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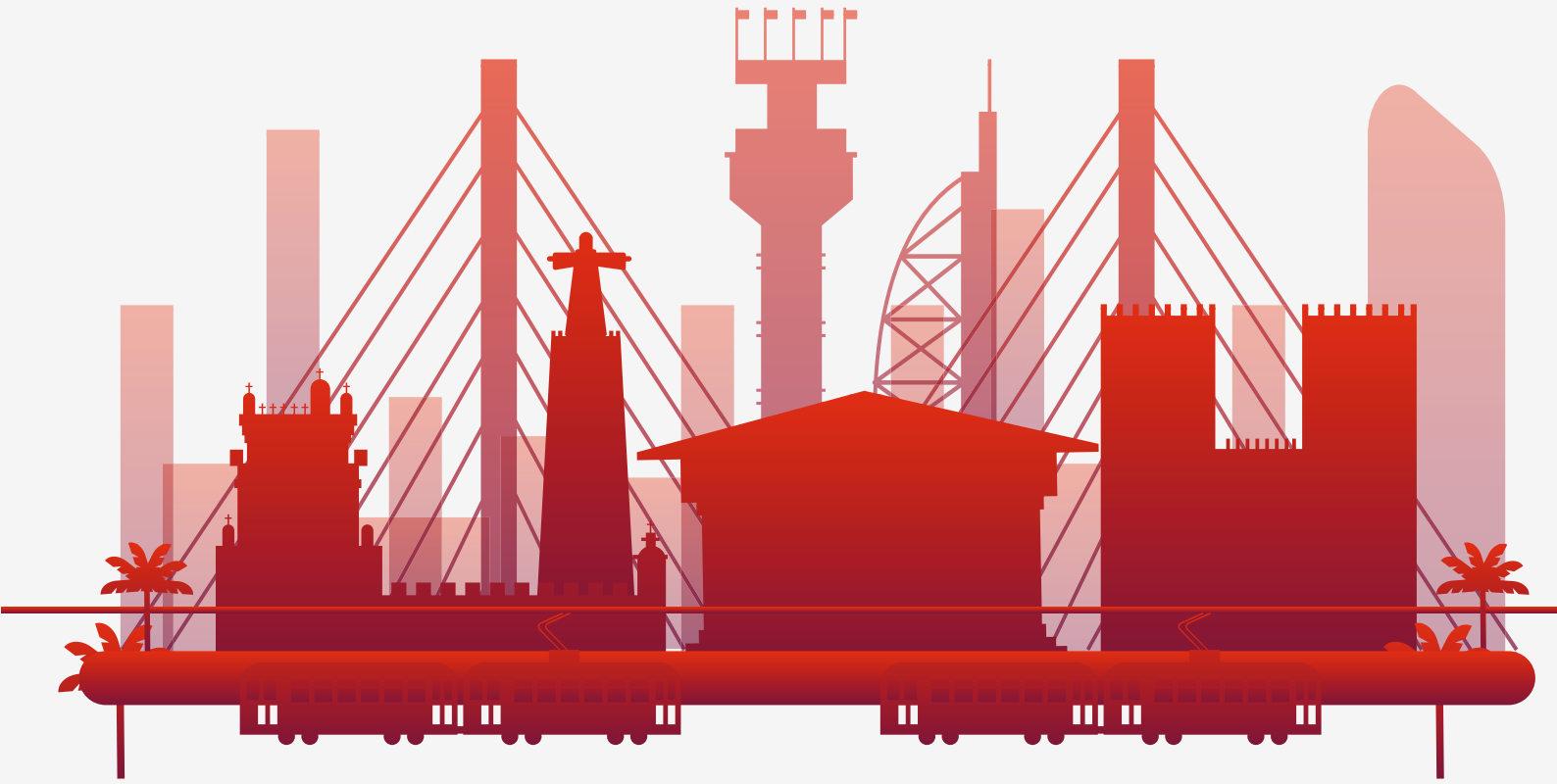

Abstract Book

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Oral presentations

OR-01

Unexpected cause for a PTT prolongation in a bleeding patient. A case report

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Plasma prekallikrein (PK) deficiency is a rare autosomal-recessive defect, mainly associated with KLKB1 gene mutations. An unexpected isolated prolonged activated partial thromboplastin time (aPTT) in a patient without history of bleeding is often the initial hint. This condition usually causes no health problems.

We herein report a case of PK deficiency diagnosed in the setting of unexpected bleeding that promoted an investigation.
A 78-year-old man with previous medical history of diabetes mellitus, hypertension and dyslipidemia, was admitted to our hospital with rectal bleeding that had started 24 hours before. He didn't have abdominal pain, vomits, weight loss or anorexia.
While waiting in the emergency department, the patient presented blood mixed in the stools. Rectal examination revealed the presence of blood. There were no visible anal fissures or hemorrhoids.

Analytical work on admission: Hemoglobin 15.8 g/dL; Platelets 241000/mL; Leucocytes 8000/mL; Normal renal and hepatic function.
aPTT 80.0 seg [20.9-34.9]; PT 10.6 [8.4 – 14.4]; INR 0.9.
aPTT synthafax = 24.30 seg [22.4"-32.9"]
aPTT 15 min = 22.2 seg [20.9"-34.9"]

The patient was admitted for colonoscopy, vigilance and to complete the study of his coagulopathy.
The isolated prolonged aPTT was confirmed in a second sample. The patient had no personal or family history of spontaneous or excessive bleeding. He had been submitted to eye and dental surgery the year before and didn't present abnormal bleeding.
A mixture of pooled plasma containing every coagulation factor with the patient's plasma in a 1:1 ratio completely corrected the prolonged aPTT, suggesting that the prolonged aPTT was due to a factor deficiency.

Intrinsic factors dosage revealed: Von Willebrand Factor (FvW) Ag: 212%; FvWRco 132 %; FVIII 153%; FIX 105%; FXI 92%; FXII 68%.
[FvW Ag: Blood group (BG) O - 48.2-140.8%; BG A/B/AB 66.1-176.3%; FvWRco: - BG O -

48.2-201.9%; BG A/B/AB - 60.8-239.8%; FVIII 50-150%; FIX 66-150%; FXI 65-150%; FXII 50-150%]
Since the mixing study suggested factor deficiency and the levels of the studied intrinsic pathway factors were normal, we assumed that the prolonged aPTT was due to a deficiency of one of the intrinsic pathway contact factors (HMWK or prekallikrein), which confer no hemorrhage risk. Dosing of contact factors are not available at our hospital but since the patient needed urgent colonoscopy, we indicated that it could be safely perform.

Colonoscopy revealed diverticulosis without active bleeding. The patient was discharged after 3 days without further surgical intervention.
Before the patient was discharged, we sent a sample to a coagulopathy reference centre for contact factor dosing which revealed: PK = 0,0 U/mL.

In this setting, a prompt investigation was required because this patient could´ve needed factor replacement therapy for surgery or to stop the bleeding. It turned out that the cause of the aPTT prolongation was due to a contact factor deficiency, which does not confer bleeding risk.

Although contact factors deficiency is very rare, it must be taken into account when investigating possible causes for prolonged aPTT. A correct diagnose may avoid treatment with unnecessary factor replacement therapy and may avoid delaying necessary procedures.

OR-02

Antiphospholipid syndrome and refractory immune thrombocitopenic purpura - A series of unfortunate events

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We present the complex case of a man diagnosed with both antiphospholipid syndrome and immune thrombocitopenic purpura and the challenge of managing these two demanding entities together, balancing the thrombotic and hemorrhagic risk associated.

A 26 years-old healthy man was diagnosed with antiphospholipid syndrome (lupus anticoagulant ratio 3.6; anticardiolipin IgG 272 GPL U/mL, IgM negative; anti-beta2 glicoprotein IgG 1138 RU/mL, IgM negative - confirmed in second determination >12 weeks apart) following a cerebral venous thrombosis. Patient was started on warfarin for a target INR of 2-3.

At 32 years-old, the patient had an episode of acute abdominal aorta thrombosis and thrombectomy followed by illiofemoral bypass was conducted. The INR target was raised to 3-4.

At 40 years-old, he develops petechia and persistent thrombocytopenia (platelets <20x10^9/L), is diagnosed with immune thrombocytopenia purpura and started on corticosteroids and azathioprine. Due to refractory thrombocytopenia, the attending physician decided on a splenectomy. The platelet count normalizes in the first few years post-procedure.

He had a spontaneous intracranial bleeding at 43 years-old. The platelet count dropped again but stabilizes at 60-90x10^9/L after reintroduction of immunosuppression. Three years later, he develops a spontaneous subdural hematoma. At admission with an INR of 4.6 (under warfarin) and 36x10^9/L platelets. From this point on he was followed up at our derpatment. Due to sustained thrombocytopenia, the patient received high-dose corticosteroids and rituximab. He was discharged on prednisolone 40mg/day and therapeutic low-molecular-weight heparin. Platelets reach a new high of 110x10^9/L, prednisolone is tapered to 10mg/day and warfarin is restarted. During an episode of acute cholangitis, an abdominal CT scan surprisingly shows a normal-sized spleen, an accessory spleen that was not removed in the surgery 6 years before.

After a severe cutaneous reaction following the second administration, rituximab is stopped and the patient is once again very dependent on steroids (15-30mg/day) to sustain platelet level >30 x10^9/L. Simultaneously, it gets progressively harder to maintain a therapeutic INR. It was decided that the patient should undergo another splenectomy. The surgery was laborious due to adhesions from the previous intervention. Platelet count rapidly normalizes, but surgical complications lead to a prolonged admission in the ICU, with multiple infectious complications. While in the ICU, and on therapeutic enoxaparin, he develops an acute thrombosis of the left common femoral artery prompting a transfemural amputation. He was discharged 5 months later with severe decline of global health status.

The patient is readmitted 20 days later with abdominal sepsis and acute kidney failure. During this admission the patient is diagnosed with urotelial malignany but deemed unfit for treatment. Thrombocytopenia dropped once again to a plateau of 20x10^9/L and he was kept on enoxaparin, with no further bleeding or thrombotic events. The admission results in death due to refractory status epilepticus, 200 days after elective second splenectomy, at 48 years of age.
The unfavorable outcome of this case exemplifies the sheer complexity of managing the coagulation balance in a patient with thrombophilia and a bleeding disorder.

OR-03

Recurrent Thrombosis in Behçet's Disease and the Challenge of Anticoagulation – A Case Report

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Background
Behçet disease (BD) is a complex systemic inflammatory disease. Vascular involvement is one of the most common features with patients suffering from recurrent vascular events especially venous thrombosis. Most of the times, these vascular manifestations are associated with signs of inflammatory activity. The inflammatory nature of BD promotes endothelial dysfunction, coagulation and platelet activation leading to inflammation-induced thrombotic events.

Material and methods
We describe a report of a 35-year-old man, with history of psoriasis diagnosed during childhood, that was referred to our institution for further evaluation of arthralgias associated with recurrent thrombotic events. In 2019, the patient was diagnosed with superficial vein thrombosis (SVT) in the right lower limb for which he was treated with enoxaparin 80mg bid, during 12 days, with complete recovery. Two months later, after a laparoscopic surgical intervention, the patient experienced fever, malaise and night sweats and had an episode of right sided deep vein thrombosis (DVT) (right common iliac vein and right external iliac vein). Laboratory examination showed only increased c-reactive protein (CRP) and rheumatoid factor; the thrombophilia screening performed (protein C, protein S and antithrombin deficiencies, factor V Leiden and factor II gene mutations, antiphospholipid antibodies) was negative. The patient began enoxaparin (1mg/Kg bid) followed by warfarin. Even under anticoagulation with INR within therapeutic range the patient presented, 9 months later, a recurrent DVT (right distal femoral vein and right popliteal vein); he also had dolorous skin nodules (apparently erythema nodosum) and mucocutaneous ulcers in oral cavity. Therapeutic with warfarin was switched to low molecular weight heparin (LMWH) and later, to dabigatran. Four months later, under treatment with dabigatran, another DVT has diagnosed (left popliteal vein) and the patient switched to LMWH followed by warfarin.

Results
After this variety of clinical manifestations, diagnosis of BD was made. The patient started systemic corticoid therapy and methotrexate, and then switched to colchicine. Since then, he did not experience any clinical exacerbations or any other thrombotic event.

Conclusion
With this case, we point out the importance of an early diagnosis of BD aiming to reduce morbidity and mortality associated with complications of this disease, such as thrombotic events. As a chronic systemic condition, BD leads to a pro-inflammatory state. Inflammation disturbs pro and anti-coagulant equilibrium promoting coagulation through several processes. Patients often experience recurrent vascular thrombosis, being the lower extremity DVT the most common. Several clinical symptoms that occur simultaneously with thrombotic events, such as constitutional symptoms, erythema nodosum and mucocutaneous ulcers suggest the inflammatory nature of thrombosis in BD. Because of that, as some studies suggest, vascular thrombotic events in BD should be prevented with immunosuppressant rather than with anticoagulants. Duration of anticoagulation must be individualized according to individual risk.

OR-04

Anticoagulation in obese and post-bariatric surgery patients: Always the same?

