin lesions, or nodules. Clinical examination revealed a 5-cm, oval, irregularly demarcated, painless, and poorly mobile mass (Fig. 1a). Submandibular and cervical lymph nodes were enlarged to 2 cm, mobile, and painless. Laboratory tests showed elevated serum ACE (124 U/L; n.v. 13.3-63.9), ESR 17 mm/hour, normal calcium, and negative Quantiferon, with normal liver and renal function. Ultrasound revealed solid, rounded or ovoid hypoechoic formations in the right parotid, with regular margins and vascularized at ECD, the largest of 29x15 mm, attributable to pathological lymph nodes. Other similar formations were present in the anterior extension of the gland (Fig. 1b). MRI confirmed nodules up to 17 mm in the right parotid parenchyma, in the ipsilateral submandibular and supraclavicular region, with ectopic margins, intense restriction of diffusion and reduced central enhancement (Fig. 1c and 1d). Needle biopsy of the most vascularized lesion described a non-necrotizing granulomatous process with granulomas consisting of epithelial histiocytes (CD68 positive), giant cells and interposed lymphocytes. No signs of infection or malignancy were found. Chest CT excluded pulmonary involvement, while the left parotid was normal. The definitive diagnosis was isolated parotid sarcoidosis. The patient was treated with oral prednisolone (25 mg for 14 days, then tapered over 21 days). After 2 months, the parotid enlargement had completely resolved.
Learning points for clinical practice
Salivary gland sarcoidosis is rare, with unilateral involvement of the parotidgland even rarer. It often presents with painless swelling, as in the casedescribed, and may be confused with neoplasms, infections, or other inflammatory diseases. Ultrasound has been helpful in recognition, whiledefinitive diagnosis was confirmed by needle biopsy, which revealednoncaseating granulomas typical of sarcoidosis.



DIFFERENTIAL DIAGNOSIS OF PRION DISEASES IN THE VAST CHAPTER OF DEGENERATIVE ENCEPHALOPATHIES: A CHALLENGE FOR THE INTERNIST

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Prion diseases or transmissible spongiform encephalopathies are part of the large chapter of degenerative diseases of the central nervous system. The cause is prions, that is, altered forms of the prion protein (PrP) normally present in various organs, particularly in the brain. Two clinical cases of prion disease found occasionally in patients admitted to the Emergency Department of the Internal Medicine department are described.
First case: M, aged 55, accesses the Emergency Department for a state of psychomotor agitation. Blood tests, electrocardiogram and chest x-ray within limits. The brain CT shows lacunar ischemic outcomes and phenomena of cortico-subcortical atrophy. He performs psychiatric consultation: ideic dissociation, derailment of thought and logical leaps, poor awareness of state, anxiety, intact sensorium. He denies anti-conservative and hetero-aggressive ideation and/or intentions. Reported psychiatric history is silent up to the previous 2 months, period in which the current psychiatric symptoms appeared for which a specialist prescribed valproate, pregabalin and quetiapine. No indication for hospitalization in a psychiatric specialist environment. If agitation, promazine im, valproatemia (at upper limits), ammoniaemia (in range) and neurological evaluation are recommended. At the neurological visit: no pyramidal or extrapyramidal signs, no focal deficit; useful execution of the following tests in hospitalization in an internal medicine environment: Ecodoppler TSA, EcoTT, EEG, lipid, vitamin, thyroid and glycated hemoglobin; which are all within normal limits and MRI of the brain and brainstem without and with contrast medium: "... substantially symmetrical enlargement of the Sylvian fissures with increased representation of the cortical sulci, more evident in the fronto-temporo-parietal area on both sides, in relation to reduced tissue trophism... enlargement of the temporal horn, in relation to reduced trophism of the hippocampus of both cerebral hemispheres, with a slightly more evident finding on

the right... alteration of the signal, hyperintense in T2-weighted sequences involving both hippocampi, in particular the body-tail on the right... Slight reduction of trophism of the head of both caudate nuclei, with a slightly hyperintense signal... right. The corpus callosum is thinned as a whole. The mesencephalon is slightly thinned ... No pathological enhancement ..." The findings described suggest the diagnostic hypothesis of an initial neurodegenerative form such as AD or CBD. A neurological reassessment is performed: diagnostic spinal tap (film array, cytophysical, cytochemical, and all screening for any paraneoplastic, immune-mediated and prion pathologies on the CSF: prot 14-3-3 research; prot RT-QuIC research; codon 129 polymorphism of the PRNP gene and mutation screening, sample sent to the ISS). All tests are negative except for the positivity of the RT-QulC (real-time-quaking-induced conversion) which supports the clinical suspicion of MCJ.
Second clinical case: F of 56 years taken to the emergency room for a fall to the ground with full consciousness; reported disturbance of balance for about 3 months and dysarthria for 3 weeks. In previous anamnesis left venous thrombosis and right cerebral ischemia, secondary epilepsy and favism under therapy with coumadin according to INR and levetiracetam. Blood tests, chest x-ray, ECG, echocardiogram (within limits except for flagging of the SIA apparently without shunt) and cranial CT scan within limits. The neurological consultation recommends brain MRI with intracranial arterial and venous MRI angiogram: "...focal signal alteration, hyperintense in T2 and FLAIR sequences and characterized by marked restriction of diffusivity, involving the putamen and the caudate nucleus in a bilateral and symmetric manner; concomitant analogous signal alteration in the bilateral fronto-parital para-falcal cortical area, more evident on the right and at the level of the temporo-occipital gyrus and right parahippocampal. Millimetric hyperintense focus in T2 and FLAIR of nonspecific gliotic significance is appreciable in the right paratrigonal white matter. Concomitant faded signal alteration, hyperintense in T2-FLAIR of the periaqueductal gray matter. The MRI angiogram does not show significant visualization defects involving the main vessels ...". Neurological reassessment is performed: the findings described in the supratentorial encephalic area do not appear to have a univocal interpretation, as it is not possible to exclude an alteration of inflammatory-infectious significance (prion disease?), less likely an alteration of toxic-metabolic significance (negative tests); a liquor examination is essential. The patient is subjected to a spinal tap and the liquor tests show a positive search for the prion protein, confirming the clinical suspicion of Creutzfeldt-Jakob prion disease.
Conclusion: these are very rare diseases (incidence is 1-2 cases per million/year), difficult to diagnose differentially, with a very long latency. After the appearance of the first symptoms, the disease evolves rapidly. There is no cure and the outcome is often fatal.

ENHANCING ORAL AND PSYCHOLOGICAL HEALTH IN HOMELESS INDIVIDUALS WITH ALCOHOL USE DISORDER: A MULTIDISCIPLINARY PROTOCOL

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Introduction: Homeless individuals with Alcohol Use Disorder (AUD) face overlapping medical, psychiatric, and social challenges, often compounded by poor oral health and limited access to coordinated care. This study aimed to evaluate the impact of a multidisciplinary protocol combining dental treatment, psychological support, and medical care in this high-risk population.
Study Objective: This pilot protocol aimed to evaluate the impact of an integrated care pathway combining dental and general health interventions in homeless patients with AUD, assessing improvements in oral health and psychological well-being.
Methods: A prospective cohort of 32 patients—93.75% male, mean age 51 years (SD = 9.2)—was followed at five timepoints over several months. Interventions included professional dental hygiene, psychological assessment, and general medical follow-up. Data were collected on oral health indicators (FMPS, FMBS, DMFT), psychometric measures (SADQ, Zung, SCL-90, SF-36), and treatment adherence. One-year retention probability was estimated using Kaplan-Meier survival analysis.
Results: During follow-up, 15.2% of patients discontinued care: 6.1% died, 3% were incarcerated, 3% experienced psychiatric decompensation, and 3% dropped out voluntarily. The estimated one-year retention rate was 56%, though potentially underestimated due to censored data.
Oral health indicators showed favorable trends: Full Mouth Plaque Score decreased from 0.70 (SD = 0.29) to 0.63 (SD = 0.19), and Bleeding Score dropped from 0.29 (SD = 0.26) to 0.17 (SD = 0.13). DMFT declined slightly from 10.10 (SD = 3.05) to 9.75 (SD = 1.26), suggesting modest clinical improvements. A significant negative association was observed between DMFT and perceived physical oral pain (coefficient = -1.79, p = 0.017).
Psychometric assessments indicated potential benefits. The SADQ score decreased from 23.7 to 19.3 (coefficient = -2.05, p = 0.034), indicating reduced alcohol dependence. The SF-36 domain "role limitations due to emotional problems" improved significantly (coefficient = 11.11, p = 0.0026). The OHIP score decreased from 4.54 to 3.57, reflecting improved oral-related quality of life. Other measures (Zung, SCL-90) showed non-significant trends toward improvement.
Two patients (6.25%) were diagnosed with precancerous oral lesions during opportunistic screenings, highlighting the importance of routine examinations in underserved populations.
Conclusion: This pilot study suggests that an integrated care approach may contribute to improvements in oral health, psychological well-being, and retention in care among homeless individuals with AUD. While results are preliminary, they underscore the value of multidisciplinary strategies tailored to complex patient populations.

FRAIL, FEBRILE, AND CULTURE-NEGATIVE: THE VALUE OF IMAGING IN A SILENT SPINAL INFECTION

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Introduction: Post-surgical spinal infections are rare but potentially serious complications, particularly in elderly and frail patients. Clinical presentation may be subtle, and in the absence of microbiological confirmation, imaging and clinical reasoning play a central role in guiding therapeutic decisions.
Case presentation: A 78-year-old woman with a history of vertebral stabilization was later submitted to hardware removal and vertebroplasty. Approximately two weeks later, she developed persistent fever, nausea, anorexia, dehydration, worsening low back pain, and progressive functional decline. Oral antibiotics administered at home were ineffective. On admission, she appeared sarcopenic, dehydrated, hypoalbuminemic (1.8 g/dL), asthenic, with normocytic anemia and C-reactive protein of 174 mg/L.
Thoraco-abdominal CT revealed soft tissue abnormalities near the spine. Contrast-enhanced MRI showed a large area of altered signal in the posterior paravertebral soft tissues from D11 to S1, extending into the posterior epidural space between L1 and L5, with particulate content and peripheral enhancement but no spinal cord compression. No clear disc involvement was observed. The radiologist favored an inflammatory or infectious etiology.
To better characterize the collections, a whole-body 18F-FDG PET/CT was performed. It revealed metabolic activity in the left paravertebral soft tissues at L4, with no bone or disc involvement, effectively ruling out osteomyelitis or spondylodiscitis. A Quantiferon-TB test was negative. CT-guided drainage yielded only serous fluid, and all cultures (blood, urine, and drained fluid) were negative.
With no surgical indication confirmed by orthopedic consultation, exclusive medical therapy was initiated with intravenous meropenem and vancomycin, continued for six weeks. The empirical choice accounted for culture negativity and suspicion of deep post-surgical infection, aiming to cover Gram-positive organisms (including MRSA) and Gram-negative aerobes, including ESBL-producing Enterobacteriaceae.
The antibiotic therapy was combined with intensive supportive care including IV hydration, nutritional support, correction of metabolic imbalances, and early physiotherapy. Clinical condition gradually improved: fever subsided, inflammatory markers decreased, functional status recovered, appetite normalized, and lumbar pain resolved. Follow-up MRI documented a significant reduction of the collections, with no epidural involvement.
Discussion: The lack of microbiological confirmation posed a major diagnostic challenge. PET imaging played a pivotal role, confirming the inflammatory nature of the collections and excluding osteomyelitis, allowing for effective conservative management. Differential diagnoses—such as spondylodiscitis, post-vertebroplasty hematoma, spinal malignancies, psoas abscess, sterile inflammation, and spinal tuberculosis—were systematically excluded through imaging, clinical evolution, and specific tests.
In frail patients, a multidisciplinary and individualized approach can avoid unnecessary invasive procedures and improve clinical outcomes. This case underlines the importance of adapting diagnostic and therapeutic pathways to the patient's overall condition, especially when standard microbiological or radiological data are inconclusive.
Conclusions: This case demonstrates that culture-negative spinal infections can be successfully diagnosed and managed through advanced imaging and integrated clinical reasoning. PET proved decisive in guiding a conservative, non-surgical strategy. Prolonged antibiotic therapy combined with multidisciplinary

support led to complete resolution.
Educationally, the case highlights the limitations of a microbiology-centered approach in frail patients and encourages clinicians to value functional imaging and clinical integration. The clinical reasoning pathway described here may serve as a replicable model in internal medicine, especially in managing complex, culture-negative infections where a personalized and thoughtful approach can significantly impact outcomes.

IMMUNE CROSSROADS: OVERLAPPING AUTOIMMUNE MANIFESTATIONS EMERGING DURING PACLITAXEL-BASED CHEMOTHERAPY

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Background: The intersection between cancer therapy and autoimmune disorders presents a complex clinical challenge. Chemotherapeutic agents can modulate immune responses, either triggering autoimmune flare-ups or unmasking latent syndromes. This is especially pertinent in patients with pre-existing immune dysregulation, where cytotoxic stress may act synergistically with underlying immunological instability, leading to atypical and hard-to-classify clinical manifestations. Despite the growing use of immunomodulatory therapies in oncology, there is limited understanding of how traditional cytotoxic regimens interact with autoimmune predisposition. Clinicians must maintain high suspicion for systemic immune reactions in cancer patients, even in the absence of overt rheumatologic diagnoses.
Case presentation: A 49-year-old woman of Moroccan origin was diagnosed in July 2024 with a localized triple-negative breast cancer (cT2N2). Her past medical history was notable for type I diabetes mellitus, a serologically positive but unconfirmed diagnosis of celiac disease, and suspect autoimmune hepatitis with persistent elevation of liver transaminases and positive ANA (>1:640, speckled pattern) but negative anti-smooth muscle and anti-LKM antibodies. Given the risk of immune-related adverse events, immunotherapy was contra-indicated. Neoadjuvant chemotherapy with weekly paclitaxel was therefore initiated by August 2024. Following initiation of paclitaxel, the patient developed progressive dermatologic symptoms including erythema, infiltration, and des-quamation of the central face with seborrheic dermatitis features. Neurodermatitis was also suspected on the posterior neck. Despite topical therapies, symptoms worsened, prompting dermatologic and immunologic reevaluation, with the initial diagnosis of atopic chronic dermatitis. By September 2024, the treatment was interrupted after nine cycles due to severe dermatologic toxicity.
After admission for the diagnostic assessment of the dermatologic toxicity, blood workup revealed leukopenia, anemia, elevated ANA (1:1280), and strong positivity for anti-SSA (>1:185) and anti-SSB (>1:320) antibodies, with borderline anti-dsDNA levels. Direct Coombs test was positive. Complement levels (C3, C4) and immunoglobulin levels were within normal ranges. Capillaroscopy and antiphospholipid panels were unremarkable. Imaging showed erosive joint changes in the wrist, a mild pericardial effusion (9 mm), and early fibrotic changes in the lungs. DLCO testing revealed a mild restrictive defect, and the Schirmer test confirmed ocular dryness. Despite a brief improvement in cutaneous symptoms, a systemic flare occurred on November 22, 2024, with the appearance of "puffy hands," palpebral edema, fever up to 39°C with chills, nausea, and a new erythematous lesion on the right foot. Blood cultures were negative, and no specific organ involvement could be identified. Liver function tests remained stable. Advanced diagnostic steps, including salivary gland biopsy, skin biopsy and direct immunofluorescence, were planned to clarify the autoimmune phenotype. Histologic examination of the skin biopsy revealed interface dermatitis, compatible with systemic connectivitis, while direct im-munofluorescence revealed deposits of IgGs. Salivary gland biopsy revealed lymphocytic infiltrates that, however, were not diagnostic for Sjogren syndrome. Overall, such constellation of features—cutaneous involvement, polyserositis, systemic symptoms, serological autoimmunity, and skin immune infiltration—suggests a possible drug-induced or chemotherapy-exacerbated connective tissue disorder with no clear diagnostic classification, in a patient with a likely underlying subclinical systemic autoimmune predisposition. After the completion of the diagnostic workup, systemic steroid therapy followed by hydroxychloroquine was initiated, with good control of symptoms. Abdominal CT scan performed during the hospitalization revealed two liver metastases leading to the initiation of systemic therapy with trastuzumab-deruxtecan, currently ongoing.
Conclusions: This case exemplifies the complex interplay between chemotherapy and autoimmunity, particularly in patients with a background of immune dys-regulation. The onset of a systemic autoimmune-like syndrome during neoadjuvant chemotherapy for triple-negative breast cancer highlights the need for multidisciplinary evaluation and flexible treatment planning. Clinicians should be aware that cytotoxic therapy may unmask or trigger immune reactions that mimic systemic connective tissue diseases, even in the absence of established criteria. Careful monitoring, broad immunologic testing, and prompt dermatologic and rheumatologic collaboration are essential in managing such atypical presentations.

SEX DIFFERENCES IN FUNCTIONAL CAPACITY AND HAEMODYNAMIC FEATURES IN PATIENTS WITH DILATED CARDIOMYOPATHY (DCM) WITH SIMILAR CLINICAL CHARACTERISTICS

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Background: /Introduction: Dilated cardiomyopathy (DCM), defined by left ventricular dilatation and systolic dysfunction, is the most prevalent form of cardiomyopathy which may lead to chronic heart failure (HF). However, precise characterization of clinical and imaging phenotypes remains incomplete. While HF has been extensively studied in literature, there is a notable lack of research on DCM, particularly concerning sex differences. DCM is more prevalent in men than in women, and it is well-known that men experience a worse prognosis, characterized by higher all-cause and cardiovascular mortality rates and an increased risk of sudden cardiac death.
Purpose: This study aims to integrate echocardiographic, cardiac magnetic resonance (CMR), and cardiopulmonary exercise testing (CPET) data to deepen the understanding of sex differences in DCM.
Methods: After excluding patients with incomplete data, the study involved 58 DCM patients referred to our outpatient cardiology clinic. Two cohorts of male and female patients were compared, matched for age, symptom perception, HF bio-humoral markers, treatments, and cardiovascular risk factors.
Results: Despite similar demographic, clinical, and bio-humoral characteristics and left ventricular stroke volume indexed (LV SVi) at rest, men exhibited a more advanced LV dysfunction, biventricular dilatation and dysfunction compared to women- see Picture1. Furthermore, men showed greater right ventricle-pulmonary artery uncoupling. In terms of exercise functional capacity, women demonstrated greater aerobic capacity, as reflected in higher peak oxygen consumption (peak VO2) values, expressed as percentage of the predicted value normalized for age, sex, and height, as well as improved oxygen pulse. Additionally, men exhibited an increased minute ventilation to carbon dioxide production (VE/VCO2) slope. Although no significant differences were found in the presence or extent of late gadolinium enhancement (LGE) between the sexes, there was a trend towards a larger septal localization of LGE in men compared to women.
Conclusions: This study reveals significant sex differences in patients with DCM: men exhibited poorer haemodynamic and cardiopulmonary findings. The investigation of the pathophysiological bases of these differences could provide a more comprehensive characterization of DCM patients leading to more personalized management strategies.