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As the prevalence of obesity continues to increase worlwide, bariatric surgery is increasingly an option. The extent to which both alter the efficacy of anticoagulants is not negligible and should be appreciated.

We report the case of a 55 year-old woman, obese (127Kg, body mass index (BMI) > 40Kg/m2) submitted to a gastric bypass 6 days before admission, being discharged under enoxaparin 40mg for thromboprophylaxis. She was admitted to the emergency department due to a psychotic episode, being hospitalized in Psychiatry, mantaining enoxaparin 40mg id. On the 6th day of hospitalization, she presented with sudden diaphoresis, hypotension, cyanosis and syncope. Upon observation, she was pale, sweaty, hypotensive (systolic blood pressure 85mmHg) and tachycardic (135bpm), with oxygen saturation 96% with oxygen therapy at 3L/min. Blood tests showed D-dimers 11372ng/mL and High Sensitivity Troponin 182ng/L. The electrocardiogram revealed sinus tachycardia and S1Q3T3 pattern. Chest CT

showed a massive pulmonary thromboembolism (PE). The transthoracic echocardiogram revealed dilation of the right ventricle with longitudinal and radial dysfunction, presenting with McConnell and 60/60 signs. It also showed a hyperdynamic left ventricle with marked systo-diastolic D-shape. Intermediate-high-risk PTE was assumed and, after multidisciplinary team discussion, the patient was transferred for a tertiary center for in situ fibrinolysis, followed by unfractionated heparin for 48 hours. She transferred back with the indication to start rivaroxaban. However, given the recent bariatric surgery and it´s expected absorptive deficits, it was decided to start tinzaparin 175UI/Kg for 3 months. The patient subsequently underwent right heart catheterization, which did not reveal signs of pulmonary hypertension.

This case highlights the pharmacokinetic changes of anticoagulation in obese patients, as well as the peculiar environment of post-bariatric surgery. In fact, while the conventional dose of prophylactic enoxaparin is 40mg id, in patients with a body mass index (BMI) > 40Kg/m2 a dose of 0.5 mg/kg 1 or 2id should be used, depending on the thrombotic risk, which probably accounts for the justified the PE in our case.

Among direct oral anticoagulants (DOACs), only rivaroxaban and apixaban - in standard doses - are recommended for PE treatment and prophylaxis of obese patients, regardless of weight and BMI. In the post-bariatric surgery period, however, changes in the bioavailability of drugs taken by oral route result either from the reduction of absorptive surfaces or from the decrease in caloric intake. Thus, current recommendations encourage the use of parenteral anticoagulation in the immediate postoperative period, considering the introduction of vitamin K antagonists or DOACs only after the 4 weeks and with pharmacological absorption monitoring. At this point, apixaban (which is primarily absorbed in the upper gastrointestinal tract) is expected to undergo minor pharmacokinetic changes, requiring however additional studies to prove its efficacy.

OR-05

Severe thrombocytopenia in secondary antiphospholipid syndrome

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Background
Antiphospholipid Syndrome (APS) is a systemic autoimmune disorder defined by arterial or venous thrombosis with or without obstetrical morbidity, along with persistent antiphospholipid antibodies. It may be either primary or associated with an underlying etiology (36.2%), particularly systemic lupus erythematosus (SLE). Moderate thrombocytopenia is also a common manifestation (20-50%), with higher occurrence in secondary APS, and is likely associated with more severe disease.

Material and methods
Clinical case report.

Results
68-year-old woman, with a history of hypertension, dyslipidemia, obesity, peripheral artery disease, SLE (with mild thrombocytopenia at presentation), APS (3 transient ischemic strokes at a young age, necrotic lesions with subungual hemorrhage in both hands, no history of miscarriages, but of prematurity) and atrial fibrillation (CHADS2VASC: 6). Medicated with hydroxychloroquine, acenocoumarin and aspirin. She was admitted to the emergency department of a tertiary hospital, with easy bruises, epistaxis, gingivorrhagia and hematuria. Analytical study revealed an hemoglobin of 12.3g/dL, severe thrombocytopenia <5.000/uL (231.000/uL one month prior) and an international normalized ratio (INR) of 3.4. Further investigation showed positive antiplatelet antibodies, negative direct Coombs test, no flare evidence of immunological diseases (normal ds-DNA, no complement consumption, low sedimentation rate and no other organ dysfunction) and negative serological viral markers. A diagnosis of immune thrombocytopenia (ITP) was assumed, anticoagulation was suspended and the patient began treatment with vitamin K and three pulses of methylprednisolone 1g, followed by prednisolone 1mg/kg/day, with initial improvement [platelet count (PLT) 24.000 -> 36.000 -> 48.000]. Anticoagulation was restarted with enoxaparin 40mg (every 12h) with later adjustment to 70mg (every 12h) given the absence of complications, high thrombotic risk and weight of the patient (98Kg). Due to a new drop in platelet count and supratherapeutic anti-Xa levels (1.35 IU/mL), enoxaparin was held, and heparin-induced thrombocytopenia was ruled out, with negative anti-PF4 antibodies. The patient received two courses of intravenous immunoglobulin (80mg daily), with progressive recovery of platelet count, resuming anticoagulation with acenocoumarin and enoxaparin. Reviewing the anamnesis, the patient had a respiratory infection a month prior to the onset of hemorrhagic symptoms, which may have been a precipitating factor of ITP. At discharge she had no evidence of active bleeding, improvement of bruises, a platelet count of 146,000/uL, receiving indication to maintain acenocoumarin, enoxaparin and prednisolone (0.8mg/Kg/day for 2 weeks), with short-term reassessment of blood count and INR control.

Conclusion
The presence of thrombocytopenia is an important independent risk factor for mortality in SLE and APS. Severe thrombocytopenia is relatively uncommon in APS patients. The approach to immunosuppression and anticoagulation must be individualized, considering the increased risk for both bleeding and thrombosis. Corticosteroids and intravenous immunoglobulin are first line treatment in primary ITP and secondary ITP associated with SLE and APS. A reasonable anticoagulation approach can be extrapolated from guidelines for thrombocytopenic cancer patients with history of thrombosis, full-dose enoxaparin for PLT >50.000/uL, half-dose enoxaparin for PLT 25.000 - 50.000/uL, and no anticoagulation for PLT<25.000/uL.

OR-06

Ulcerative Colitis and The Heart Ought to Be Far Apart. A Case Report

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Introduction
Left ventricular (LV) thrombi usually occur in the setting of global or regional LV systolic dysfunction and are extremely rare in patients with mild/absent LV wall motion abnormalities. Inflammatory bowel disease (IBD) has been known to increase the risk of thrombosis in the venous and arterial systems, predominantly in the active phases of the disease. The occurrence of LV thrombus during an IBD exacerbation is rare, nonetheless, physicians should be familiarized with this association and possible thromboembolic complications.

Case Presentation
We present a 51 year-old man who had been diagnosed with ulcerative colitis one year ago. Since the diagnosis, the patient was hospitalized twice, once for basilar artery thrombosis-related ischemic stroke and a second time due to cytomegalovirus-induced esophagitis with mediastinal extension and myopericarditis. At that time, the transthoracic echocardiogram (TTE) revealed a mildly reduced left ventricular ejection fraction with segmental hypokinesia in a non-ischemic pattern, mainly of the basal and mid-inferior, lateral and anterior walls.
A few months later, the patient was evaluated for sudden-onset oppressive chest pain with mandibular and right arm irradiation. No other relevant symptomatology was reported. The electrocardiogram revealed an ST-segment elevation myocardial infarction of the inferior wall. Coronary angiography showed complete occlusion of the posterior descending and first posterolateral branch arteries. Thrombi aspiration on both arteries and balloon dilatation of the posterolateral artery was performed. Blood work revealed an expected rise in troponin and an unexpected exuberant thrombocytosis (platelets > 1000 x 10^9/L).

At the time of this hospitalization, the patient was already having bloody and mucopurulent diarrhea for two months. Gastroenterology colleagues observed the patient and ultimately confirmed an ulcerative colitis exacerbation. He was started on immunosuppressive therapy.

The post-myocardial infarction TTE demonstrated mildly reduced left ventricular ejection fraction, with hypokinesia of the basal and mid segments of the inferior and inferolateral walls and of the interventricular septum. Apart from these findings, a round, mobile, hyperechogenic, pedunculated 6x9mm mass was evidenced in the normally contracting apical region and confirmed by using an ultrasonographic enhancing agent. The patient was started on a vitamin K antagonist, maintaining antiplatelet therapy with clopidogrel.

At the present moment, the patient is awaiting a new echocardiographic evaluation and has his ulcerative colitis under control.

Conclusion and Discussion

The case presented showcases an exacerbated ulcerative colitis patient with echocardiographic evidence of a thrombus in a normally contracting apex, who had an arterial thromboembolic complication. The myocardial infarction was believed to be secondary to partial embolization of the LV thrombus. Similar cases have been described in the literature, with inflammation, autoimmunity and pharmacotherapy being responsible for the heightened thrombogenicity of this disease. Some experts support the use of prophylactic anticoagulation during IBD exacerbations, however, clinical trials are necessary to prove this practice.

OR-07

Platypnea-Orthodeoxia Syndrome: Dyspnea that improves in a supine position

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Platypnea-orthodeoxia syndrome is a rare condition characterized by dyspnea and hypoxia that worsens in an upright position and improves in the supine position, and can result (among other causes) from inter-atrial communication defects, with consequent hypoxemia due to a right-to-left shunt. The most frequently described cause is right-to-left interatrial shunting from a patent foramen ovale (PFO) or an atrial septal defect (ASD), however, this condition is often asymptomatic. Furthermore, not all patients with inter-atrial communication develop right-to-left shunt.

We present the case of a 67-year-old man with a history of paroxistic atrial fibrillation, ischemic stroke, dyslipidemia, and hypertension, followed up in a cardiology clinic for ascending aortic aneurysm (52mm) and aortic bicuspid valve. He initially went to the emergency service due to progressive shortness of breath, especially during moderate exertion, dry cough and rhinorrhea in the last 1 week. He also reports exacerbated constipation in the past few days with infrequent bowel movements and very hard stools. He denied chest pain, palpitations, orthopnea, paroxysmal nocturnal dyspnea, lower limb edema or fever.

At admission due to significant desaturation, he was observed in the emergency room. Gasometrically, with a PaO2 of 35mmHg with FiO2 80%, and refractory to greater oxygen supply. Analytically, there was no elevation of inflammatory parameters, and pulmonary CT angiography was performed to rule out pulmonary embolism or parenchymal lesions.

Clinically, the patient was in good general condition, despite maintaining oxygen saturation that seemed to vary with position: he desaturated in an upright position, with almost normalization of PaO2 in the right lateral decubitus and supine positions, raising the suspicion of a right-to-left shunt. Due to this suspicion, the patient was hospitalized, and a transesophageal echocardiogram was performed, confirming the presence of a PFO with spontaneous right-to-left flow, thus explaining the oscillating hypoxia. It should be noted that there was a significant episode of constipation in the days prior with evident abdominal distention, which may have contributed to facilitating the inter-atrial flow similar to a sustained Valsalva maneuver. The patient underwent percutaneous correction of the inter-atrial defect with an Amplatzer device, with normalization of PaO2 at the time of discharge.
This is a rare condition, but should always be suspected in patients who present with unexplained and refractory hypoxemia despite oxygen supply. Transesophageal echocardiogram is often sufficient to make the diagnosis, and the consequent correction of the inter-atrial defect not only resolves hypoxemia but also prevents the occurrence of systemic paradoxical embolism (stroke, acute myocardial infarction).

OR-08

When the Heart Strikes Back: A Case Report of a Cardioembolic Stroke Due to Fulminant Prosthetic Valve Endocarditis

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Introduction
The migration of cardiac vegetations in infective endocarditis (IE) can result in life-threatening embolic events. Embolism is a common occurrence in IE, affecting 20-50% of patients and frequently causing strokes, which are associated with elevated morbidity and mortality rates. The brain and spleen are the most frequently affected sites of embolism in left-sided IE.

Case report
A female patient, aged 43, presented to the Emergency Department with status epilepticus. She had a pre-existing medical history that included cured hepatitis C, previous alcohol abuse, biological mitral prothesis with previous endocarditis episode in 2009, pacemaker device and atrial fibrillation that was being managed with anticoagulation therapy. She was originally admitted to the Cardiology service approximately one week prior to this presentation with acute decompensated heart failure due to new-onset severe mitral regurgitation. Transthoracic echocardiogram (TTE) and transesophageal echocardiogram (TEE) at that time did not show evidence of vegetation or intracardiac thrombus. Blood analysis showed no increase in inflammatory biomarkers, and blood cultures were negative.
Upon presentation after status epilepticus, she was admitted in intensive care unit. Brain computed tomography revealed multiple infarct lesions compatible with diffuse septic

metastasis in the context of infective endocarditis. Blood cultures on admission grew methicillin-sensitive Staphylococcus aureus. She was treated with flucloxacillin and gentamicin, and a new TEE study was obtained. The echocardiogram showed a large sessile, mobile mass, attached to the mitral prosthetic valve. The patient developed multiorgan dysfunction with rapid onset of cardiac and respiratory failure and passed away after 5 days of treatment.