Variables	Men (N 37, 64%)	Women (N 21, 36%)	p-value
Age (years)	57.89 ± 13.22	58.86 ± 14.60	0.798
NYHA class			0.762
class 1	6 (16%)	5 (24%)	
class 2	19 (51%)	10 (48%)	
class 3	8 (22%)	6 (29%)	
class 4	1 (3%)	0	
NT-proBNP (pg/mL)	1221.00 [580.95-3521.00]	588.40 [252.10-1082.80]	0.104
Echocardiography			
TAPSE (mm)	20.17 ± 5.24	21.72 ± 4.01	0.267
TRV (m/s)	2.44 ± 0.38	2.33 ± 0.41	0.391
sPAP (mmHg)	31.00 [25.00-38.00]	29.00 [25.00- 32.00]	0.346
TAPSE/sPAP (mm/mmHg)	0.65 [0.44-0.77]	0.81 [0.64-0.87]	**0.024**
CPET parameters			
AT (% of VO2 predicted)	44.94 ± 20.71	49.22 ± 28.76	0.665
VO2 AT (mL/kg/min)	13.20 [10.75-14.25]	10.60 [8.35-11.45]	**0.018**
Peak VO2 (mL/kg/min)	14.96 ± 4.71	13.71 ± 3.57	0.301
Peak VO2 (% of predicted)	55.53 ± 13.11	65.90 ± 18.44	**0.016**
VE/VCO2 slope	31.45 [27.70-35.70]	28.30 [24.85-32.00]	**0.027**
VO2/WR (mL/min/watt)	9.12 ± 1.80	9.24 ± 2.20	0.834
O2 pulse (mL/bpm)	10.61 ± 2.95	8.85 ± 2.18	**0.021**
O2 pulse (%)	80.28 ± 14.78	107.80 ± 19.07	**<0.001**
CMR parameters			
LVEF (%)	31.35 ± 12.42	41.62 ± 13.34	**0.005**
RVEF (%)	45.72 ± 14.55	61.24 ± 10.14	**<0.001**
LV SVi (mL/bpm/m2)	40.94 ± 12.29	39.77 ± 8.22	0.675
LVMi (g/m2)	110.68 ± 30.64	83.75 ± 19.42	**0.001**
LV EDVi (mL/m2)	129.55 [108.04-164.90]	105.36 [78.35-117.31]	**0.001**
LV ESVi (mL/m2)	88.73 [64.11-130.39]	61.53 [39.14-83.54]	**0.003**
RV EDVi (mL/m2)	80.40 [65.60-119.06]	56.03 [50.21-70.82]	**<0.001**
RV ESVi (mL/m2)	37.78 [29.70-84.83]	22.08 [16.54-26.50]	**<0.001**
LGE (%)	1.87 [0.00-6.08]	0.01 [0.00-4.63]	0.390
LGE +	25 (68%)	10 (48%)	0.103
LGE septal localisation	15 (60%)	5 (50%)	0.197

THE ROLE OF THE MULTIDISCIPLINARY TEAM IN THE MANAGEMENT OF COMPLEX CASES OF PATIENTS WITH LIVER DISEASE IN A PERIPHERAL HOSPITAL

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Background: A multidisciplinary approach has been shown to improve the management of several diseases. The present study aims to evaluate the role of a multidisciplinary approach in complex cases of liver disease, ranging from focal liver lesions to hepatocarcinoma and biliary tract disease.
Methods: Since November 2023, 32 cases of patients referred to the Liver Disease Outpatient Clinic of Barone Lombardo Hospital were discussed multidisciplinary. The team consisted of internists, radiologists, oncologists, surgeons and an endoscopist. The initial proposals of clinicians were compared with the decisions taken by the team to evaluate the appropriateness of prescribing radiologic exams and the need for referral.
Results: Among all the included patients (32), the median age was 57, 19 patients (59%) were female, 18 patients (56%) had liver disease. 23 patients have been discussed for diagnostic scope, 6 for therapeutical decision and 3 for both. The mean follow-up period is 197 days (28-330). A total of 8 CT scans, 12 MRIs and 1 Positron Emission Tomography scan were saved as determined by the team versus the individual physician's initial assessment. No patients were referred to a secondary or tertiary hospital. No adverse events were reported during the follow-up period.
Conclusions: The multidisciplinary approach improves the appropriateness of prescribing radiological examinations with consequent reduction of costs, adverse events related to the use of contrast and a better allocation of resources. Moreover, the multidisciplinary team avoids unnecessary referrals to secondary and tertiary hospitals.

BURNOUT AMONG YOUNG INTERNISTS ACROSS THE MEDITERRANEAN COUNTRIES: A PRELIMINARY RESULT OF A SURVEY

Vassallo G.A.[1], Dionisi T.[2], Abida H.[3], Berrim M.R.[4], Uyaroglu O.A.[5], Lemouaden R.[6], Amine M.[7], Salzano A.[8], Letifi W.[3], Pietrantonio F.[9], Romano M.[10], Delcea C.[11], Abdallah Y.[12], Gasbarrini A.[2], Addolorato G.[2]
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Background: and Aims: Burnout among physicians is associated with poor productivity at work, dissatisfaction and regrets about career choices. The present study aims to evaluate the prevalence of burnout and its main associated factors among young Internists across the Mediterranean Countries.
Methods: The survey was conducted across Mediterranean countries by the Young Internists Groups of each National Society of Internal Medicine. Data were collected through an online questionnaire. Data from Algeria, Egypt, Italy, Lebanon, Morocco, Tunisia and Turkey were analyzed.
Results: Data from 181 young Internists (age < 40 yrs) working in universities and non-teaching hospitals were collected. The median age was 29 years. Burnout was reported by 40,3% of respondents. The main associated factors were a high workload (60.2 %), insufficient time in family and social life (56.9 %), sleep deprivation (40.9%) and financial instability (33.1 %). Only 8.6% reported the presence of a support system to deal with burnout inside their hospital.
Conclusions: Burnout is very common among young Internists across Mediterranean Countries and it is associated with a high workload, insufficient time in family and social life, sleep deprivation and financial instability. Strategies to prevent burnout among young Internists should be identified and a support system to deal with burnout should be present in every hospital.

WORK OVERLOAD AMONG YOUNG INTERNISTS ACROSS THE MEDITERRANEAN COUNTRIES: A PRELIMINARY RESULT OF A SURVEY

Vassallo G.A.[1], Dionisi T.[2], Abida H.[3], Berrim M.R.[4], Uyaroglu O.A.[5], Lemouaden R.[6], Amine M.[7], Salzano A.[8], Letifi W.[3], Pietrantonio F.[9], Romano M.[10], Delcea C.[11], Abdallah Y.[12], Gasbarrini A.[2], Addolorato G.[2]
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Background: and Aims: Work overload, stress and anxiety among physicians are associated with medical mistakes and poor quality of care. The present study aimed to evaluate the prevalence of overwork, its main causes and consequences among young Internists across Mediterranean Countries.
Methods: The survey was conducted across Mediterranean countries by the Young Internists Groups of each National Society of Internal Medicine. Data were collected through an online questionnaire. Data from Algeria, Egypt, Italy, Lebanon, Morocco, Tunisia and Turkey were analyzed.
Results: Data from 181 young Internists (age < 40 yrs) working in universities and non-teaching hospitals were collected. The median age was 29 years.Excessive workload was reported by 57.9% of respondents. The main reasons for excessive workload were spending more hours at work than was required by the hospital (68%), not having any day off after a nightshift (63.1%), excessive number of patients seen (26.9%), too much time dedicated on paperwork and administrative duties (78.3%). Finally, according to 70.2% of respondents, excessive workload was the main cause of stress and anxiety.
Conclusions: Work overload is very common among young Internists across Mediterranean Countries. It is caused by excessive time spent at work, lack of rest, high number of patients managed and paperwork. Work overload is associated with stress and anxiety. Strategies to reduce work overload among young Internistsacross Mediterranean Countries should be identified.

AN ULTRASOUND/ELASTOGRAPHY SCREENING EXPERIENCE FOR METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD) IN A HIGH-RISK POPULATION: PREVALENCE AND FACTORS ASSOCIATED WITH MASLD AND LIVER FIBROSIS

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Background And Objectives: Patients with obesity, type 2 diabetes mellitus (T2DM), and metabolic syndrome are at increased risk of developing metabolic dysfunction-associated steatotic liver disease (MASLD), metabolic dysfunction-associated steatohepatitis (MASH), and advanced liver fibrosis. We evaluated the prevalence and severity of MASLD, as well as the diagnostic performance of a sequential algorithm using the Fibrosis-4 (Fib-4) index and liver stiffness (LS) measurement, in a prospective cohort of patients with severe obesity, T2DM, and metabolic syndrome followed at a tertiary care center.
Methods: Consecutive patients with severe obesity, T2DM, and metabolic syndrome under the care of obesity specialists, diabetologists, internists, and endocrinologists at the Civil Hospital of Baggiovara, University Hospital of Modena, AOU of Modena, underwent liver ultrasound for steatosis (SLD) assessment, Controlled Attenuation Parameter (CAP) measurement via Fibroscan®, and LS evaluation using both Fibroscan® and 2D-Shear Wave Elastography (2D-SWE).
Results: A total of 218 patients were enrolled, with a median age of 54.6 [43.9–61.8] years; 47.7% were male. Obesity, T2DM, hypertension, and dyslipidemia were present in 83.5%, 29.4%, 51.8%, and 63.3% of cases, respectively.SLD, defined as ultrasound-detected steatosis and/or CAP ≥ 248 dB/m, was found in 188 patients (86.2%), with MASLD being the attributed cause in 95.7% of cases.
SLD was significantly associated with BMI (p=0.001), HOMA-IR (p<0.001), triglycerides (p<0.001), AST (p=0.012), ALT (p<0.001), GGT (p=0.007), and the presence of liver fibrosis (p=0.022).
Fifty patients (22.9%) had elastographic evidence of liver fibrosis, defined as LS ≥8 kPa by Fibroscan®, or ≥8 kPa by 2D-SWE in cases of Fibroscan® failure (11 patients, 5.0%).
Liver fibrosis was significantly associated with male sex (p<0.001), BMI (p=0.007), systolic blood pressure (SBP) (p=0.019), HOMA-IR (p=0.005), AST (p<0.001), ALT (p<0.001), GGT (p<0.001), and the presence of SLD (p=0.022), and inversely associated with LDL (p=0.028) and HDL cholesterol (p=0.014). Forty-five patients (20.6%) had a Fib-4 score ≥1.3 (≥2.0 if over 65 years). The performance of Fib-4 in detecting elastographic evidence of liver fibrosis was: Sensitivity 32.0%, Specificity 82.7%, Positive Predictive Value (PPV) 35.6%, Negative Predictive Value (NPV) 80.3%, and diagnostic accuracy 71.1%.
Application of the 2024 EASL-EASD-EASO algorithm (sequential Fib-4 and LS via Fibroscan®) yielded a diagnostic accuracy of 82.6%, identifying 20 patients (9.2%) requiring hepatology referral (8 with Fib-4 ≥2.67 and 12/37 with Fib-4 between 1.3/2.0 and 2.67 and LS ≥8 kPa) and 198 patients (90.8%) not requiring referral (173 with Fib-4 <1.3/2.0 and 25/37 with Fib-4 between 1.3/2.0 and 2.67 and LS <8 kPa).Among the 173 low-risk patients (Fib-4 <1.3/2.0), 34 (19.7%) had LS ≥8 kPa. These patients were more often male, younger, had higher prevalence of severe obesity (BMI >40 kg/m²), evidence of SLD, lower HDL cholesterol, and higher SBP and ALT levels. In multivariate analysis, male sex [OR (95% CI) 3.82 (1.48–9.85), p=0.006] and BMI > 40 kg/m² [OR (95% CI) 4.13 (1.54–11.09), p=0.005] were independently associated with LS ≥8 kPa among patients with low-risk Fib-4.
A stricter definition of elastographic fibrosis—requiring LS ≥8 kPa on both Fibroscan® and 2D-SWE (12 patients, 5.9%)—improved Fib-4 performance (Sensitivity 58.3%, Specificity 81.3%, PPV 16.3%, NPV 96.9%, diagnostic accuracy 79.9%) and algorithm accuracy (95.1%), with only 5/161 (3.1%) low-risk patients showing LS ≥8 kPa, suggesting that use of a single elastographic method may overestimate fibrosis.Fifteen patients underwent liver biopsy based on screening results, revealing MASH in 8 (53.3%) and fibrosis stage F2 or higher in 8 (53.3%), including 2 with cirrhosis.
Conclusions: Sequential screening for MASLD using Fib-4 and LS measurement accurately identifies high-risk patients requiring hepatology referral. Severe obesity is significantly associated with LS ≥8 kPa even in patients with low-risk Fib-4 scores. False negatives from Fib-4 are greatly reduced using a stricter fibrosis definition requiring LS ≥8 kPa on both Fibroscan® and 2D-SWE. Thus, dual elastographic assessment may outperform Fibroscan® alone in predominantly obese populations.

HEPCIDIN DYNAMICS PREDICT OUTCOMES IN COVID-19 PATIENTS TREATED WITH INTERLEUKIN INHIBITORS

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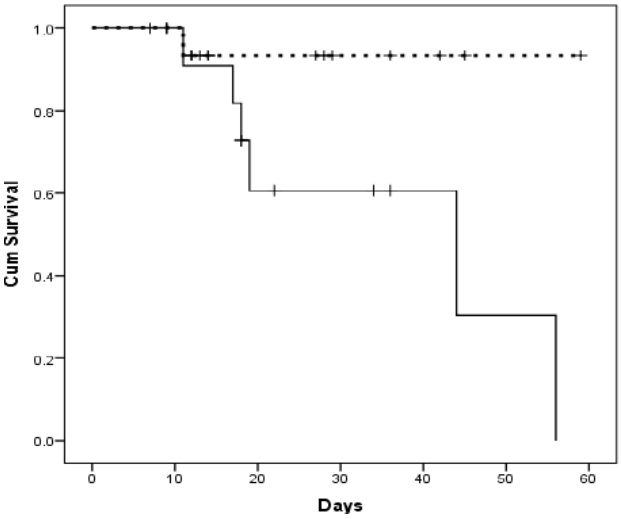
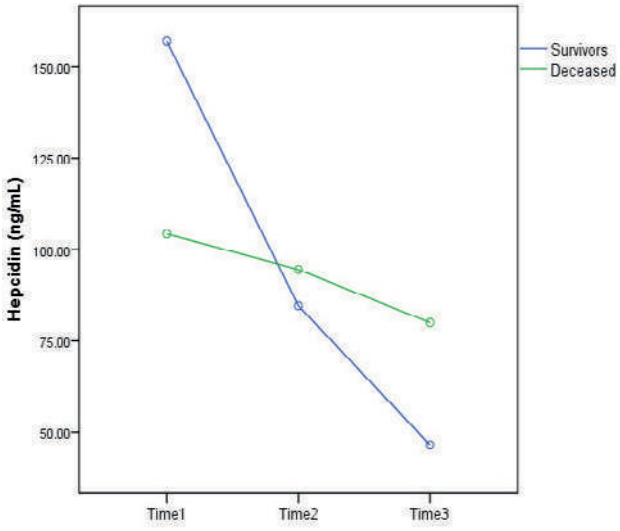
Background: iron metabolism and its key regulatory hormone, hepcidin, play a pivotal role in infection and inflammation. However, the prognostic value of iron metabolism markers in SARS-CoV-2 infection remains poorly defined.
Methods: We conducted a retrospective observational study examined a cohort of 30 patients admitted to an internal medicine unit between March and April 2020 for COVID-19 infection. Serial measurements of hepcidin and other iron-related parameters were performed at baseline, 3 days, and 7 days after administration of anti-IL-1 receptor or anti-IL-6-receptor therapies. The primary outcome was in-hospital mortality.
Results: Baseline iron and inflammatory markers did not significantly differ between survivors and non-survivors. Hepcidin levels correlated positively with C-reactive protein (r=0.57, p < 0.001) and inversely correlated with serum iron (r= - 0.3, p= 0.006) at baseline and 3 days after post-treatment. Notably, the percentage change in hepcidin levels from baseline to day 3 after anti-IL therapy emerged as the only independent predictor of in-hospital mortality in multivariate analysis. A hepcidin %-drop ≤ 39% had a specificity of 85.71 (95% CI 42.1 - 99.6) and a sensitivity of 73.91 (95% CI, 51.6 - 89.8) for predicting mortality.
Conclusions: Hepcidin dynamics are strongly associated with clinical outcomes in COVID-19. Monitoring hepcidin trends represents a promising, easily measurable approach to stratify risk in patients treated with interleukin inhibitors and may complement existing biomarkers in infection management.





CELIAC DISEASE AND SJÖGREN'S SYNDROME: A CONTROVERSIAL ASSOCIATION

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Introduction: Celiac disease (CD) is a chronic immune-mediated enteropathy triggered by gluten intolerance, due to an abnormal T-cell response to HLA-DQ2-bound gluten peptides, in genetically predisposed patients with HLA-DQ2/DQ8 allels. According to international guidelines, duodenal biopsy is the gold standard for diagnosis, though high-titer anti-tissue transglutaminase IgA antibodies ≥10 times the upper limit of normal are highly predictive.
Sjögren's syndrome (SjS) is a complex systemic autoimmune disease marked by the triad of sicca symptoms, fatigue and joint pain, with sicca symptoms persisting more than three months, after the exclusion of possible differential diagnosis (2016 ACR/EULAR classification), often accompanied by vasculitis, lung, kidney, neurologic, gastrointestinal involvement or malignancy. The interplay of genetics, estrogens and environmental triggers may promote autoreactive B and T-cells proliferation and activation; IL-10 and 6 may drive B-cell immortalization and potential lymphoma. Anti-SSA/Ro and anti SS-B/La, rheumatoid factor (RF) and antinuclear antibodies (ANA) are present in 85% of cases.
Gastrointestinal (GI) manifestations are common in Sjs: esofageal, gastric and bowel dysmotility, pancreatic or liver dysfunction, CD affects up to 15% of patients, autoimmune hepatitis and primary biliary cholangitis in 10% cases. While the link between CD and connectivitis diseases like systemic lupus erythematosus (SLE), primary SjS (pSjS) and systemic sclerosis is debated, but co-occurrence is more frequent in CD patients (≈30%) compared to the 3-9% reported in the general population.
We present a case series of CD and primary SjS evaluated in our centre.
Case 1. A 41-year-old woman with SLE, positive ANA 1:160, anti-DsDNA antibodies, thrombocytopenia, arthralgia, treated with hydroxicloroqiune, metylprednisolone, Azatyoprine, SjS with xeropthalmia and xerostomia (positive SS-A 272 U/mL and Schirmer test), Hashimoto thyroiditis, microcytic anemia, mild hypoalbuminemia, Shönlein Henoch vasculitis, history of cerebral stroke with minimal residual weakness on the left side of the body (negative antifosfolipid syndrome, thrombophilia, smoking or dyslipidemia), steroid-induced osteoporosis with vertebral fractures presented with bloating, chronic fatigue, weight loss, suspected gluten intolerance. Despite negative serology, duodenal biopsy confirmed celiac disease. After starting a gluten-free diet and immunosuppressive therapy, her sicca symptoms improved with less need for tear substitutes.
Case 2. A 41-year-old woman presented with asthenia, diarrhea and weight loss (-10 kg in the last month). She had a history of three spontaneous abortions, Hashimoto's thyroiditis, SjS with positive anti SSA/Ro >10 U/mL and FR >20 IU/mL, treated with pilocarpine and methylcellulose-based eye drops. Serology showed positive ANA 1:640, IgA deamidated gliadin antibodies (30 U/mL) and tissue transglutaminase IgA antibodies (tTG-IgA 60 U/mL), negative anti-endomysium antibodies. The duodenal biopsy confirmed the clinical suspicion of celiac disease.
Case 3. A 58-year-old woman complaining progressive fatigue, itching, abdominal discomfort and diarrhea with dark stools. Laboratory tests showed: sideropenic anemia and elevated transaminases, rising the suspicion of celiac hepatitis. Serology was positive for tTG-IgA > 200 U/mL and anti-endomysium antibodies, and the biopsy confirmed celiac disease (Marsh IIIb). She later developed xerophthalmia and xerostomia, and recurrent dental caries. Anti SSA/Ro, anti SSB/La, ANA and RF were all positive.
Discussion: There is growing evidence of a meaningful association between pSjS and CD, potentially driven by a shared genetic predisposition, gut permeability, molecular mimicry, post-translational changes of luminal proteins, immune dysregulation, microbiota alterations and environmental factors. Approximately 5-12% of patients diagnosed with pSjS also have CD, compared to 1% of the general population. CD is the most common immune-mediated comorbidity of pSjS that impacts the GI tract. Furthermore, ongoing inflammation is frequently observed in the small bowel mucosa of nonceliac patients with pSjS.
This case series highlights the complex and possibly underestimated association between CD and pSjS. Although the coexistence of these two conditions remains a matter of debate, our experience suggests that their concurrence may not be incidental. In all three patients, CD was diagnosed in the context of pre-existing pSjS or vice versa, and in one case, gluten-free diet (and immunosuppression) led to an improvement in systemic and sicca symptoms. This reinforces the importance of maintaining a high index of suspicion for CD in patients with SjS who present with gastrointestinal complaints, anemia or nutritional deficiencies, even in the absence of positive serology. Further research is needed to clarify the immunological and clinical relationship between CD and pSjs, and to assess whether routine screening for CD in patients with pSjS should be adopted in clinical practice.