Conclusion
IE is a challenging condition to diagnose, as it can present with a range of symptoms. Early diagnosis is crucial to enable prompt implementation and acute mitral regurgitation may be the first sign of IE. Vigilance and a high index of suspicion when assessing high-risk patients can lead to better outcomes and prevent major complications associated with IE.

OR-09

Overexpression of FXII as a risk of thrombosis in patients with SAMTER syndrome, angioneurotic edema, and its association with smoking rate and hematological parameters

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Background
SAMTER syndrome (SSx), with its triad bronchial asthma, nasal polyps and aspirin allergy; It is an entity that must be recognized since many patients with asthma may have other risk factors for thrombotic events, complicating the use of antiplatelet therapy. In the world we only find 5 clinics that study SSx, in addition, a strong association between angioneurotic edema, SSx and an over-expression of coagulation FXII has been found.

Objective
To study in our SAMTER clinic the expression of FXII in patients who have developed a picture of angioedema and assess their risk of thrombosis.

Methods
A cohort of 21 patients with SxS was studied, with manifestations of angioneurotic edema secondary to aspirin and non-steroidal anti-inflammatory drugs (NSAIDs), whose clinical history, search for thrombosis factors, samples were taken for the measurement of blood count (baseline and follow-up) and FXII factor. Patients were classified as hyperactive and with normal levels of FXII. Descriptive statistics were performed on quantitative variables and frequency measurements on qualitative variables. Clinical history and hematological parameters were compared between the two study groups.

Results
A total of 21 patients were studied, 6 men and 15 women, 38% (8) were classified as hyperactive to FXII, while 71% (15) were smokers.
A strongly significant association was found between smoking rate and Hyperactivity to FXII, with respect to hematological variables: Erythrocytes hemoglobin, hematocrit and lymphocytes showing an increase in their average in hyperactives compared with those not hyperactive to FXII (Table 1, graphs 1,2 , 3,4).

Conclusion
There is a strong association between smoking rate, hematocrit, hemoglobin and erythrocytes and factor XII hyperactivity in a small cohort of patients with SAMTER syndrome and angioneurotic edema.

OR-10

Study of the antiplatelet efficacy of red yeast rice and tomato juice extract in vitro

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Background
Epidemiological studies have demonstrated the cardiovascular protective role of a healthy diet. In this context, the beneficial effects of fruits may be related to the bioactive compounds found therein. Tomatoes provide a cardioprotective effect at both the endothelial and platelet levels. In the meanwhile, growing evidence supports the use of a range of 'nutraceuticals' (constituents of food prepared as pharmaceutical formulations) including preparations of red yeast rice (RYR), which is used in traditional Chinese medicine. RYR preparations, which are used as oral supplements, have been demonstrated to be safe and effective in reducing atherosclerotic cardiovascular disease. The aim of the present study was to explore the antiplatelet efficacy of RYR (5% monacolin) and tomato juice extract (TJE).

Materials and Methods
Human platelets were isolated by whole blood from apparently healthy donors. RYR (40 μg/mL) and TJE (30 μg/mL) (Epsilon Health, GR) and their combination were studied for inhibition of aggregation of platelets induced by several agonists such as arachidonic acid (AA, 300 μM), ADP (10 μM), and thrombin receptor activating peptide-6 (TRAP-6, 10 μM). Further, we explored the level of the membrane expression of PAC-1 and P-selectin.

Results
Platelets activation with AA: TJE (30 µg/mL) exhibited 41.5 % inhibition with IC50 13.8±1.5 µg/mL. RYR (16 µg/mL) could not cause strong inhibition (less than 20 %). The combination of TJE (30 µg/mL) with RYR (16 µg/mL) exhibited 90.7 % inhibition ($p<0.05$ in comparison with TJE). Moreover, TJE exhibited 93.2±4.5 % and 57.0±18.0 % of P-selectin at concentrations of 30 µg/mL and 5 µg/mL respectively ($p<0.05$ in comparison with activated platelets). PYR did not exhibit inhibition of P-selectin. The combination of TJE (5 µg/mL) and RYR (40 µg/mL) exhibited 77.0±5.3 % inhibition of P-selectin ($p<0.05$ in comparison with activated platelets). Platelets activation with ADP: TJE (30 µg/mL) exhibited 28.6 % inhibition. The inhibition of platelet aggregation did not exceed the value of 50 % in several concentrations of TJE (30-360 µg/mL). PYR (40 µg/mL) could not exhibit inhibition (less than 5.3 %). The combination of TJE (30 µg/mL) and RYR (40 µg/mL) exhibited 45 % inhibition. Also, TJE (30 µg/mL) and PYR (40 µg/mL) could not inhibit the membrane expression of PAC-1 and P-selectin. Platelets activation with TRAP-6: TJE (30 µg/mL) exhibited 60 % inhibition, and in 360 µg/mL exhibited 90 %. The IC50 of TJE was 11.9±1.5 µg/mL. RYR (40 µg/mL) exhibited 27.4 % inhibition. The combination of TJE (30 µg/mL) with RYR (40 µg/mL) exhibited 68.1 % inhibition ($p<0.05$ in comparison with TJE). Moreover, only TJE (30 µg/mL) exhibited 46.1±17.4 % inhibition of PAC-1 and 73.5±9.7 % of P-selectin ($p<0.05$ in comparison with activated platelets). The combination of TJE (30 µg/mL) and RYR (40 µg/mL) exhibited 60.3±4.4 % inhibition of PAC-1 and 34.6±13.1 % of P-selectin ($p<0.05$ in comparison with activated platelets).

Conclusions
The combination of RYR and TJE significantly improves the inhibitory effect towards the activation of platelets mainly with AA and TRAP-6 and less on the activation with ADP. The importance of these findings needs further investigation.

OR-13

Sex-based differences in ST-segment elevation myocardial infarction: A multicentre national registry analysis

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Background
Sex differences in ST-segment elevation myocardial infarction (STEMI) are not fully understood. Female patients appear to have higher mortality.
Purpose: to establish sex-differences in Portuguese STEMI patients.

Material and methods
Retrospective multicentre analysis of STEMI patients included in the Portuguese Registry on Acute Coronary Syndromes (ProACS) between October 2010 and October 2022. Two cohorts were defined according to sex. Baseline characteristics, clinical findings, treatment and mortality were compared. Multivariate analysis was performed to assess predictors of mortality.

Results
A total of 14470 patients were included with a mean age of 64 ± 14 years, of which 26% were female. Female patients were significantly older ($p<0.001$) and with higher prevalence of several cardiovascular risk factors such as: high blood pressure ($p<0.001$), diabetes ($p<0.001$) and dyslipidemia ($p=0.015$), as well as higher reported past medical history, namely ischemic stroke/transient ischemic attack ($p=0.001$), renal disease ($p<0.001$) and dementia ($p<0.001$). On the other hand, previous coronary artery disease was less common comparing to men. Reperfusion therapy was less frequent in females ($p<0.001$), with less cases of multivessel disease ($p=0.004$). Regarding inpatient medical treatment women were less frequently prescribed medical therapy and more frequently needed inotropes ($p<0.001$). Regarding discharge medication, similar tendencies were observed, and women were less frequently referred to cardiac rehabilitation programs ($p<0.001$).
Concerning prognosis, women had more complications while at hospital, namely, congestive heart failure ($p<0.001$), ischemic stroke ($p<0.001$) and intra-hospital mortality ($p<0.001$). Similarly, women had higher thirty-day and one-year mortality ($p<0.001$) and non-cardiac hospital readmission ($p<0.001$). After multivariate analysis, female sex (OR=1.633; CI 95% [1.065-2.504]; $p=0.025$) remained as an independent factor for intra-hospital mortality but not for thirty-day and one-year mortality.

Conclusions
In our population, female patients had statistically significant differences in comparison to men regarding clinical characteristics, treatment and prognosis. Nevertheless, female sex was an independent risk factor only for intra-hospital mortality.

OR-14

Combined Use of NGS and Multiplex Ligation-Probe Amplification for Diagnosis of Congenital Fibrinogen Deficiencies. A rare or underdiagnosed cause of thrombophilia or bleeding events? A Single-Centre Study

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Background/Aim

Congenital fibrinogen deficiencies are rare and involve defects in the production or function of fibrinogen. They can be quantitative, with partial or complete absence of fibrinogen, or qualitative, with normal or reduced levels and/or abnormal functional activity. While hemorrhagic events are associated with quantitative deficiencies (afibrinogenaemia/ hypofibrinogenaemia), dysfibrinogenemias can present with bleeding, thrombosis, or both. Fibrinogen is a hexameric protein consisting of three pairs of polypeptide chains (Aα, Bβ and γ), encoded by FGA, FGB and FGG genes, respectively. Variants in these genes have been associated with fibrinogen deficiency. Our study aimed to identify the molecular defect in patients with fibrinogen anomalies, hemorrhagic diathesis, and/or thrombosis using NGS, and to design MLPA probes for the coding regions of FGA, FGB, and FGG genes to detect deletion carriers.

Material and Methods

From 2017 to 2023, a total of 29 unrelated patients and 18 relatives with suspected congenital fibrinogen deficiencies were included in the study. The molecular diagnosis was carried out using a custom panel for next-generation sequencing (NGS) targeting 43 genes. Library preparation and sequencing were performed according to IonS5 (TFS) protocol. Due to the rarity of this disorder and the lack of commercially available MLPA kits, custom MLPA probes were designed to cover all coding regions of the fibrinogen cluster. The obtained MLPA data were analyzed using Coffalyser.net software.

Results

Of the analyzed patients, 20 different variants were identified, including pathogenic, potentially pathogenic, and uncertain significance variants, in FGA (9), FGB (3), and FGG (8) genes.

Notably, ten of the identified variants were novel, including variants in FGA (p.Gly182Arg, p.Asp211Glu, and p.Gly342Glu), FGB (p.Glu240Lys, p.Asp311Tyr, and p.Tyr368*), and FGG (p.Tyr27Cys, p.Asp63Val, p.Trp360*, and p.Glu422del).
The patients were diagnosed with hypofibrinogenemia (n=5), hypodysfibrinogenemia (n=11), and dysfibrinogenemia (n=2). Two patients were diagnosed with afibrinogenemia, both of whom were homozygous for two variants in FGA (complete deletion and p.Arg181*) and presented with severe hemorrhagic manifestations. Six patients presented with thrombosis, with one carrying the FGA p.Cys64Tyr variant, which has been associated with both thrombosis and bleeding.
MLPA confirmed the total deletion of FGA that was suspected by NGS in one patient and enabled the diagnosis of an FGA deletion carrier in a familial study. In total, 11 patients were asymptomatic.

Conclusions
In this study, we identified 10 new variants in the fibrinogen cluster coding region and observed a high phenotypic variability, consistent with previous reports. A phenotype-genotype correlation was observed in the quantitative deficiencies, while dysfibrinogenaemias remain a challenge. We emphasize that functional fibrinogen deficiencies like dysfibrinogenemia and hypodysfibrinogenemia are rare causes of thrombophilia, and may be overlooked as they often exhibit normal standard coagulation tests and a lack of hemorrhagic events. Therefore, if a thrombotic event is suspected with no classical thrombophilia risk factors, testing for this rare deficiency should be considered. Our study highlights the usefulness of an integrated NGS and MLPA diagnostic strategy as a practical tool in clinical practice, enabling faster and broader diagnosis of fibrinogen hereditary anomalies.

OR-16

Genetic variants in SERPINC1 and sensitivity of activity assays for detection of antithrombin deficiency

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Background
Antithrombin (AT) deficiency, the most severe form of inherited thrombophilia, carries a high risk for venous thromboembolism, therefore, a highly sensitive assay to identify this disorder is essential. Some genetic variants are difficult to detect, and this often depends on the particular AT activity assay. The aim of this study was to compare AT activities measured by different AT activity assays in relation to the genetic background of Slovenian patients with AT deficiency.

Methods
The study included 220 adult patients, who developed idiopathic venous thromboembolism before the age of 50. 129 patients were consecutive and 91 with previously determined AT activity < 80 %. In all patients, AT activity was measured by five different AT activity assays (Innovance, Stago, Biophen IIa, Biophen Xa, HemosIL). Potential genetic variations in any of the seven exons and flanking intron regions of the AT gene SERPINC1 were determined by Sanger sequencing. In patients without such variants, the presence of structural genetic variants was investigated by MLPA.

Results
A genetic variation in SERPINC1 was found in 81 % of cases with AT activity < 70 %. 14 different point variants (9 missense and 5 nonsense variants) and one whole gene deletion were detected. The most prevalent variant was AT Padua I (c.236G>A, p.Arg79His), which was found in almost half of the patients with AT deficiency. Other variants present in our cohort were AT Basel (c.218C>T, p.Pro73Leu), AT Dublin (c.89T>A, p.Val30Glu), AT Budapest III (c.391C>T, p.Leu131Phe), AT Denver (c.1277C>T, p.Ser426Leu). In addition, some nonsense and one missense variant causing type I AT deficiency were found in individual families. A homozygous intronic variant c.41+10G>A causing type I AT deficiency was also detected. All assays showed good sensitivity for type I variants, except for the intronic variant, which was detected only by Innovance. Of the type II variants, only AT Budapest was detected by all assays. AT Dublin variant was the most difficult to detect, as all assays measured normal AT activity. AT Denver (type II variant with reactive site defect (type IIRS)) was detected only by FIIa-based assays (Stago and Biophen IIa). On the other hand, the sensitivity of each FXa- and FIIa-based assay was different for different type II variants affecting the heparin-binding site (type IIHBS). Assays with the highest sensitivity were Stago (92 %) and Innovance (92 %), followed by Biophen IIa (71 %), Biophen Xa (67 %) and HemosIL (50 %).