THE MODERATING ROLE OF ADVERSE CHILDHOOD EXPERIENCES IN THE RELATIONSHIP BETWEEN CROHN'S DISEASE ACTIVITY AND THE DEVELOPMENT OF PTS SYMPTOMS

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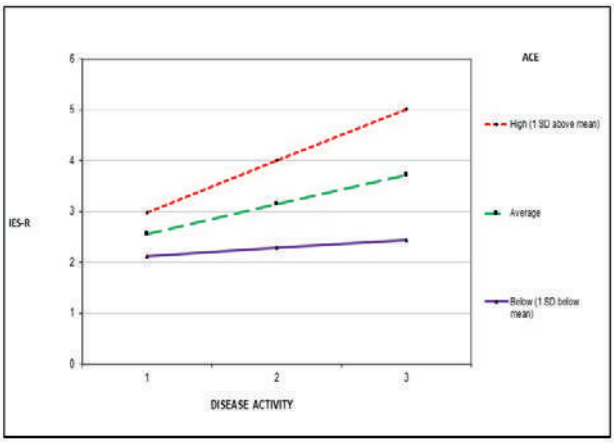
Introduction: Crohn's disease (CD) is a chronic inflammatory bowel disease (IBD) characterized by a relapsing course, debilitating symptoms, and potential long-term complications. Patients with chronic illnesses are more vulnerable to post-traumatic stress (PTS) symptoms, which may arise from both the illness itself and the diagnostic or therapeutic procedures. Studies indicate that approximately one-third of patients with IBD exhibit significant PTS symptoms, including flashbacks, nightmares, hypervigilance, and sleep disturbances, which can sometimes progress to post-traumatic stress disorder (PTSD). This study examines the moderating role of adverse childhood experiences (ACEs) in the relationship between disease activity and PTS symptoms.
Methods: This cross-sectional study included consecutive CD outpatients attending the Center for Digestive Diseases (CEMAD) at Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Rome. Participants completed two self-report questionnaires: the Revised Impact of Event Scale (IES-R) and the Adverse Childhood Experiences (ACEs) questionnaire. Disease activity was evaluated using the Harvey Bradshaw Index. Data were analyzed using Pearson correlation coefficients and moderated regression analyses in SPSS software (version 27).
Results: A total of 172 CD patients were included. Of the total sample, 48 patients (31.2%) exhibited a score of 33 or higher on the IES-R, suggestive of PTSD. Correlation analyses showed that ACEs scores were significantly associated with all IES-R subscales: intrusion ($r = .405$, $p < .001$), avoidance ($r = .348$, $p < .001$), and hyperarousal ($r = .363$, $p < .001$). Additionally, patients with higher ACEs scores had significantly more severe disease activity ($r = .272$, $p < .001$). The highest ACEs scores were related to psychological abuse. Hierarchical regression analysis further demonstrated that the relationship between CD activity and the overall IES-R score was significantly stronger among patients with high ACEs scores ($b = .21$, $p < .001$) compared to those with medium ($b = .12$, $p = .005$) or low scores ($b = .06$, $p = .291$) as illustrated in Figure 1.
Conclusions: The findings suggest that adverse childhood experiences increase psychological vulnerability in patients with Crohn's disease, influencing the course of the illness. Integrating psychological assessment into clinical practice appears essential to improve the overall management of IBD and to prevent the worsening of post-traumatic symptoms.



A TWICE NEGLECTED DISEASE: A RARE CAUSE OF HEART FAILURE ASSOCIATED WITH RURAL POVERTY. A CASE REPORT

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Introduction: Endomyocardial fibrosis (EMF) is a rare form of restrictive cardiomyopathy, predominantly seen in tropical and subtropical regions. This condition is characterized by fibrous deposition in the ventricular endocardium, leading to impaired diastolic function. It is a disregarded disease associated with poverty, particularly in rural areas of Sub-Saharan Africa, South America, and Asia. Only rare cases have been reported from Ethiopia to date. Despite its neglected status, EMF is believed to be one of the most common causes of restrictive cardiomyopathy worldwide.
The disease is characterized by the fibrosis of the endocardial surface of the apex of one or both ventricles, that leads to restrictive heart physiology and progressive congestive heart failure (CHF). Notably, the prevalence of ventricular thrombi is increased in this condition. Furthermore, EMF is more commonly associated with ascites due both to increased hydrostatic pressure and to increased vascular permeability on inflammatory basis.
The underlying pathophysiology of the disease remains largely unclear. One theory suggests that Loeffler endocarditis (a cardiomyopathy secondary to diffuse eosinophilic infiltration of the myocardium) and EMF may be part of the same disease spectrum. Infections and environmental factors (such as magnesium deficiency, cassava intake and malnutrition) have been proposed as contributing factors, but a clear and consistent association has never been demonstrated.
The diagnosis is challenging: the disease should be suspected in individuals with CHF in or from endemic areas and is based on echocardiographic findings, such as the presence of endomyocardial plaques, obliteration of the ventricular apex, presence of thrombi, atrioventricular-valve dysfunction due to adhesion of the valvular apparatus to the ventricular wall.
Case report: A 33-old man, from a rural Kebele in Oromia region in Ethiopia, presented to our hospital for severe dyspnoea at rest, and bilateral leg swelling. The patient was admitted to the medical ward with the diagnosis of acute CHF. He denied any previous medical history and home medications.
At the admission, the patient was afebrile, alert, presented peripheral oedema and a systolic murmur in the mitral area. Vital parameters were normal, with stable hemodynamic. Lung examination revealed bilateral crackles. Abdominal evaluation demonstrated a tense abdomen and bilateral flank dullness.
An echocardiography was performed and demonstrated normal size left ventricle (LVDd 52 mm) with severe global hypokinesia, reduction of the ejection fraction (20%) and evidence of diastolic dysfunction. Left atrium was enlarged (LAVi 70 ml). The mitral valve was moderately regurgitant. Tricuspid valve showed regurgitation, with augmented PAPs of 45 mmHg.
The apex of the left ventricle appeared obliterated by a non-homogeneous hyperechoic lesion suggestive for fibrosis with increased thickening of the basal inflow tract papillary muscle. Cava vein was found enlarged (22 mm) and non-collapsing during inspiration.
Furthermore, at the abdomen ultrasound, a moderate ascites was found. No signs of liver disease were present. A grade 3 venous excess ultrasound (VExUS) score suggested a cardiogenic ascites.
Therapy for CHF was started, including furosemide 40 mg tid, enalapril 5 mg od, spironolactone 25 mg od and atenolol 25 mg bid. In the night after the admission, patient's condition repentantly worsened, and he suddenly died.
Conclusion: Our experience suggests that, although considered neglected, EMF should be considered as a as differential diagnosis in all patients with HF from rural areas whit suggestive echocardiographic features and/or ascites of verified cardiogenic origin.
Early recognition and treatment of this condition, in fact, could help reducing mortality related to CHF and to the complications of ventricular thrombi.

BEHAVIORAL AND ANTHROPOMETRIC DETERMINANTS OF EXCESSIVE ALCOHOL CONSUMPTION: EVIDENCE FROM THE BRFSS 2015

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Introduction: Excessive alcohol consumption is one of the leading preventable causes of morbidity and mortality in the adult population. Identifying behavioral and sociodemographic characteristics associated with this behavior can support the development of more effective prevention strategies.
Methods: Data were obtained from the 2015 Behavioral Risk Factor Surveillance System (BRFSS), a national survey coordinated by the Centers for Disease Control and Prevention (CDC) that collects self-reported health-related information from the adult population in the United States. The final sample included 253,680 individuals, with a mean body mass index (BMI) of 28.4. A binary logistic regression was performed to explore the association between excessive alcohol consumption (dependent variable) and the following predictors: fruit consumption, vegetable consumption, BMI, and sex. Odds ratios (ORs) and 95% confidence intervals (95% CI) were calculated.
Results: The model was globally significant (χ^2 = 1318, $p < 0.001$), with a McFadden's R^2 of 0.012. Fruit consumption was associated with a lower likelihood of excessive alcohol use (OR: 0.661; 95% CI: 0.638–0.684; $p < 0.001$), whereas vegetable consumption was paradoxically associated with an increased risk (OR: 1.419; 95% CI: 1.352–1.489; $p < 0.001$). Female sex (OR: 0.959; $p < 0.001$) and higher BMI (OR: 0.959; $p < 0.001$) were also protective factors.
Conclusions: The analysis of BRFSS 2015 data shows that specific dietary habits and individual characteristics, such as sex and body mass index, are significantly associated with excessive alcohol consumption. These findings may help guide future preventive strategies and educational interventions targeting at-risk groups.

SCLEROSTIN INHIBITION DURING HORMONAL ADJUVANT THERAPY FOR EARLY BREAST CANCER

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Cancer Treatment Induced Bone Loss (CTIBL) is an imminent risk of fracture condition that needs an early therapy with rapid antifracture response. The occurrence of a frailty fracture further increases the risk of subsequent events determining a condition of very high imminent risk of fractures. Actually, antiresorptive agents, mainly Denosumab, are recommended in this condition while Teriparatide is unadvised. The overexpression of sclerostin both as a consequence of adjuvant hormone therapy and by breast cancer cells themselves makes the use of Romosozumab rational in this setting[1,2].
The aim of this study is to compare the effects on Bone Mineral Density (BMD) and Trabecular Bone Score (TBS) of Romosozumab and Denosumab in CTIBL with very high imminent risk of fracture.
In a prospective 12 months open label case-control study, 15 Early Breast Cancer women on aromatase inhibitors (BC) with severe CTIBL (≥1 fragility fracture in the last 2 years) starting Romosozumab 210 mg/month (ROMO-BC) where matched by age, BMD, prevalent fracture with 15 BC starting Denosumab 60 mg/6 months (DNB-BC) (Fig.1). Patients with other osteometabolic diseases, actual or previous corticosteroid treatment or serum 25(OH)D <50 nmol/L were excluded. All subjects were supplemented with Vitamin D and calcium during the study and were naïve for previous bone modifying agents. Spine and Hip DEXA scans (Hologic Discovery A) for BMD, TBS and vertebral morphometry were performed at 0, 6 and 12 months along with biochemistry for Bone Turnover Markers.
Patients in the two groups were comparable for baseline characteristics (Tab.1). Lumbar spine BMD increased significantly more in ROMO-BC vs DNB-BC at 6 months (+3.2±0.92% vs +2.26±0.61%, p=0.002) but the difference wasn't significant at 12 months (+5.26±0.81% vs +4.53±0.96%, p=0.051). Total Hip

BMD increased significantly more rapidly in ROMO-BC than DNB-BC (+2.7±0.65% vs +1.2±0.71%, p=0.001 at 6 months and +3.4±0.69% vs +2.11±0.72%, p=0.001 at 12 months). TBS improved significantly more at 6 months in ROMO-BC vs DNB-BC (+2.08% vs +0.9%, p=0.002), but the improvement was similar at 12 months in the two groups (+2.49% vs +2.17%; p=0.39).Regarding bone turnover markers, both Romosozumab and Denosumab determined a significant reduction in CTX levels throughout the study, although the reduction in this marker was more pronounced with Denosumab (at 12 months -62% with ROMO and -92% with DEN); Romosozumab, but not Denosumab, was also associated with an increase in P1NP (+5% at 12 months). Neither new fractures or adverse events were reported in both groups.
These preliminary data suggests that Romosozumab might be a suitable alternative to Denosumab in aromatase inhibitors-induced CTIBL at very high risk of fracture, permitting a rapid recovering of BMD and TBS. Further studies are required to confirm these preliminary results and to establish the efficacy of Romosozumab in reducing the risk of fractures in this setting.