Conclusion
Type I variants can generally be detected by all AT activity assays, while detection of AT Dublin variant remains challenging. In addition, FIIa-based assays tend to be more sensitive to type IIRS variants compared to FXa-based assays. On the other hand, some FXa- and FIIa-based assays are more sensitive to type IIHBS variants than others, diminishing the role of coagulation factor used in the assay. Because not all variants can be detected by only one activity assay, the introduction of molecular methods or other prospective methods such as mass-spectrometry to detect AT deficiency seems reasonable.

OR-17

Etiology of Cerebral Venous Thrombosis: Retrospective Analysis of a 15-year Period in a Tertiary Hospital

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Background
Cerebral venous thrombosis (CVT) is an uncommon form of stroke and venous thromboembolism (VTE). Its pathogenesis remains unclear but inherited or acquired risk factors can contribute to its development.
The aim of this study is to review our hospital data concerning patients with CVT and its etiology investigation.

Materials and Methods
We retrospectively evaluated patients admitted to a Portuguese tertiary hospital, due to an acute diagnosis of CVT, from 2005 to 2020. Besides age and gender, we evaluated the presence of inherited thrombophilias (antithrombin, protein C and S deficiencies, Leiden factor V or prothrombin gene mutation), acquired risk factors (including oral contraceptive medication, pregnancy, obesity, active cancer, systemic inflammatory disease) and previous VTE events. A p value of 0.05 indicates statistical significance. Analyses were performed with SPSS Statistics software.

Results
Our study included 181 patients - 145 females (80,1%) with mean age 38.16 years (SD 11.80); 36 males with mean age 43.22 years (SD 16.75); p=0.038.
Inherited thrombophilias were identified in 51 patients (28.2%) - prothrombin gene mutation (17; 9.4%) and protein S deficiency (12; 6.6%) were the most common.
At the time of the CVT event, 96 patients (66.2% of female participants) were under oral contraceptive medication, 34 of them (18.8%) had no other identifiable cause for CVT. Other frequently found risk factors include: obesity - 38 patients (21.1%); systemic inflammatory diseases (inflammatory bowel disease or antiphospholipid syndrome) - 35 patients (19.3 %); vasculitis - 20 patients (11%); hematological diseases - 20 patients (11%); active infection - 19 (10.5%); active cancer - 17 (9.4%). At the time of the diagnosis of CVT, 2 patients were pregnant and 2 were in the puerperium (2.76% of females). Among all patients, 18 (9,9%) had a previous history of VTE; none of these patients was under anticoagulant treatment.
In our sample, it was not possible to identify any risk factor for CVT in 20 patients (11.1%)

Conclusions
In our study, CVT was more common among young female patients, with oral contraceptives presenting as an identifiable important risk factor. Pregnancy at the time of the event was not as frequent as demonstrated in previous studies, but all females in childbearing age were advised to reinstate treatment with subcutaneous heparin if ever pregnant.
Along with inherited thrombophilia, oral contraceptive medication and obesity - recognised as major risk factors for CVT -, in our sample, systemic inflammatory diseases also arise as an important subjacent possible cause for thrombosis.
With the emergence of the COVID-19 pandemic in 2020, this infection has been identified as a new CVT trigger - nonetheless, no patients were identified in our sample. From 2021 on, after the studied period, vaccine-induced immune thrombotic thrombocytopenia was also recognized as a possible cause of CVT.
The role of inflammation and other atypical conditions in the development of thrombosis is a subject of interest going forward, as idiopathic thrombosis still has a high frequency in our population.

OR-18

Systolic Blood Pressure and Pulse Pressure are predictors of future cardiovascular events in patients with true resistant hypertension

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Background
Cardiovascular (CV) and cerebrovascular events are mostly caused by arterial hypertension. The most severe outcomes are associated with resistant hypertension (RH), which has an estimated prevalence of approximately 10–18% among patients receiving treatment for arterial hypertension. Due to the heightened risk of CV events associated with RH, accurate cardiovascular prognosis is crucial. According to the European Society of Cardiology, RH is commonly diagnosed based on office BP that should be confirmed by ambulatory blood pressure monitoring (ABPM) or home blood pressure monitoring (HBPM). ABPM is preferred as it eliminates the often-observed white coat effect, thereby providing a more realistic and homogeneous sample. ABPM is mandatory for resistant hypertension diagnosis, but its use for prognosis is limited. This study aimed to identify the most precise predictors of future cardiovascular events when diagnosing RH through ABPM, which is considered to be approximately 41% more accurate than HBPM by some experts.

Material and methods
This observational longitudinal study involved 258 patients, with a mean age of 60.4 ± 11.2 years and 61.2% of them being male. The patients underwent 24-hour ABPM in a hypertension unit between 1999 and 2019. All patients included in the study had a mean systolic blood pressure (SBP) of ≥130 mmHg on 24-hour ABPM, or SBP ≥135 mmHg during the daytime while taking the highest tolerable doses of at least three antihypertensive agents, including a diuretic. Alternatively, they had controlled blood pressure with four or more antihypertensive agents. The primary outcomes of the study were global cardiovascular events, which included cerebrovascular, coronary, and other cardiovascular events. The mean follow-up period for the patients was 6.0 ± 5.0 years.

Results
Sixty-eight cardiovascular events were recorded, of which 63 were non-fatal and 5 were fatal. Patients who experienced these events were generally older and had higher rates of both chronic kidney disease and prior cardiovascular events. The study found that an increment of 1 standard deviation in 24-hour systolic blood pressure, night systolic blood pressure, and 24-hour pulse pressure were independent predictors of global cardiovascular events, with respective hazard ratios (HRs) of 1.44 (95% confidence interval [CI] 1.10-1.88), 1.35 (95% CI 1.01-1.80), and 1.39 (95% CI 1.02-1.89). In addition, patients with a pulse pressure > 60 mm Hg of 24 hours, daytime, and nighttime, analyzed as a categorical variable, had a significant HR related to future cardiovascular events in a multivariate Cox analysis, with respective HRs of 1.95 (95% CI 1.01-3.45), 2.15 (95% CI 1.21-3.83), and 2.07 (95% CI 1.17-3.67). Kaplan Meier survival analysis of 24-hour pulse pressure, daytime, and nighttime > 60 mmHg showed a worse cardiovascular outcome (Log Rank <0.05).

Conclusion
In conclusion, ABPM-based RH diagnosis was deemed crucial and is a fundamental tool not only for the diagnosis of resistant hypertension, but also for predicting future cardiovascular events.

OR-19

Treatment of Cerebral Venous Thrombosis: Retrospective Analysis of a 15-year Period in a Tertiary Hospital

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Background
Cerebral venous thrombosis (CVT) is a rare cerebrovascular disease that, despite its low mortality rate, can result in adverse neurologic outcomes. Occasionally, the obstruction of cerebral sinus caused by CVT can lead to secondary intracranial hemorrhage. Nonetheless, its treatment, which must be started immediately after diagnosis, includes anticoagulant treatment as a fundamental cornerstone.
The aim of this study is to review our hospital's experience in the acute management of CVT events, as in its treatment in the long term.

Materials and Methods
We retrospectively evaluated patients admitted to a Portuguese tertiary hospital, due to an acute diagnosis of CVT, from 2005 to 2020. Besides age and gender, we evaluated the presence of risk factor for CVT, personal history of venous thromboembolism (VTE), treatment with anticoagulants (agent and timing), CVT recanalization, hemorrhagic complications, and VTE recurrence. Analyses were performed with SPSS Statistics software.

Results
Our study included 181 patients (80.1% females) with mean age 39.17 years (SD 13.1).
In our center, 108 patients (59.7%) immediately started treatment with low molecular weight heparin (LMWH), while 56 (30.9%) started with unfractionated heparin (UFH). Hemorrhagic complications associated with initial anticoagulation occurred in 6 patients (3.3%). Craniectomy was performed in 6 patients (3.3%), due to elevated intracranial pressure refractory to medical treatment. Subacute recanalization of the occluded cerebral sinus or vein was achieved partially in 80 patients (44.2%) and fully in 42 patients (23.2%); no data was obtained for 32 participants (17.7%).

After acute treatment with heparin, 153 patients (84.5%) continued anticoagulant treatment with warfarin. Direct oral anticoagulants (DOACs) emerged as a therapeutic agent after 2017 - 18 patients diagnosed subsequently were treated with dabigatran, representing 45% of all patients diagnosed in that period.

In our sample, 69 patients (38.1%) maintained anticoagulant treatment for 9 to 12 months and only 7 patients (3.9%) were anticoagulated for less than 9 months. In 81 patients (44.7%), treatment was prolonged beyond 12 months, among which 58 (32%) have an indication for permanent anticoagulation. Among patients who eventually interrupted anticoagulant treatment, 8 (4.4%) presented subsequent VTE - 3 of those presented recurrent CVT.

In our sample, there was no mortality chargeable to CVT.

Conclusions
In our study, as in the existing literature, LMWH or UFH are the preferred anticoagulant agents for the acute treatment of CVT, as they simultaneously promote recanalization of the CVT and prevent its propagation. Both agents have proven to be safe, even in patients with intracerebral hemorrhage secondary to CVT.
After the acute phase, it is known that anticoagulant treatment allows to prevent CVT and VTE recurrence. Interestingly, in our study, it is possible to observe the paradigm change in long-term anticoagulation after CVT - DOACs (namely dabigatran) only recently presented as agents as efficient as warfarin, with a better safety profile. The optimal duration for this treatment is not well defined - in our sample, most patients maintained treatment for at least 9 months; 32% had an indication for permanent anticoagulation.

OR-20

Sex-based differences in patients with unstable angina – A single-centre retrospective study

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Background
Coronary artery disease (CAD) is a major cause of morbi-mortality globally. There seems to be different pathophysiology and risk factors in CAD among men and women, which result in different clinical phenotypes and symptoms. We aim to study and describe sex-based differences regarding baseline characteristics, clinical and diagnostic features and outcomes in patients with unstable angina (UA).

Material and methods
Single-centre retrospective cohort study of patients admitted with UA and subjected to coronary angiography from January 2015 to April 2022. Data regarding cardiovascular (CV) risk factors, medication, clinical history, echocardiography and coronary angiography was collected. Significant CAD was defined as ≥70% stenosis or positive functional evaluation of a major epicardial coronary artery. 1-year major cardiovascular adverse events (MACE) were defined as all-cause mortality, CV mortality, acute myocardial infarction, stroke, urgent revascularization and stent thrombosis. Statistical analysis was performed with SPSS v28.

Results
This study included 166 patients of which 47 were females (28.3%). Female patients were older (67±11 vs 63±11 years, p=0,017) and less frequently former smokers (4.3% vs 36.1%, p<0,001). Previous history of CAD was less frequent in women (23,4% vs 39,8%,p=0,046) as was the prescription of aspirin (28.3% vs 47.9%, p=0,023). There was no differences in the time "pain to coronary angiography" (less than 72h) (57,4% vs 53,8%,p=0,669); number of vessels affected (1-vessel) (39,1% vs 57,9%,p=0,146); success of revascularization strategy (85% vs 85,7%,p=1,000) and median in-hospital length of stay (2 vs 2 days, p=0,514). Similarly, aetiology was comparable between groups, with significant CAD being the most common finding (40,4% vs 53.8%,p=0,121). Discharge medication was identical between groups with exception of aspirin, more prescribed in male patients (75,9 vs 52,3%, p=0,004). There were no differences in left ventricular ejection fraction between male and female patients (59% vs 60%, p=0,747). Median follow-up was 1518 days and we found no difference in 1-year MACE (4,4% vs 6,2%, p=0,668).

Conclusion
Women presenting with suspected UA were older than men, with similar CV risk factors, except for smoking status. In our cohort we found no difference in clinical characteristics, angiographic findings and outcomes based on biologic sex of patients.

OR-21

Defective Fibrinolysis Driving Hemostatic Challenges

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Background
Hemostasis is a complex physiologic process that maintains circulating blood in a fluid state and enclosed in a proper system.
Fibrinolysis, the final stage of hemostatic activation, is the gradual digestion and removal of the fibrin clot as vascular healing occurs.
Two activators of fibrinolysis, tissue plasminogen activator (TPA) and urokinase plasminogen activator (UPA) convert fibrin-bound plasminogen into the principal enzyme of the fibrinolytic system, plasmin, which hydrolyzes fibrin, restoring blood vessel patency.
Plasminogen activator inhibitor-1 (PAI-1) is the main inhibitor of plasminogen activation, inactivating both TPA and UPA. Alpha2-antiplasmin (α2AP) rapidly binds and inactivates any free plasmin. Thrombin-activatable fibrinolysis inhibitor (TAFI) functions as an antifibrinolytic enzyme.