Bibliography:

1. Kyvernitakis I, Rachner TD, Urbschat A, Hars O, Hofbauer LC, Hadji P. Effect of aromatase inhibition on serum levels of sclerostin and dickkopf-1, bone turnover markers and bone mineral density in women with breast cancer. J Cancer Res Clin Oncol.2014;140(10):1671-1680.
2. Bojanić K, Bilić Ćurčić I, Kuna L, et al. Association of Wnt Inhibitors, Bone Mineral Density and Lifestyle Parameters in Women with Breast Cancer Treated with Anastrozole Therapy. J Clin Med. 2018;7(9):287.

	DENOSUMAB	ROMOSOZUMAB	p
Age (years)	62.0 (45-73)	62.5 (53-71)	0.33
AI Therapy Duration (years)	3.0 (1-4)	3.0 (1-5)	0.45
Lumbar Spine BMD (g/cm2)	0.744 (0.631-0.894)	0.726 (0.623-0.879)	0.80
LS T-score	-2.75 (-3.6/-1.5)	-2.90 (-3.8 /- 1.5)	0.59
Total Hip BMD (g/cm2)	0.77 (0.50-1.17)	0.74 (0.597-1.07)	0.86
TH T-score	-1.7 (-2.6/ -0.3)	-1.6 (-2.4/-0.4)	0.89
TBS	1.19 (1.123-1.39)	1.19 (1.123-1.390)	0.87
P1NP (ug/mL)	90,0 (67-122)	89,0 (65-110)	0,52
CTX (ng/mL)	0.781 (0.412-1.023)	0.778 (0.577-1.123)	0.86
SDI	2 (1-3)	2.2 (1-3)	0.68

AUTOIMMUNE HEPATITIS AND MASLD OVERLAP AS AN ATYPICAL INITIAL PRESENTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE REPORT

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Background: Systemic lupus erythematosus (SLE) is a complex autoimmune disorder with heterogeneous clinical manifestations affecting multiple organ systems, including the kidneys, skin, hematologic system, and central nervous system. Although less frequently emphasized, hepatic involvement occurs in approximately 19% to 60% of cases. The spectrum of liver pathology in SLE ranges from metabolic dysfunction–associated steatotic liver disease (MASLD) - particularly in the presence of systemic inflammation and metabolic comorbidities - to cirrhosis, which remains relatively uncommon, occurring in only 1–2%[1] of cases.
We present the case of a 46-year-old male patient diagnosed with end-stage cirrhosis, in whom serological findings were suggestive of underlying SLE.
Case presentation: A 46-year-old overweight male with a history of smoking and hypertension was referred for evaluation of chronic fatigue, elevated liver enzymes (AST ×3 ULN, ALT ×1.5 ULN), hyperbilirubinemia (total 2.2 mg/dL, direct 0.8 mg/dL), anemia (Hb 8.6 g/dL), and thrombocytopenia (platelets 108,000/μL) at Liver Unit, Policlinico di Foggia.
As part of his medical history, he had previously been hospitalized for fatigue and persistent fever (T>38.5 °C), anemia, elevated liver enzymes, and hyperbilirubinemia. CT imaging at that time revealed hepatomegaly with irregular contours, ascites, and pleural and pericardial effusions, suggestive of advanced liver disease. Infectious causes were excluded, and given the positive ANA titers, a corticosteroid tapering regimen was initiated. The patient showed clinical improvement and was discharged with instructions for outpatient follow-up.
During hospitalization, autoimmune screening confirmed positive ANA at a titer of 1:160, while anti-LKM1 and anti-SMA antibodies were negative. Abdominal ultrasound and PET imaging confirmed advanced cirrhosis, with no evidence of neoplastic or myelolymphoproliferative disease. Liver biopsy demonstrated end-stage cirrhosis with severe microvesicular steatosis involving approximately 70% of hepatocytes, and histological features suggestive of immune-mediated injury.
Based on the 2019 EULAR classification criteria, the patient reached a total score of 23 (threshold ≥10), confirming the diagnosis of systemic lupus erythematosus. In light of the coexisting conditions, a diagnosis of liver cirrhosis secondary to overlapping SLE and MASLD was established. Corticosteroid therapy was reintroduced, resulting in significant clinical and biochemical improvement over the months following discharge.
Conclusions: This case highlights an uncommon overlap between systemic lupus erythematosus and metabolic dysfunction–associated steatotic liver disease as contributing factors to end-stage cirrhosis. ANA positivity, a high EULAR score, and a favorable response to corticosteroid therapy, together with histological features of immune-mediated injury and marked steatosis, support a dual etiology of liver cirrhosis. This underscores the need to consider autoimmune liver involvement in patients with metabolic risk factors and advanced liver disease.

Bibliography:

[1]Youssef W. I., Tavill A. S. Connective tissue diseases and the liver. Journal of Clinical Gastroenterology. 2002;35(4):345–349. doi: 10.1097/00004836-200210000-00012

PARANEOPLASTIC HYPERSENSITIVITY-LIKE IMMUNE DYSREGULATION IN ATYPICAL CHRONIC LYMPHATIC LEUKEMIA

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Introduction: Chronic lymphatic leukemia (CLL) is the most common adult leukemia in the Western World, characterized by the accumulation of mature monoclonal B-lymphocytes in lymphoid tissues and bone marrow. Clinical course is variable, ranging from indolent course to aggressive disease which can evolve into B-cell prolymphocytic leukemia or diffuse large B-cell lymphoma (Richter's transformation). Cutaneous manifestations are rare, they can arise from direct leukemic infiltration, cutaneous Richter's syndrome, immune dysregulation, paraneoplastic syndromes (vasculitis, pemphigus, pemphigoid-like lesions, Sweet syndrome), drug-induced reactions or infections. Symptomatic CLL may present with lymphadenopathy, cytopenia, splenomegaly, hepatomegaly and constitutional symptoms. First-line treatment includes Bruton tyrosine kinase inhibitors and BCL2 inhibitors, with PI3K inhibitors, CAR T-cell therapy, and allogeneic stem cell transplantation reserved for advanced or refractory cases.
Case report: A 51-year-old man with a recent history of atypical CLL treated with chemotherapy up to six months previously, presented with elevated polyclonal IgE levels (2451 IU/mL), pruritus, chronic relapsing urticaria, fatigue, artromyalgia, night sweats. New CT scans of the chest and abdomen were normal; superficial lymph node ultrasound showed inhomogeneous tissue structures and poorly defined hilar architecture.
Lymph node biopsy showed proliferation of prolymphocytes, immunolymphoblasts, small lymphocytes and mast cells. Immunohistochemistry showed a CLL-compatible profile (CD20+, CD79a+, CD5+, LEF1+, BCL2+), weak CD23 and IRF4 expression, absence of markers suggestive of transformation (cyclin D1, SOX11, CD10, BCL6, CD30), moderate proliferative activity (KI67: 5–30%). No evidence of EBV. Venetoclax was started and the patient was referred for immunological consultation. Allergy history and prick tests were negative. The patient denied insect bites before the urticarial rash, Raynaud's, arthralgia, photosensitivity, sicca symptoms, dyspepsia, cardiovascular, respiratory or neurological changes. Laboratory investigations were unremarkable except for elevated β2-microglobulin (2.99 mg/L); autoimmune and infectious panels were negative. Skin manifestations resolved with cetirizine 10 mg/day and the patient remained clinically stable at three-month follow-up.
Discussion: This case highlights an atypical presentation of CLL relapse, marked by non-atopic elevated IgE levels and chronic pruritic urticaria, raising the suspicion of eosinophilic dermatosis of hematologic malignancy (EDHM). Systemic symptoms, high IgE and skin involvement without an allergic context may signal disease progression or transformation.
The differential diagnosis of elevated IgE is broad and includes atopic conditions, parasitic infections, viral, mycobacterial or fungal diseases, (human immu-

nodeficiency virus, cytomegalovirus, Epstein Barr virus, tuberculosis, leprosy, candidiasis, pulmonary aspergillosis), tobacco smoking, autoimmune disorders like eosinophilic granulomatosis with polyangiitis, nephrotic syndrome, monogenic primary immune deficiencies (pediatric patients) with an atopic phenotype, graft-versus-host disease and some hematological malignancies as IgE-secreting multiple myeloma, Hodgkin's lymphoma. Recurrent urticaria could rise the suspicion for urinary or respiratory tract infections, EBV, HBV, H. pylori, Hashimoto thyroiditis, Schnitzler syndrome, cryoglobulinemia, mastocytosis, connective tissue diseases but they were ruled out. This findings suggest that elevated IgE and urticaria may result from a paraneoplastic, Th2-mediated immune response, characterized by isotypic switching, mast cell activation, eosinophilic recruitment, all of which are implicated in the pathogenesis of EDHM.

EDHM is a chronic, relapsing pruritic skin disorder occurring in patients with various hematologic neoplasms, most often CLL, presenting in different forms, from erythematous papules to blisters, urticaria or ulcers. The pathogenesis is poorly understood, a type-2 immune response plays a central role, with local excess of interleukin-4 and interleukin-5, which promotes eosinophil production, differentiation and migration. Chemotherapy may also play a role in EDHM development.

Histological and immunohistochemical findings confirmed active CLL with moderate proliferative activity, evidenced by the presence of prolymphocytes, immunoblasts, and a KI67 up to 30%, suggesting clonal evolution or disease acceleration. The initiation of venetoclax, a BCL2 inhibitor, was appropriate for relapse. Biopsy of the skin lesions was not performed due to clinical resolution with antistaminics, consistent with EDHM (not with neoplastic infiltration). This aligns with prior reports of EDHM usually responding to symptomatic treatment. While the prognostic significance of EDHM remains unclear, its occurrence here coincided with disease relapse, marking a more aggressive disease course, as in the few cases reported in the literature.

LOW HDL CHOLESTEROL IS A SENTINEL MARKER FOR HEPATIC STEATOSIS IN METABOLIC SYNDROME: IMPLICATIONS FOR TARGETED SCREENING STRATEGIES

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Introduction: The complex relationship between dyslipidemias and metabolic health remains incompletely understood. While attention has historically focused on elevated low-density lipoprotein cholesterol (LDL-C), reduced high-density lipoprotein cholesterol (HDL-C) may signal broader metabolic disturbances. This study investigated whether reduced HDL-C functions as an indicator of metabolic syndrome components and hepatic dysfunction in a well-characterized cohort of patients referring to our institution for overweight or obesity.

Materials and methods: This cross-sectional investigation included patients evaluated at the Metabolic Health Clinic of San Raffaele Hospital between January 2023 and October 2024. HDL status was categorized as low (<55 mg/dL in females; <45 mg/dL in males) or normal. Assessments included comprehensive anthropometrics (BMI, waist measurements, body composition ratios), biochemical parameters (lipid fractions, liver enzymes, glycemic indices), and hepatic ultrasonography. Multivariate statistics incorporated correlation analyses and network analysis of metabolic interrelationships.

Results: The study included a total of 496 patients, with 193 (39%) presenting low HDL-C levels and 303 (61%) having normal HDL-C values. Reduced HDL-C demonstrated robust associations with multiple metabolic perturbations. Anthropometric parameters revealed significantly increased adiposity across multiple measures in the low HDL-C group: BMI (+11.7%; 28.6 vs 25.6 kg/m², p<0.001), waist circumference (+6.4%; 100.0 vs 94.0 cm, p<0.001), and waist-to-height ratio (p<0.001). Quantitative correlation analysis confirmed strong inverse relationships between HDL-C concentrations and measures of central adiposity.

Biochemical profiling revealed hepatic involvement with substantially elevated ALT in the low HDL-C group (+21.7%; 28.0 vs 23.0 U/L, p<0.001) alongside marked hypertriglyceridemia (+47.5%; 146.0 vs 99.0 mg/dL, p<0.001). Ultrasonographic assessment demonstrated pronounced differences in hepatic steatosis prevalence, with 57% higher frequency in the low HDL-C group (33% vs 21%, p=0.006).

Network analysis identified dense interconnections between HDL-C and metabolic parameters, with HDL-C functioning as a central node within a tightly clustered metabolic syndrome constellation. Cardiometabolic risk factor profiling showed significantly increased arterial hypertension prevalence (+30.8%; 51% vs 39%, p=0.012) in the reduced HDL-C cohort, alongside higher smoking rates (+47.1%; 25% vs 17%, p=0.039). Gender distribution analysis revealed male predominance in the low HDL-C group (42% vs 33%, p=0.041).

Conclusion: Our findings establish reduced HDL-C as a powerful indicator of underlying metabolic dysfunction and hepatic steatosis. The observed patterns suggest that HDL-C levels reflect integrated metabolic health through complex biological pathways connecting lipid metabolism, adiposity, and liver function. These observations support implementing targeted metabolic screening strategies utilizing HDL-C as an initial filter, as individuals with reduced HDL-C warrant comprehensive evaluation for metabolic syndrome components and hepatic steatosis, even in the absence of overt obesity.

SARCOPENIC OBESITY IN TYPE 2 DIABETES MELLITUS: PREVALENCE AND PREDICTORS

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Background: Diabetes mellitus (DM) is a recognized risk factor for sarcopenic obesity (SO), a condition characterized by the coexistence of abdominal obesity (AO) and reduced skeletal muscle mass and function. We implemented routine screening for SO in a diabetes outpatient clinic to assess its prevalence and associated factors in type 2 diabetes mellitus (T2DM) patients.

Methods: We evaluated outpatients with T2DM using bioelectrical impedance analysis (BIA) to measure skeletal muscle mass (MM) and the handgrip strength test to assess muscle function (MF). Physical activity (PA) was estimated using the International Physical Activity Questionnaire (IPAQ). SO was defined as the presence of (1) AO (waist circumference [WC] ≥88 cm in women and ≥102 cm in men), (2) low skeletal muscle index (SMI, calculated as MM/weight), and (3) low MF, diagnosed based on the cut-points recommended by ESPEN and EASO.

Results: We included 109 participants, of whom 65 (59.6%) presented with AO. Among these, 11 (16.9%) were diagnosed with SO. Participants with SO showed a trend toward male gender (81.8% vs. 53.7%, p=0.080) and a lower prevalence of elderly individuals (27.3% vs. 57.4%, p=0.068) compared to those without SO (Table 1). Isolated low SMI or MF was detected in 25.9% and 22.2% of participants without SO, respectively. We compared BMI and WC among participants with normal SMI/MF, low MF or SMI, and SO(low SMI/MF) (Figures 1 and 2). BMI correlated positively with MM (Spearman's rho 0.314, p=0.011) but negatively with SMI (rho -0.29, p=0.019) (Figure 3). No significant correlation was found between WC and MM or SMI. Logistic regression adjusted for sex and age identified BMI as a significant predictor of low SMI (OR 1.17, 95% CI [1.04–1.31], p=0.007), but not of SO. No variables predicted low MF.

Conclusions: A significant proportion of patients with T2DM present with AO and SO, characterized by low SMI and reduced MF. Our findings underscore that while higher BMI is associated with increased MM, it is inversely correlated with SMI, emphasizing the importance of adjusting MM for body weight to accurately identify SO. Further studies are needed to explore the determinants of reduced MF and to establish targeted interventions for SO in diabetic patients.

Table 1. Comparison between participants without or with SO

Variable	No SO (n=54)	SO (n=11)	P
Sex (M, %)	53.7	81.8	0.08
Age (years)	70.0 [64.0; 59.9]	70.0 [79.0; 76.0]	0.318
Elderly (age ≥65y, %)	57.4	27.3	0.068
Overweight/obesity (%)	68.5	90.9	0.099
Low physical activity (%)	51.9	54.5	0.870

Data are % or median [25°;75° percentile]

Figure 1. Body mass index

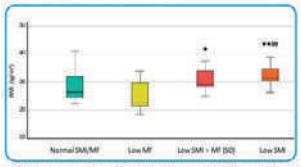
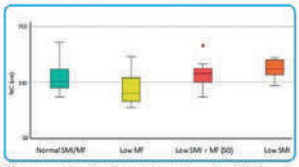
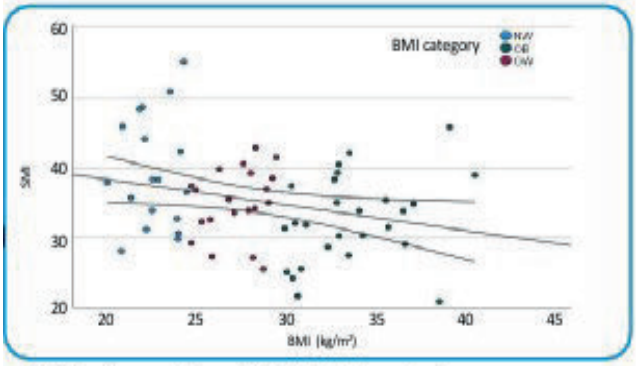


Figure 2. Waist circumference



BMI, body mass index; SMI, skeletal mass index; MF, muscle function; SO, sarcopenic obesity; WC, waist circumference. * p=0.013 vs. low MF; **p<0.001 vs. low MF; ##p=0.008 vs. normal SMI and MF

Figure 3. Correlation between BMI and SMI



BMI, body mass index; SMI, skeletal mass index

DIRECT ORAL ANTICOAGULANT FOR THE TREATMENT OF PORTAL-SPLANCHNIC VEIN THROMBOSIS, A COHORT STUDY

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Background: Portal/splanchnic vein thrombosis (PSVT) is a relatively rare condition that can lead to portal hypertension and gastrointestinal bleeding. While it can be linked with tumors, inflammatory bowel diseases, infections, and hypercoagulable states, cirrhosis is the leading cause, with a prevalence of up to 25% among patients on the transplant waiting list. According to the Baveno VII guidelines, anticoagulant therapy is the treatment of choice to recanalize the vessel and prevent complications. Low-molecular-weight heparins (LMWH) have been the most commonly used treatment, achieving up to 80% recanalization in non-cirrhotic patients and 42% in cirrhotic patients. Direct Oral Anticoagulants (DOACs) are also suggested as alternatives, but data supporting their use in PSVT remains limited.
Aims: To evaluate the efficacy and safety of direct oral anticoagulants in the treatment of PSVT.
Methods: We performed a retrospective cohort analysis of patients with PSVT treated with anticoagulants from November 2023 to January 2025 at our outpatient hepato-thrombotic clinic, a multidisciplinary collaboration between hepatologists and thrombosis experts established in 2023. All patients initiated on anticoagulants were followed per clinical protocol at 3, 6, and 12 months, with imaging assessments (Doppler ultrasound, CT angiography, and/or abdominal MRI). During the follow-up, we recorded radiologic signs of recanalization and the occurrence of minor and major bleeding according to the ISTH definition.
Results: 37 patients with PSVT were treated with anticoagulants during the study period (mean age 65±10 years, male 75%). 29 patients had cirrhosis due to the following causes: alcohol-related (n=18, 49%), autoimmune (n=2, 18%), HCV/HBV (n=3, 8%), dysmetabolic (n=3, 8%), and other causes (n=3, 8%). In patients with cirrhosis, the CHILD-Pugh mean score was A6. Overall, 25 (73%) patients were initiated on a DOAC, while 12 (32%) were treated with LMWH. The most commonly used DOAC was apixaban (n=19), followed by rivaroxaban (n=4) and edoxaban (n=2). In 8 out of 12 patients on LMWH, a DOAC was not initiated due to concerns about hemorrhagic complications or ineligibility (e.g. CHILD-Pugh classification C). Patients on DOAC therapy were followed for an average of 253 days, during which complete or partial PSVT recanalization was observed in 18 (72%) patients (9 with complete and 9 with partial recanalization). Only one patient on DOACs experienced minor bleeding, and no major bleeding events were observed. One patient died during follow-up due to spontaneous bacterial peritonitis complicated by hepatorenal syndrome. After a period of full-dose anticoagulation lasting 6 to 12 months, 19 patients were switched to a prophylactic dose of DOAC.
Conclusions: DOACs appear to be safe and effective in treating PSVT, both in patients with and without cirrhosis. However, the limited number of enrolled patients and the relatively short follow-up period prevent drawing definitive conclusions.