Material and methods
Report on the current knowledge of genetic and environmental risk factors on fibrinolysis disorders, addressing the need for a holistic approach to provide comprehensive management and prophylactic strategy.

Results
There is a delicate equilibrium between the activators and inhibitors in the fibrinolytic cascade. When these components are out of balance, excessive fibrinolysis can cause uncontrolled bleeding and impaired endogenous fibrinolysis can lead to pathologic clotting.
Strongly contributing to disease morbidity in a widening spectrum of clinical disorders, acquired and inherited dysregulation of the fibrinolytic system is associated with diverse and unpredictable clinical phenotypes ranging from the trauma induced coagulopathy, to rare congenital bleeding disorders, to venous and arterial thrombosis as observed in the antiphospholipid syndrome.
Yet diagnosis of a hyperfibrinolytic hemorrhagic tendency or a hypofibrinolytic thrombotic predisposition is challenged by the lack of currently available and well-established global assays of fibrinolysis, precluding the pursued improvement of patient care and health.

Conclusion
Deeper knowledge of the fibrinolysis intricacy and development of validated laboratory tests are warranted as they are essential to understand findings, predict thrombotic events, diagnose hypercoagulable conditions, and resolutely convey targeted treatment to deleterious imbalances of the fibrinolytic pathway.

OR-22

Red Blood Cell Exchange Therapy in Sickle Cell Anemia: stroke prophylaxis

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Background
Automated red blood cell exchange (RBCX) is a critical therapeutic intervention for managing various complications associated with sickle cell anemia (SCA), including primary and secondary stroke prevention (recommendation 1A, category I, by American Society for Apheresis). RBCX offers several advantages, including rapid reduction of pathological erythrocytes containing hemoglobin S (HbS) without increasing blood viscosity or fluid overload and reduced risk of iron accumulation.
Stroke is a common serious complication of SCA and affects approximately 10% of patients before the age of 20. Without chronic exchange transfusions, stroke may recur in 46-67% of patients within 3 years of the initial event.

Our study aims to share our experience in RBCX as a primary and secondary stroke prevention strategy in patients with SCA.

Material and methods

This retrospective observational cohort study included 9 patients with SCA undergoing chronic RBCX at our hospital center for primary or secondary stroke prophylaxis between January 2017 and April 2023.

Results

A total of 173 RBCX procedures and 9 patients were screened for inclusion in the study: 6 females (67%) and 3 males with an average age of 31 [22-48]. The genotype was mainly homozygous (Hb SS), 8 (89%), and only 1 Hb SM0; there were also 3 (33%) patients with the Moya-Moya pattern and 1 (11%) with the Bantu/Bantu haplotype.

Seven (78%) patients underwent RBCX for secondary stroke prevention, and 2 (22%) for primary stroke prevention due to cerebral-vascular abnormalities detected by MRI. Only 1 patient had a recurrent stroke while on chronic RBCX.

The RBCX procedure is usually executed with a frequency of 4/4 weeks. The patient on chronic RBCX for a longer time has been receiving treatment for 288 weeks, whereas the most recent patient has only been receiving treatment for 16 weeks. Patients following initiating chronic RBCX exhibit an average reduction in Hb S of 23,5% [0,2-43,6].

In total, 1081 packed RBCs were transfused, an average of 6 [5-8] per procedure. None of the patients developed alloantibodies after initiating RBCX.

The findings on iron excess were irregular. On average, ferritin blood levels declined by 608,8 ng/ml; however, 3 patients experienced increases to values above 1000 ng/ml, and 2 patients maintained levels with virtually no change.

Conclusions

Overall, our SCA patients on chronic RBCX have shown a reduction in HbS levels and a low stroke recurrence rate without an iron overload increment. Poor adherence to treatment may explain recurrent strokes when on chronic RBCX, as well as elevated blood ferritin levels.

Although chronic RBCX increases patients' exposure to RBCs and related expenses, there appears to be no increased risk of alloimmunization. On the other hand, there is a negative effect on blood supply. But stroke is a leading cause of disability in SCA, and chronic RBCX remains the gold standard treatment for preventing it.

OR-23

The effect of a Berry extract on the production of Neutrophil Extracellular Traps and on platelet aggregation in vitro

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Background

Polyphenols of various plants and fruits, including berries, have - among others – antioxidant, antiplatelet and anti-inflammatory effects and play an important role in the prevention of various chronic diseases, such as cardiovascular diseases and cancer. The aim of the present study was to investigate the effect of an extract of Morus nigra (Black Mulberries) on the production of neutrophil extracellular traps (NETs) and the aggregation of platelets in vitro.

Materials and Methods

Edible mulberry fruits (Morus nigra, Black mulberries) were collected from areas of Attiki and Epirus, Greece, and extracted with a solvent system [isopropanol:water (IsoPro:W), 60:40 v/v). Neutrophils were isolated from the whole blood of healthy people by a density gradient on Histopaque-Ficoll. Neutrophils (in a density of 1.2x106 cells/mL) were incubated with the berry extract (100 μg/mL) for 10 min (37 0C, 5 % CO2) followed by the activation with phorbol myristate acetate (PMA, 100 nM) for 4 h (activated cells). The berry extract was also tested in untreated neutrophils. Netosis was measured by ELISA (Cell Death Detection ELISA PLUS, Roche) using myeloperoxidase antibody (anti-MPO, Hycult Biotech Inc). Also, platelet-rich plasma (PRP) was prepared from the whole blood of apparently healthy people. Platelets were pre-incubated at 37 °C for 10 min with the berry extract in several concentrations. Light transmittance aggregometry was performed in PRP in the presence of the agonists arachidonic acid (AA, 300 μM), ADP (10 μM), and thrombin receptor activating peptide-6 (TRAP-6, 10 μM), an agonist of the PAR-1 receptor.

Results

The berry extract inhibited netosis at 76.7±3.6 % in activated neutrophils in comparison with untreated cells. By contrast, this extract did not affect AA, ADP-, or TRAP-6 -induced platelet aggregation (less than 20%).

Conclusions: The Berry extract significantly potentially inhibited netosis but did not affect platelet aggregation induced by AA-, ADP- or TRAP-6- platelet aggregation. The composition of active ingredients as well as the underlying mechanisms of inhibitory activity of the berry components on the production of NETs are under investigation.

Acknowledgments
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OR-24

Effect of long-term storage and freeze-thawing cycles on urinary thromboxane A2 metabolite and isoprostanes

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Introduction
Biological samples are often stored for several years in biobanks before assessing specific biomarkers. Therefore, assessing their stability and reproducibility over long-term storage is of great importance to ensure reliable data and valid interpretation. Thromboxane AMis enzymatically generated in vivo largely from arachidonic acid released by activated platelets. The major metabolite of TXAMis the 11-dehydro-TXBM(TXM) which is stable and excreted in the urine. Furthermore, AA can also be non-enzymatically oxidated into FMisoprostanes with the 8-iso-prosaglandin (PG)FMMas the most abundant isoprostane measurable in human's urine. Both metabolites have been shown in large prospective cohorts to reflect the degree of in vivo platelet activation and lipid peroxidation, respectively. In particular the TXM, is able to predict major vascular events and death in large perspective studies and trial's subgroups.

Aims
This study investigated the long-term stability the TXM, 8-iso-PGFMMand creatinine as control molecule, in human urine samples stored at -40°C over years. We also evaluated the effect of freezing and thawing cycles on the same metabolites.

Methods
One-ml urine samples were extracted, assayed for TXM and 8-iso-PGFMM and creatinine for the first time according to the original protocol and study, stored at -40°C and then thawed and measured again in a time interval spanning from 2 and 10 years from the first measurement. Samples were from healthy individuals (n=57), patients with diabetes mellitus (n=45), myeloproliferative neoplasms (n=249) and solid cancers (n=331).

To evaluate the effects of freezing and thawing, urine samples were sequentially frozen and thawed for 10 times. Some samples were added with the antioxidant (4-hydroxy-TEMPO 10mM) immediately after collection and then underwent freezing and thawing sequences. After 2,4,6,8 and 10 cycles we measured TXM, 8-iso-PGF2M, creatinine and peroxides.

Results
TXM (n=676), 8-iso-PGF2M (n=117) and creatinine (n=638) levels were expressed as % of the first measurement, and their concentrations were reproducible in urine stored up to 10 years and highly correlated (TXM: rho=0.99, P<0.0001; 8-iso-PGFMM: rho=0.98, P<0.0001;creatinine: rho=0.99, P<0.0001).
Over 10 cycles of freezing and thawing cycles the values of TXM and creatinine were highly reproducible (TXM: 95-8±14; creatinine: 100.7±5.7% of the measurement at baseline, n=10), while 8-iso-PGFMM concentrations showed a significant increase starting from the fifth cycle of thawing (rho=0.98, P<0.001, n=10). When 4-hydroxy-TEMPO, was added, 8-iso-PGFMM levels remained stable (103.1±3.3% of the baseline at cycle 10, n=5). We also measured a significant increase in oxidation species after the 4th freezing and thawing cycle (fold increase 24.4±15 vs. baseline, n=3).

Conclusion
TXM, 8-iso-PGFMM and creatinine appear stable in urine samples stored at -40° for up to 10 years. TXM and creatinine appear stable even after multiple freeze-thawing cycles while 8-iso-PGFMM levels increase after 5 cycles of thawing likely due to increase in reactive oxygen species generated in the urine samples. These data are relevant when measuring biomarkers in samples stored in biobanks over long time, or when the same samples undergo multiple cycles of freezing and thawing, which apparently trigger the generation of reactive oxygen species in the urine.

OR-25

Reducing variability in light transmission aggregometry: The role of internal quality control and laboratory outcomes

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Background
Light transmission aggregometry (LTA) it's the gold standard for platelet function testing. Our workflow comprises essentially patients with bleeding disorders or taking antiplatelet agents as well as liver transplant protocol and other surgery context.
We implemented this method in March 2018 and overpassed 1000 analysed samples in five years. Standardisation of LTA improved in the last decade. Our trained staff is committed to internal quality control (IQC) for reducing the heterogeneity in performance.

Materials and Methods

We checked platelet rich plasma (PRP) pools prepared from citrated whole blood samples, collected within 4-6 hours, in SD Innovation TA-4V (Stago). The repeatability tests (consecutive determinations) included adenosine diphosphate (ADP), thrombin receptor-activating peptide-6 (TRAP), epinephrine (EPI), arachidonic acid (ARA), collagen (COLL) and ristocetin (RISTO) at different concentrations. Our primary endpoint it's to achieve a coefficient of variation (CV) less or equal to 10%. Repeated measurements express the variability degree. Besides that, we achieved geometric mean of maximum aggregation (MA) results for RISTO low (secondary endpoint). We carried out 84 IQC exercises corresponding to 284 tests (Excel computational procedure for observational data) and associated them with preventive maintenance (PM) versus corrective maintenance (CM).

Results

Precision (CV) and Accuracy (Mean) in LTA – Total of Exercises / Tests
Agonists and Concentrations:
ADP 2 µM
ADP 10 µM
TRAP 10 µM
TRAP 50 µM
EPI 5 µM
EPI 25 µM
ARA 1 mM
COLL 2 µg/mL
COLL 10 µg/mL
RISTO 1.5 mg/mL
PM - CV ≤10%: 67 / 224; CV >10%: 9 / 34
CM - CV >20%: 4 / 16
RISTO 0.5 mg/mL - PM: 4 / 10 (Mean: 6.08)
PRP - PLT: 102-230x10^9/L

Conclusions

Almost all the time, scheduled PM was suitable, however, we point out one situation that required CM by the manufacturer prior to keep up the routine.
After cleaning the channels (when CV >10%) and CM, we performed always IQC exercises (allocated in PM – CV ≤10%) to start again.
Cleaning and following control by the manufacturer overtook procedures fulfilled in-house.
We tailor IQC exercises for troubleshooting equipment and whenever batch switches, unexpected results occurs, storage of reagents, specimen transport or handling are uncertain.
Indeed, repeatability remains a pivotal concept in unchanged conditions – same instrument and operator, and repeating during a short time.
All values of RISTO 0.5mg/mL were within the normal range (MA <10%).
We would like to optimise PLT count in PRP to 150-250x10^9/L.

Precision is important to reduce variability and mistakes. Accuracy is essential to avoid systematic errors. Identification of the root of the problems for recurrence prevention of nonconforming events and management of revisions in work instructions ensures better practices and reliable results.

OR-26

"In utero" thromboembolic events and diagnosis of factor V Leiden

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Background
Thromboembolic events in the pediatric age are more common in neonates. Although environmental and genetic risk factors interact in these cases, it has been described the role of factor V Leiden mutation in the development of arterial and venous thrombotic events in neonates and children. We present a case of an extensive "in utero" thrombosis with left renal vein thrombosis and cicatricial nephropathy diagnosed with Factor V Leiden.

Material and methods: We report a clinical case of a 4-year-old male patient referred to our consultation for thrombophilia testing. The child had a history of occlusive thrombosis of the inferior vena cava, hepatic vein, common iliac vein, and left renal vein "in utero" diagnosed shortly after birth. Consequently, he had a cicatricial nephropathy and decreased left renal function (~9%). He was born in a foreign hospital, so the only medical information that could be accessed was a report that the mother was carrying. The delivery occurred by an emergency cesarean section due to non-reassuring fetal status and the child was born with right hemiparesis. The mother mentioned that he had been treated with low molecular weight heparin (LMWH) for 4 months, but she was unable to specify whether any studies had been carried out. Recently, the pediatrician had required a brain MRI because of the hemiparesis and the exam showed a sequelae lesion on the left brain, possibly of ischemic origin. When enquired, the mother denied any pregnancy complications or family history of thrombotic events.

Results
As this child had extensive venous thrombosis and a suspicion of an arterial thrombotic event, a study of inherited and acquired thrombophilic defects was performed. The results were as follows: antithrombin III and protein C activity and protein S level were normal; lupus anticoagulant and anticardiolipin/anti-M2 glycoprotein antibodies were negative; prothrombin 20210 mutation was negative, but a heterozygous factor V Leiden (FVL) mutation was detected.

Conclusions
The risk of recurrent venous thromboembolism (VTE) is 1.4-fold higher in factor V Leiden heterozygotes compared to patients without FVL. Therefore, a multidisciplinary discussion should be held to decide whether the child would benefit from starting indefinite anticoagulation. The thrombosis site, the number of events and other risk factors must be considered for an individualized decision.

OR-27

Effect of EPA, DOACs and their combination on platelet activation

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Background
Omega-3 fatty acids exhibit pleiotropic effects, through numerous molecular mechanisms, including antiplatelet activity. Eicosapentaenoic acid (EPA) is commonly prescribed in patients with hypertriglyceridemia, often alongside Direct Oral Anticoagulants (DOACs), such as the FXa inhibitor, Rivaroxaban and the thrombin inhibitor, Dabigatran. The aim of the present study was to investigate the effect of EPA, Rivaroxaban, Dabigatran (the active metabolite), as well as the possible synergistic effect of EPA/DOAC combinations on platelet activation, induced by the PAR-1 receptor agonist, TRAP-6.

Materials and Methods
Platelet Rich Plasma (PRP) was prepared from citrated blood of healthy volunteers and adjusted to 250.000 platelets/μl. PRP was pre-incubated at 37°C for 10min with EPA, Rivaroxaban, Dabigatran, or the EPA/DOAC combinations in various concentrations prior to aggregation with TRAP-6 (10μM). The inhibitory activity was determined by Light Transmittance Aggregometry. The appropriate concentrations of EPA or each DOAC to achieve an inhibitory activity of 15-25% were used in experiments where the EPA/DOAC combinations were studied.

Results
EPA inhibits platelet activation in a dose dependent manner (IC50=964,13μM). Rivaroxaban exhibits maximal inhibition at 10μM (24.4±7.3%) and Dabigatran at 40μM (17.2±3.6%) The combination of 250μM EPA (23.9±4.9% inhibition) with 4μM Rivaroxaban (20.1±5.3% inhibition) inhibited platelet aggregation by 80.99±15.2%. Accordingly, the combination of 250μM EPA with 40μM Dabigatran resulted in 17.5±6.7% inhibition of platelet activation.

Conclusion
The combination of EPA and Rivaroxaban exhibited a synergistic antiplatelet activity towards TRAP-6 induced platelet activation. In contrast, the inhibitory effect of the combination of EPA with Dabigatran was not differentiated from that observed in the presence of each individual compound. These results may be clinically important in patients receiving both EPA and a DOAC.

Acknowledgements
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OR-28

Platelets Dysfunction as a Potential Marker of Severity in Pulmonary Embolism Patients

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Background
Platelets are essential components of the coagulation cascade, with physiopathologic impact on the development of innumerous thromboembolic diseases, such as pulmonary embolism (PE).
The platelet index - 'Platelet Distribution Width' (PDW) – measures platelets' size variation or anisocytosis. Studies have shown an association between an augmented PDW value and platelet activation, but despite of their routine measurement, their use as a gravity indicator for PE is reduced.

Material and Methods
Single center cross-sectional study comprising 141 patients admitted to the emergency department due to PE with an echocardiographic evaluation at diagnosis time. Statistical analysis of data was performed using Independent-Samples T Test.

Results
The total population (n=141) was subdivided in two groups – with - 51,1% - and without right ventricle dilation – 48,9%. There weren´t significant differences between the two groups on gender (p=.108), history of previous PE (p=.542), Chronic Obstructive Pulmonary Disease (p=.091) and intra-hospital death (p=.056).
On comparison, the patients in the subgroup with right ventricle dilation were older (70,1 vs 63,9 years, p<.05), had a higher percentage of positive I-troponin (86,8 vs 38,5%; p<.05) and BNP at admission (81,6 vs 47,4%; p<.05) and were submitted more frequently to fibrinolytic therapy (22,5 vs 1,4%, p<.05).

Patients with right ventricle dilation had a higher PDW value (16,2% vs 15.2%; p=.026) and lower total platelet count (200,7 vs 226,1 X 10E9/L; p=.043).

Conclusion
The study suggests that patients with right ventricle dilation have a higher PDW value and lower total platelet count when in comparison with patients without right ventricle dilation. These findings suggest a possible association between platelet indices and imagiologic gravity indicators on PE.

OR-29

Thrombophilia assessment during arterial thrombosis

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Background
Thrombophilia represents a hypercoagulable state which increases the risk of venous thrombosis and would also be associated with arterial thrombosis. Although discussed, screening for thrombophilia abnormalities is carried out during these pathologies with variable results.
The objective of this study is to analyze the results of the thrombophilia assessment carried out in patients with arterial thrombosis.

Material and methods
This is a monocentric and retrospective study that included patients with arterial thrombosis who were referred to the laboratory for hereditary thrombophilia assessment and search for antiphospholipid antibodies between 2014 and 2022. The assessment included the search for Lupus anticoagulant (LA) by means of 2 tests: Time of Activated Cephalin and Diluted Russel Viper Venom Time, the search for anticardiolipin (aCL) and anti-M2-glycoprotein I (aM2GPI) antibodies of the IgG type by ELISA method, an assay for protein S (PS) and C (PC), antithrombin (AT) as well as the search for resistance to activated protein C (RPCA) by functional methods.

Results
A total of 67 patients (33 women and 34 men) were included. The average age of the patients was 39 years old. Ischemic Stroke (IS) was the main indication (77.6%), followed by arterial thrombosis of variable location (13.4%) then Myocardial Infarction (MI) (8.9%). Thrombophilia assessment was positive in 23.8% of patients. We found a PS deficiency in 13.1% of cases

(7 IS and 1 MI), an AT deficiency in 5% of cases (1 IS, 1 renal artery thrombosis, 1 central retinal artery thrombosis) and RPCA in 5.4% of patients (3 IS). LA was detected in 2 patients among the 67 (2.9%) including one with IS. No cases of protein C deficiency were noted and the search for aCL and aB2GP1 was negative in the cases tested.

Conclusions
We report a high frequency of protein S deficiency and AT deficiency and a low frequency of anti-phospholipid antibodies during arterial thrombosis. These results are similar to those reported in certain studies; however, they must be interpreted with caution considering the small number of participants.

OR-30

Gender-based disparities in clinical and procedural outcomes after rotational atherectomy

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Introduction
The presence of extensive calcification in coronary arteries is a hallmark of patients undergoing percutaneous coronary interventions (PCI) with rotational atherectomy (RA), and the prognosis of such patients may vary based on their sex.

Aim
This study aimed to assess whether there are differences in the occurrence of adverse clinical events and long-term outcomes after rotational atherectomy (RA) between males and females.

Methods
We retrospectively enrolled all consecutive adult patients who underwent RA at our single center between 2012 and 2022. Clinical features and in-hospital outcomes were compared between sexes. major adverse clinical events (MACE-9 was defined as the composite of total death, myocardial infarction, coronary revascularization, stroke, and hospitalization because of heart failure.

Results
For a total of 97 samples, the number of men (68;66.7%) is much larger than the women (29; 28.4%). Women were older, 76.31 years versus 72.83 years for men (t = 1.71; 95% CI: -0.561:7.515; p<0.091)
The highest mortality rate happens at the age-group 80-89 years, being observed a total of 28 deaths in the follow up (7 women, 21 men) in the whole sample, being the differences

between genders not statistically significant (Mann-Withney=804.5; p=0.518)
For a total of 44 positives, both genders, the differences for Diabetes Mellitus 2 are again not statistically significant (MW=30; p=0.609). Regarding hypertension, the majority of patients (87%) are hypertensive, but once again, no significant among genders (MW=894.5; p=0.222) However there are significant differences (MW=691.5; p=0.003) in smoking, where men (36%) largely exceed women (7%).

Conclusion
The study concluded that women may be more vulnerable to in-hospital complications following RA ICP procedures.

Poster presentations

P-01

Clinical benefit of right coronary artery chronic total occlusion PCI

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Background
Coronary chronic total occlusions (CTO) are relatively common findings in the context of coronary angiography. The indication for revascularization of this type of lesions remains controversial. Right coronary artery (RCA) is often affected in this context, and the clinical benefit of treatment through percutaneous coronary intervention (PCI) is not consensual. Our aim was to analyze if RCA CTO patients will benefit in terms of clinical outcomes (recurrence of angina and/or heart failure (HF) symptoms) and hard outcomes (myocardial infarction and/or death) when compared to left coronary artery (LCA) CTO patients.

Material and methods
Retrospective study between 2019/2020, with a mean follow-up of 2 years, composed of n=177 patients undergoing CTO-PCI. Created two groups (RCA CTO group and LCA CTO group). Categorical variables are presented as frequencies and percentages, and continuous variables as means and standard deviations, or medians and interquartile ranges for variables with skewed distribution or a significant Shapiro-Wilk test. Multivariate analysis was performed using logistic regression. P value < 0.05 indicates statistical significance.

Results
A total of 177 patients were identified, with a mean age of 65±11 years, 82.5% male. 75% showed hypertension, 40% with diabetes, 73% with dyslipidemia, 18% with obesity and HF in 15%. RCA CTO group were younger with a mean age of 63,6±10,3 (p=0.047), more use of contralateral access (p<0.001), better creatinine clearance 80.8±24.9 (p=0.038) and a poor left ventricular function (LVEF) at baseline 45.4±10.8, but without statistical significancy (p=0.066). Both groups improved LVEF after intervention (p<0.001). Symptoms recurrence occurred in 15% of patients after 2 years. Total symptoms recurrence was significant higher in RCA CTO group (24% vs 9%, p=0.018), mainly derived by HF symptoms (15% vs 4%, p=0.013), with RCA CTO vessel being an independent predictor for HF symptoms recurrence after PCI, when compared to LCA CTO vessel (p=0.015, OR 4.92, 95% CI 1.37 to 17.7). Myocardial infarction and death were low after 2 years, without difference between groups.

Conclusion
Revascularization of CTO lesions by PCI was associated with low rates of symptoms recurrence,
and clinical outcomes showed no differences regardless of the CTO artery treated. RCA-CTO showed less benefit in reducing the recurrence of HF symptoms.

P-02

Possibility of mini-invasive sampling method in determination of direct oral anticoagulants – A pilot study

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Background
Direct oral anticoagulants are widely used in many indications to prevent various thromboembolic events. This group of anticoagulants has a rapid onset and offset of action, fewer drug and food interactions, a wider therapeutic window, and a more predictable pharmacological effect than vitamin K antagonists. As we can observe a growing number of patients taking of them, monitoring plasma levels might be beneficial and even mandatory in some circumstances. Minimally invasive methods of peripheral blood collection are an alternative to conventional blood sampling by venepuncture. In addition, optimised collection devices are coming to the fore, allowing minimally invasive sampling even in the home environment. The main aim of this pilot study is to show the possibilities of the so-called volumetric absorptive microsampling (VAMS) technique in the monitoring of direct oral anticoagulants, which allows fast, accurate and hematocrit-independent sampling of a peripheral blood sample.

Material and methods
Mitra sticks (the VAMS-based collecting device) have been implemented for peripheral blood collection. Extraction conditions and a sample preparation method were optimised to determine apixaban, dabigatran, edoxaban and rivaroxaban in peripheral blood. The extracts were analysed using our in-house validated liquid chromatography-tandem mass spectrometry method (LC-MS/MS). Measured blood levels were compared against the same patients' plasma levels to determine the blood/plasma ratios.

Results
During the optimisation of extraction conditions, the best responses for all analytes have been reached using 200 µL of 1% formic acid in methanol. The extracts were evaporated, resuspended in 120 µL of water and analysed by LC-MS/MS method. Six patients were enrolled in our study to check the trough level (immediately before drug administration) and the peak level (2 hours after drug administration). All drugs' blood/plasma concentration ratios ranged from 0.5 to 0.8. The measured trough blood levels were 58 ng/mL for apixaban (n=1), 15 ng/mL for dabigatran (n=1), 36 and 35 ng/mL for edoxaban (n=2), and 10 and 30

ng/mL for rivaroxaban (n=2). The peak blood levels were 111 ng/mL for apixaban (n=1), 31 ng/mL for dabigatran (n=1), 353 and 169 ng/mL for edoxaban (n=2), and 95 and 284 ng/mL for rivaroxaban (n=2). After recalculation by blood/plasma concentration ratios, all measured values are in recommended therapeutic ranges published by International Council for Standardization in Haematology.