ANALYSIS OF THE EFFECT OF THERAPY ON EXERCISE CAPACITY IN PATIENTS WITH ANDERSON-FABRY DISEASE

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Background: and Aim: Fabry disease (FD) is a rare X-linked lysosomal storage disorder caused by mutations in the GLA gene, which encodes the enzyme α-galactosidase. The accumulation of globotriaosylceramide (Gb3) in various tissues and organs underlies the clinical manifestations of the disease, which range from muscular involvement to renal, peripheral nervous system, and cardiac complications. Due to its X-linked inheritance, disease manifestations are more severe in males, whereas females generally present milder forms, likely due to X-chromosome lyonization. FD patients exhibit a wide range of symptoms related to Gb3 accumulation in multiple organs and tissues, among which fatigue and asthenia are among the most frequently reported. In this study, we aimed to analyze the effect of enzyme replacement therapy (ERT) on exercise capacity in FD patients.
Methods: FD patients who had undergone at least one bicycle ergometer stress test at our clinic were included in the analysis.
Results: From February 2021 to September 2022, we enrolled 59 patients. Table 1 summarizes the main characteristics of the study population and the key ergometer stress test parameters. Patients receiving ERT showed lower lactate concentrations at peak exercise (with a trend toward statistical significance compared to untreated patients), which translated into a statistically significant difference in lactate levels from baseline to peak exercise. No significant differences were found in demographic characteristics or other stress test parameters. Patients on ERT had been receiving therapy for 57 ± 53 months.

Table 1. Demographic characteristics of the study sample and main results by mean of bicycle ergometer test in the whole cohort and in the two subgroups.

Whole semple
(n=59)
No ERT
(n=28)
ERT
(n=31)
p-value
0.038

For a subgroup of 15 patients who had started enzyme replacement therapy since our first evaluation we were able to evaluate the effects of this treatment in relation to the cardiopulmonary exercise test, as shown in Table 2.

Table 2. Ergometer stress test at baseline and follow-up
Baseline
(n=15)
Follow-up
(n=15)
P value
0.034
0.034
0.050

As shown in Table 2, in the subgroup of patients who had initiated ERT, after a mean follow-up period of 14 ± 5 months, we observed an increase in exercise duration of approximately 90 seconds (from 399 ± 123 seconds at baseline to 539 ± 239 seconds at the final follow-up; p = 0.034), along with an increase in METs from 8.7 ± 2.7 at baseline to 11.7 ± 5.2 at follow-up (p = 0.034).
Conclusions: The initiation of ERT in patients with Fabry Disease is associated with an improvement in exercise capacity, reflected by increased exercise duration and METs.

Moreover, patients undergoing long-term enzyme replacement therapy exhibited reduced metabolic acidosis, as assessed by lactate production during exercise, compared to those not receiving therapy.

AKI AND METFORMIN: AN EXPLOSIVE COMBINATION?

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Introduction: Metformin is the first-line treatment for type 2 diabetes mellitus, due to its efficacy and favorable safety profile. However, its use in patients with acute kidney injury (AKI) has traditionally been subject to caution due to the risk, albeit rare, of lactic acidosis. Current guidelines suggest a more individualized approach, but data on the use of metformin in acute settings are still limited. This study aims to evaluate the association between metformin therapy and in-hospital mortality in patients with AKI.
Materials and methods: A machine learning algorithm was used to identify all admissions with a diagnosis of acute kidney injury (AKI) at the Emergency Department of the IRCCS Istituto Clinico Humanitas, in the period between 01/01/2015 and 28/02/2024. Out of a total of 3852 identified cases, clinical data relating to 503 patients were manually collected. Among these, 70 patients were affected by diabetes mellitus treated with metformin. The association between metformin use and mortality in patients with AKI was subsequently analyzed.
Results: The mean age of patients included in the analysis was 77.1 years, while that of patients treated with metformin was 77 years. Among the 70 patients treated with metformin, 28 had a concomitant diagnosis of chronic renal failure (CRF), with stage 3 being the most frequent (75% of cases), only one patient in stage 4 and no patients in stage 5.The overall in-hospital mortality was 7.95% (40 deaths out of 503 patients), while in the subgroup treated with metformin it was 7.14%.Treatment with metformin was not associated with an increase in mortality; on the contrary, it emerged as a potential protective factor, although not statistically significant (OR: 0.86; p = 0.77), probably due to the limited number of events.No significant association was observed between metformin use and the need for dialysis (OR: 1.02; p = 0.98).
Discussion: The results of this study suggest that metformin use is not associated with increased in-hospital mortality or the need for dialysis in patients with acute kidney injury (AKI). The trend toward a possible protective effect, although not statistically significant, is consistent with recent evidence suggesting its safety even in the presence of moderate renal impairment. However, interpretation should be cautious, considering the retrospective nature of the study and the limited number of patients in the metformin-treated subgroup.
Conclusions: Metformin does not appear to worsen in-hospital prognosis in patients with acute renal failure. These data support a more balanced clinical approach in the management of hypoglycemic therapy in the acute phase. Further prospective studies on larger case series are desirable to confirm these observations and better define the indications for drug suspension in the presence of renal failure.

HEPATIC FIBROSIS INDICES CORRELATE WITH MICROVASCULAR REMODELLING: RESULTS FROM A MASLD PATIENTS' COHORT

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Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) conveys an increased cardiovascular risk. Fibrosis-4 Index (FIB-4 Index) and AST to Platelet Ratio Index (APRI) are two scores for the non-invasive assessment of hepatic fibrosis in MASLD patients while Fatty Liver Index (FLI) is a surrogate score of steatotic liver. Hypertension is characterized by microvascular remodelling, which has a known prognostic significance in terms of cardiovascular events. Whether hepatic fibrosis and microvascular remodelling indices correlate in MASLD and hypertension is unknown.
Aim: Assessing the correlation between indices of hepatic fibrosis and microvascular remodelling in hypertensive patients with or without MASLD.
Methods: 23 participants were recruited: 20 met MASLD's diagnostic criteria (13 hypertensives and 7 normotensives) and 3 hypertensive patients without any hepatic disease. Patients with diabetes, cancer, autoimmune diseases and other hepatic diseases were excluded to avoid a possible confounding effect on microvascular remodelling parameters. Retinal arteriolar morphology was assessed by Adaptive Optics. Blood chemistries were performed to compute APRI, FIB-4, FLI.
Results: FIB-4 directly correlates with the retinal external and internal arteriolar diameter (rho = 0.434; p = 0.049 and 0.581; p = 0.006, respectively), the wall cross-sectional area (WCSA), (rho = 0.665; p = 0.001), and age (rho = 0.661; p = 0.001). A direct correlation was observed between WCSA and age (rho = 0.460; p = 0.027). APRI and FLI didn't show any significant correlation with remodelling parameters.
Conclusions: Among FLI, APRI and FIB-4 only the latter showed a significant correlation with retinal arteriolar morphology. Moreover, FIB-4 is directly correlated with outward hypertrophic remodelling, a vascular morphological impairment resulting from inflammatory and pro-oxidant damages.

	AH-MASLLD (n.13)	AH (n.3)	MASLD (n.7)
Age (year)	52,1 ± 14,6	61,3 ± 4,1	46,3 ± 11,2
SBP (mmHg)	133,6 ± 10	140,3 ± 18,6	126,8 ± 15,6
DBP (mmHg)	87,3 ± 8,8	89,3 ± 12,2	85,5 ± 8,4
HR (bpm)	74,5 ± 10,2	73 ± 15,7	69,4 ± 15,2
BMI (kg/m²)	29,2 ± 5,1	25,2 ± 3,7	27,3 ± 2,6
Waist circumference (cm)	105 ± 12	96 ± 10	99,1 ± 4,1
FIB-4 SCORE	1,15 ± 0,7	1,2 ± 0,7	0,99 ± 0,2
APRI SCORE	0,32 ± 0,1	0,3 ± 0,72	0,4 ± 0,1
FLI	67,1 ± 27,6	54,3 ± 17,9	64,1 ± 29,1

Fig.1. Data are expressed as mean ± standard deviation. AH: arterial hypertension, SBP. Systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate, BMI: body mass index, WCSA. Wall cross sectional area, WLR: wall lumen ratio.

	AH-MASLD (n.13)	AH (n.3)	MASLD (n.7)
Internal Diameter (µm)	95,8 ± 11,5	92,9 ± 7,3	92,6 ± 12,9
External Diameter (µm)	119,7 ± 12,1	109,4 ± 4,4	116,2 ± 12,8
Wall thickness (µm)	11,9 ± 0,8	13,2 ± 1,2	12 ± 0,4
WCSA (µm²)	4075,6 ± 617,2	4436,8 ± 760,2	3935,5 ± 542,9
WLR	0,25 ± 0,03	0,29 ± 0,005	0,27 ± 0,03

Fig.2. Data are expressed as mean ± standard deviation. AH: arterial hypertension, SBP. Systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate, BMI: body mass index, WCSA. Wall cross sectional area, WLR: wall lumen ratio.