Conclusion

In this pilot study, we evaluated the minimally invasive collection method of blood samples for monitoring direct oral anticoagulant therapy. Introducing the VAMS technique might help increase the patient's adherence to the treatment, as it allows home sampling without the assistance of trained personnel. In addition, dried collection sticks might be delivered for analysis, packed in envelopes, and sent via standard postal services. Thus, we believe that volumetric absorptive microsampling using a commercially available device (Mitra stick) is a promising tool for routine therapeutic monitoring of direct oral anticoagulant therapy.

P-03

Mass spectrometry-based method for routine monitoring of direct oral anticoagulants

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Background

Direct oral anticoagulants (DOACs) are used for stroke prevention in patients with non-valvular atrial fibrillation, for the treatment and secondary prevention of venous thromboembolic disease and as thromboprophylaxis after hip or knee replacement surgery. In the indications mentioned above, they replace the vitamin K antagonist – warfarin. Compared with warfarin, one of the advantages of these drugs is no need for laboratory testing to monitor coagulation and dose adjustment. However, therapy monitoring can be helpful in some situations, such as before surgical procedures and during adverse effects (thrombosis/haemorrhage). For these purposes, we developed a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method to simultaneously quantify apixaban, dabigatran, edoxaban and rivaroxaban in human plasma.

Material and methods
Human plasma sample pre-treatment was done by a one-step extraction procedure using Ostro 96-well plate. Analytes were separated by gradient elution over 4.2 min and consequently detected on a triple quadrupole tandem mass spectrometer using positive electrospray ionization. The developed method was validated according to the European Medicine Agency guideline for validating bioanalytical methods.

Results
Initially, we optimized the detector parameters to reach the best response and selectivity for each analyte. The chromatographic separation conditions were tested during the next step to achieve optimal separation and symmetrical peak shapes. Retention times were 1.01 min for dabigatran, 1.55 min for edoxaban, 2.03 min for apixaban and 2.07 min for rivaroxaban. All analytes had a quantification concentration range of 3.0 to 1000 ng/ml. The method was validated according to EMA guideline on bioanalytical method validation for selectivity, carry-over, linearity of calibration curves, a lower limit of quantification, precision and accuracy, extraction recovery, dilution integrity, matrix effects and stability under different conditions (short-term stability, long term stability – two months at -20°C, freeze and thaw stability and post-processing stability). Finally, the developed and fully validated method was applied to determine the DOACs plasma levels in real clinical samples from patients treated with one of the drugs. The samples were taken just before the drug administration (trough level) and two hours after drug administration (peak level), so the differences in the pharmacokinetics of patients could be seen. The measured trough plasma levels ranged from 86 to 287 ng/mL for apixaban (n=14), 36 to 164 ng/mL for dabigatran (n=8), 31 to 43 ng/ml for edoxaban (n=3) and 12 to 111 ng/mL for rivaroxaban (n=10). The peak concentrations ranged from 196 to 633 ng/mL for apixaban (n=14), 79 to 214 ng/mL for dabigatran (n=8), 190 to 375 ng/ml for edoxaban (n=3) and 139 to 419 ng/mL for rivaroxaban (n=10). Considering the published recommended therapeutic reference ranges, we can conclude that the vast majority of our results are in recommended ranges.

Conclusion
We developed and validated a sensitive and high throughput LC-MS/MS method for simultaneously quantifying four DOACs. This method has several advantages, including low sample volume, short run time and simple and fast sample pre-treatment, making it suitable for implementation in the routine management of patients treated with these drugs.

P-04

Predictors of major adverse cardiovascular events in patients with unstable angina in the high-sensitivity troponin era - Single-centre retrospective study

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Introduction
Since the introduction of high-sensitivity troponin assays, unstable angina (UA) became a less diagnosed type of acute coronary syndrome. There are few common biomarkers with the potential to predict the development of adverse outcomes in patients with UA. Finding better biomarkers, especially simpler and readily available, may help improving cardiovascular (CV) long-term outcomes. We aim to test different biomarkers (creatinine, troponin and N-terminal pro B-type natriuretic peptide (NTproBNP)) and assess their sensitivity and specificity to determine major adverse cardiovascular events (MACE) in patients admitted with UA in the high-sensitivity troponin era.

Methods
Single-centre retrospective cohort study of patients admitted with UA and subjected to coronary angiography from January 2015 to April 2022. Two cohorts were defined according to troponin assays available – high-sensitivity cardiac troponin I (hs-cTn) vs. conventional cardiac troponin. Data regarding CV risk factors, medication, clinical history, echocardiography and coronary angiography was collected. Significant coronary artery disease (CAD) was defined as ≥70% stenosis or positive functional evaluation of a major epicardial coronary artery. MACE were defined as all-cause mortality, CV mortality, acute myocardial infarction, stroke, urgent revascularization and stent thrombosis. Statistical analysis was performed with SPSS v28.

Results
This study included 166 patients of which 119 males (72%) with mean age 64 years old. Past medical history was remarkable for typical CV risk factors, namely excess weight (80%), dyslipidemia (77%) and history of smoking (43%), and 35% had previous history of CAD. After coronary angiography, 50% of patients were found to have significant CAD. 14% suffered MACE (median follow up of 4years). No differences were found between the two cohorts, except for dyslipidemia, which was more frequent in the hs-cTn group (85% vs 70%, p=0,029). After introduction of hs-cTn in October 2018, 72 patients were admitted with UA, of which 10% had MACE in the long term follow up (median 1,8years). After receiver operator characteristic (ROC) curve analysis, NT-proBNP was the only biomarker with acceptable

performance to discriminate MACE. The optimal cut-off level of 189pg/ml predicted long-term MACE with a sensitivity of 80% and a specificity of 74% [ROC area under the curve (AUC) 0,750, 95% CI: 0,531-0,969]. On the other hand, troponin assays (initial value, maximum value and troponin variation), with AUC of 0,432, 0,541 and 0,553, respectively, and creatinine, with AUC of 0,626 had poor discriminatory power.

Conclusion
UA patients have a low risk of MACE. NT-proBNP may be a useful variable to select those who are at higher risk of MACE and thus help clinitians to intensify drug therapy and advocate lifestyle changes in this selected population.

P-05

Microparticle procoagulant activity in major β-thalassemia patients

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Background
Mthalassemia has been associated with a hypercoagulability state and a high risk of thromboembolic complications. The mechanisms of thrombotic events are still unclear and would be related to a higher expression of microparticles (MP). We aimed to study microparticles procoagulant activity in major Mthalassemia patients using thrombin generation assay (TGa).

Material and methods
12 adults major Mthalassemia patients and 12 age and gender matched normal controls were enrolled in the study. Blood samples were collected from patients before transfusion. Platelet-free Plasma was obtained after three successive centrifugations at room temperature (two centrifugations at 1500 g for 15 min and the third one at 13000 g for 2 min). Samples were aliquoted and stored at -80°C until use. TGa was performed according to CAT method using MP reagent(Stago, France). the studied parameters were: Lag Time(Lag T), thrombin peak, time to peak (tt peak), Velocity index (Vi) and the endogenous thrombin potential (ETP)

Results
The mean age of major Mthalassemia patients was 26 years [18 – 36]. The sex ratio was 1.58. All patients were splenectomised and regularly transfused. Both thrombin peak and ETP were significantly decreased in patients compared to controls (thrombin peak = 202,28 vs 281,12 ; p = 0,006, ETP = 817,7 vs 1197,37 ; p = 0,001). However, no significant difference was found in Lag Time, Vi and ttpeak between patients and controls (Lag T = 7,83 vs 8,3 ; p = 0,5, Vi = 86,91vs 141,18 ; p = 0,12, ttpeak = 10,33 vs 10,91 ; p = 0,63).

Conclusion
Using TGa, microparticle procoagulant activity in adult major Mthalassemia regularly transfused patients was not increased in comparison with healthy individuals.

P-06

Thrombin generation assay using frozen-thawed PRP in major β-thalassemia patients

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Background
Unlike standard tests, Thrombin generation assay (TGA) is a functional test allowing a more global exploration of the haemostatic process. TGA is usually ran on Platelet poor plasma as it is the most standardized and documented assay. Other types of matrixes can be used, such as whole blood, Platelet rich plasma and frozen-thawed Platelet-Rich Plasma (ft-PRP). Nevertheless, the contribution of frozen thawed PRP-Thrombin generation assay (ft-PRP TGA) to the identification of thromembolic risk in certain diseases such as thalassaemia remains unclear. We aimed to study the hypercoagulability state in major Mthalassemia patients using ft-PRP TGA.

Material and methods
The study population included 13 adults major Mthalassemia patients and 11 age and gender matched healthy volunteers. Patient samples were taken prior to transfusion. Blood samples were centrifuged at 200 g for 8 min to obtain Platelet-rich Plasma then were aliquoted and stored at -80°C until use. TGA was performed according to CAT method using PRP reagent (Stago, France). the studied parameters were : Lag Time (Lag T), thrombin peak, time to peak (tt peak), Velocity index (Vi) and the endogenous thrombin potential (ETP)

Results
The mean age of major Mthalassemia patients was 26 years [18 – 36]. The sex ratio was 1.62. All patients were splenectomised and regularly transfused. The comparison between thrombin potentials obtained in patients and controls was assessed by means of the Mann–Whitney U test and was equal to : Lag Time (Lag T = 2,5 vs 2,17 ; p = 0,3), thrombin peak (peak = 205,7 vs 238 ; p = 0,4), time to peak (ttpeak = 4,33 vs 4 ; p= 0,4), Velocity index (Vi = 109,9 vs 118 ; p = 0,6) and the endogenous thrombin potential (ETP = 758,4 vs 831,4 ; p = 0,6)

Conclusion
Using frozen thawed PRP-Thrombin generation assay no significant difference was found between major Mthalassemia patients and controls.

P-09

Diagnostic role of high-sensitive cardiac troponin: Is it a good rule-out test for unstable angina? – A single centre analysis

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Background
Unstable angina (UA) is defined as myocardial ischemia at minimal exertion or at rest without myocardial injury. According to current guidelines, fewer UA have been diagnosed after introduction of high-sensitivity (hs) cardiac troponin (cTn) assays. Furthermore, these patients have a low risk of cardiovascular events and the optimal approach regarding selecting patients that benefit from non-elective invasive testing is not well established.
The purpose of this analysis was to determine the usefulness of hs cTn in discriminating coronary artery disease (CAD) in UA.

Material and methods
Retrospective single-centre subanalysis of 166 UA patients admitted for invasive stratification from 2015 to 2022. Two cohorts were defined according to the cTn assay used (hs-TnI vs conventional TnI) and its baseline characteristics, coronary angiography findings and associated extended major adverse cardiovascular events (MACE) compared. Receiver-operating characteristic (ROC) analysis was used to determine diagnostic accuracy of several variables.

Results
Overall, mean age was 64 ±11 years, 72% were male, significant CAD was diagnosed in 50%, the incidence of MACE was 14% and no differences between groups were found, except for dyslipidemia (p=0.029). Seventy-two UA cases (43%) were diagnosed using hs-cTn assay. After ROC analysis of this group, the diagnostic accuracy of hs-cTn for the presence of significant CAD was higher for maximum levels of hs-cTn - with adequate discriminatory power (area under the curve [AUC] 0.778; 95% CI: 0.671-0.884) - although being lower for initial values or absolute change in troponin levels (AUC 0.626 and 0.751, respectively). The cutoff value of 13.35 ng/dL for maximum levels of hs-cTn predicted CAD with a sensitivity of 80% and a specificity of 62%. Other variables, such as NT-proBNP or creatinine had low discriminatory power (AUC 0.552 and 0.582, respectively).

Conclusions
In our population of UA patients, clinical characteristics, CAD and MACE did not differ significantly regardless of the use of hs or non hs-cTn assays. Although maximum hs-cTn had an adequate discriminatory power for CAD, this was not the case for other variables. Therefore, other variables should be considered in addition to initial hs-cTn to better select those that may benefit from non-elective invasive stratification.

P-10

Establishment of a coagulation-focused outpatient clinic: An Internal Medicine and Transfusional Medicine cooperation

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The management of coagulation disorders is becoming more complex and demanding due to recent advancements in diagnosis and treatment. This development led to a need for specialized outpatient clinics focused on the diagnosis and management of these patients. We present the drive that lead to the creation of such a clinic in our hospital, its purposes and the experience from the first 3 years of practice.

Our regional hospital serves a population of 600.000 patients and lacks Hematology specialty. In 2019, one department of internal medicine and the department of transfusional medicine decided to cooperate and create an outpatient clinic focused on coagulation disorders, covering both thrombotic and bleeding diseases. Examples of referral motives were: thromboembolic event at young age; difficult anticoagulation decision/management, platelet count/function abnormalities, coagulation times abnormalities. The clinical body consists of 1 internal medicine doctor and 2 transfusional medicine doctors. The team meets every 2 weeks to discuss new referrals and discuss and decide on the most complex cases. The clinic is open to referrals from within the institution and also primary care.

In the first 3 years, 205 patients were followed-up at the clinic, amounting to 674 visits. Sixty percent of patients were female, with a mean age of 55.3±18,3 years-old [16-92]. Thrombotic disease (or its suspicion) is responsible for 71.7% of referrals (n=147). The majority of these patients had a venous thromboembolism (n=118), followed by arterial thrombosis (n=14), obstetric morbidity (n= 7), thrombocytosis (n=4) and suspected thrombophilia (n=4). In regards to thromboembolic events, 68.6% (n=81) were considered unprovoked and 76.5% (n=62) of these patients were studied for thrombophilia, with 41,9% (n=26) being diagnosed with a thrombophilia. This means that 22% of patients followed-up at the clinic after a throm-

boembolic event were diagnosed with thrombofilia (antiphospholipid syndrome, n=10; antithrombin deficiency, n=6; Leiden Factor V mutation, n=6; protein S deficiency, n=3; protein C deficiency, n=3; Prothrombin mutation, n=1; JAK-2 mutation, n=1). Most patients referred for bleeding disorders were so due to difficulty managing anticoagulation or its complications (n=30), followed by thrombocytopenia (n=13), easy bleeding/bruising (n=9), and coagulation times abnormalities (n=6).

This project is still at its infancy but represents the will to improve the care of these patients at a local level and a good example of team-work between two different but complementary specialties. The creation of such a clinic without the proper framework proved challenging, specially with the advent of the Covid-19 pandemic. There is still a lot to be done and our next goals are to further deepen the connections to primary care, educate our communities for these diseases and develop research projects.

P-11

Experience of two cases of hereditary haemorrhagic telangiectasia treated with systemic Bevacizumab

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Hereditary haemorrhagic telangiectasia (HHT) is a genetic disorder characterized by uncontrolled angiogenesis due to elevated expression of vascular endothelial growth factor (VEGF). Patients present typically with epistaxis, gastrointestinal bleeding, arteriovenous malformations, and iron-deficiency anaemia. Bevacizumab is an anti-VEGF monoclonal antibody that has been used to control bleeding symptoms in severe forms of this disease. We present two patients with HHT followed in our centre with successful bleeding control with Bevacizumab.

Case 1 is a 77-year-old man with previous history of giant cell arteritis with rheumatic polymyalgia, controlled with steroids and methotrexate. He had a long-standing history of severe epistaxis, leading to multiple visits to the emergency department (ED) and presenting at least in one episode with haemorrhagic shock. Additionally, he had a nasal septum perforation and an associated iron-deficiency anaemia. The physical examination revealed mucocutaneous telangiectasias of the face, mouth, and hands, and he also had a three-generation familiar history of epistaxis. Thoracic and cranio-encephalic CT-scans excluded arteriovenous malformations, but the endoscopy disclosed gastric angiectasias. The diagnosis of HHT was confirmed after genetic study showing a ACVRL1 mutation. The patient maintained frequent episodes of epistaxis, with an Epistaxis Severity Score (ESS) of 10. PET-scan excluded the possibility of vasculitis activity that justified this evolution.

Case 2 is a 69-year-old man with long-standing history of severe epistaxis (ESS 10), with nasal septum perforation, and iron-deficiency anaemia needing frequent transfusional support (5 units/year), as well as ischaemic cardiopathy with difficult management of antiaggregating therapy due to these blood losses. Screening for arteriovenous malformations showed no alterations, and the gastrointestinal study disclosed only two small angiectasias of the colon. Nonetheless, genetic study was requested and revealed an ENG mutation that confirmed the diagnosis of HHT.
Systemic Bevacizumab was initiated in a similar regimen in both cases: 350mg twice a month for the first 2 months and 350mg monthly from then on. In case 2, after the first year of therapy, administrations were adjusted to 350mg every two months, due to good clinical response. Additionally, they both maintained aminocaproic acid on demand and ferric carboxymaltose as needed.

Both patients reported a significant improvement in quality of life, with a reduction of ESS at the 6- and 12-month re-evaluations (6 and 6 in case 1, 4 and 3 in case 2, respectively). Both maintained epistaxis of mild to moderate severity, in case 1 still needing transfusional support in one occasion. We didn't record any adverse effects related to Bevacizumab in any patient.
Thus, in our experience, Bevacizumab seems to be a safe and a therapeutic alternative in severe uncontrolled HHT, improving quality of life, reducing emergency visits and need for transfusional support.

P-12

LDL levels in very high cardiovascular risk patients - A call for intensive lipid-lowering therapy

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Background
European Society of Cardiology (ESC) guidelines on dyslipidemias were published in 2019 updating LDL recommended values for very high cardiovascular (CV) risk patients from <70mg/dL to <55mg/dL, as lower LDL levels improve prognosis in this population. This study aims to evaluate LDL levels in a population of very high CV risk and its trend over the years, assess its prognosis impact on acute coronary syndromes (ACS) admissions and evaluate the lipid-lowering therapy medication regimen in this population.

Material and methods
Retrospective study based on the analysis of patients who were admitted due to ACS between 2017 and 2021 and that before admission were already in the very high CV risk category. LDL levels variation was assessed from 2017 to 2021. Lipid-lowering therapy regimen

was assessed using three categories: No statin therapy, statin therapy alone, and statin plus ezetimibe. Outcomes of admission were assessed according to LDL levels (≥70mg/dL or <70mg/dL) and the following endpoints were evaluated: proportion of STEMI, left ventricular disfunction (<50%), complications during admission and mortality.

Results
228 patients were included, mean age of 67 ± 11.6 years and 65% male. Overall, only 31% of the patients had LDL values < 70mg/dL (82 ± 28 mg/dL) and only 16% of the patients had LDL < 55mg/dL. Mean LDL levels in 2021 were slightly lower than in 2017, without significance (P= 0.283). ACS admission outcomes analysis revealed that patients with LDL>70 presented with a significantly higher proportion of STEMI (P=0,025) and had significantly more complications during admission (P=0,031). Analysis of lipid-lowering therapy regimens revealed that most of the patients are treated with statin alone (70,6%) and only 26.7% of the patients are treated with statin + ezetimibe.

Conclusion
Most of the patients in the very high CV risk category who are admitted due to ACS are above the ESC LDL recommended levels, translating into worse outcomes, and only a small percentage of this population is treated with combination lipid-lowering therapy. The results of this study restate the need for aggressive lipid-lowering therapy in very high CV risk patients.

P-13

Characterization of acute aortic syndromes: A 10 year-analysis

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Background
Acute aortic syndrome (AAS) is a rare, but life-threatening condition. Despite recent advances, there is lack of contemporary data describing this population.

Material and methods
We performed a retrospective analysis of patients admitted with AAS in our center in the last 10 years to characterize incidence, clinical course, risk factors and outcomes of this population.

Results
There were 75 patients admitted with AAS, 90.7% aortic dissections (72.8% Stanford type A), 6.7% intramural hematomas and 2.7% penetrating ulcers. Patients were predominantly male (61.3%), with a mean age of 67±14 years. Concerning risk factors, hypertension was the most common (66.2%), followed by dyslipidemia (33.8%), smoking (27%), diabetes

(17.6%), family history of AAS (2.7%) and connective tissue disease (2.7%). Most patients had a symptom onset <24h (71.6%) and chest pain was the most frequent complaint (52.7%), followed by abdominal pain (18.9%) and syncope (18.9%). At admission, 28.8% of patients presented in shock, 26.3% had ischemic ECG changes, 8.2% had peripheral ischemia and 6.8% had acute cerebrovascular event.
Type A aortic dissection patients (n=49) had a median aortic diameter of 51.0mm (IQR 47-58) and 32.6% had a diameter <55mm. Among these patients, 70.8% underwent surgery, 4 patients died before surgery and 8 were not eligible due to comorbidities. Median length of hospital stay was 9 days (IQR 2-19), 5 patients were reintervened due to acute complications and the in-hospital mortality rate was 39.6%. During a median follow-up time of 11 months (IQR 0-71), 4 patients (11.7%) were submitted to another aortic procedure and 4 patients (14.8%) developed a MACCE event, with an overall mortality of 24.1% (7 patients).
Patients with type B aortic dissection (n=19) were older than type A (71±15 vs 64±13 years) but had a similar clinical presentation. They were predominantly treated conservatively (70.8%). In-hospital mortality was 15.8%. During follow-up time, there were 7.1% of MACCE events and overall mortality was 31.3%.

Conclusion
In our study, arterial hypertension remained the most prevalent risk factor in AAS patients. Clinical presentation was variable and almost one-third presented in shock. Acute aortic dissection, especially type A, was associated with a high rate of in-hospital and medium-term morbidity and mortality. A significant number of patients had an aortic diameter <55mm, highlighting the importance of controlling hypertension and other cardiovascular risk factors, to early recognise patients at risk.

P-14

When anticoagulation is not enough

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Introduction
Oral anticoagulation is the gold standard of embolic stroke prevention in patients with atrial fibrillation. However, in some patients, other strategies should be followed.

Clinical case
This is the case of a 72 years-old male patient that presented an embolic thrombus to the right renal artery. Atrial fibrillation (AF) was diagnosed only a few months later, while the patient was already medicated with a direct oral anticoagulant. No strategy to control rhythm was initiated, with focus on frequency control. The patient was later referenced to the Cardiology consult due to symptomatic AF and initiated propafenone. This strategy was insu-

fficient to attain sustained sinus rhythm and later the patient had an embolic stroke to the cerebellum, whilst on anticoagulation. The patient is currently waiting AF ablation. Some of the sequelae might not be reversible.

Discussion
Anticoagulation is widely important to prevent embolism in AF. This, however, should not deviate our attention to the arrhythmia itself. Rhythm control is increasingly the recommended initial strategy in newly diagnosed AF, as it results in less mortality, lower rates of cardiac failure and better exercise tolerance and quality of life.

Conclusion
Overall, returning to sinus rhythm is superior for embolic prevention in atrial fibrillation and, as clinicians, we should not miss the window of opportunity for doing so in recently diagnosed AF.

P-15

Hemocromatose Hereditária Tipo 1 associada Trombose da Artéria Mesentérica. A proposito de um caso clínico

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Background
A Hemocromatose Hereditária tipo I é uma doença genética frequentes do ser humano, correspondendo cerca de 90% dos casos de Hemocromatose. Em Portugal, é especialmente prevalente no norte. Juntamente com as outras doenças genéticas hemocromatósicas, a hepcidina, o peptídeo central regulador do metabolismo do ferro, desempenha um papel fundamental.

Caso Clínico
Doente do género masculino de 51 anos de idade, caucasiano, com história de Sobrecarga de Ferro, Etanolismo Crónico mantido, DHC Etanólica, Úlceras Gástricas e Duodenais, HTA, Dislipidemia e Síndrome Depressivo e de Ansiedade, seguido em Consultas no Hospital de Dia de Imuno-Hemoterapia, com indicação para flebotomias terapêuticas regulares que não cumpria os tratamentos. Recorreu ao SU do HSM em Outubro de 2021 por quadro de vómitos alimentares ocasionais, diarreia de fezes escuras (2/3 dejecções dia), anorexia, dor abdominal difusa, sem irradiação, e agravamento do tremor habitual, com cerca de 3 semanas de evolução. Negava febre, pirose, azia, sintomas urinários, dispneia, toracalgia, tosse. Negou toma de fármacos anticoagulantes ou anti-agregantes, lipotimia ou perda de conhecimento, queixas urinárias, febres ou queixas sugestivas de infeção.
Apresentava níveis de ferro sérico elevados e apresentava alteração genética no gene responsável pelo metabolismo do ferro, com indicação para flebotomias terapêuticas.

Material e Metodos
Consulta de processo clínico em soistema infomático

Resultados
Hiperferritinémia, alteração da função hepática e TAC abdominal que revelou isquemia crónica intestinal. Conclui tratar-se de um caso de Trombose da Artéria Mesentérica Superior.

Conclusão
O Prognóstico deste doente é reservado dada as comorbilidades associados, a manutenção dos hábitos etílicos e incumprimento terapêutico. A probabilidade de recorrência de eventos trombo-embólicos nestes casos é muito elevada.

P-16

Outcomes of diabetic patients submitted to chronic total occlusion PCI

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Background
Coronary chronic total occlusions (CTO) are relatively common findings in the context of coronary angiography. The indication for revascularization of this type of lesions remains controversial. There is little knowledge about clinical outcomes between type 2 diabetic (DM2) and nondiabetic patients submitted to CTO by percutaneous coronary intervention (PCI). Our aim was to analyze the clinical benefit and outcomes of diabetic patients submitted to CTO PCI. Additionally, we specifically aimed to identify independent predictors to symptoms recurrence in this population.

Material and methods
A retrospective analysis was carried out of CTO patients submitted to PCI between 2019-2020. Patients were divided in two groups regarding previous DM2 (with-DM2 and without-NDM2). Composite primary outcome (recurrence of angina and/or heart failure (HF) symptoms) and secondary outcomes (myocardial infarction and death) were compared between both groups. Independent predictors of primary outcome were assessed by multivariate logistic regression. P value < 0.05 indicates statistical significance.

Results
A total of 177 patients were identified, with a mean age of 65±11 years, 82.5% male. 75% showed hypertension, 40% with diabetes, 73% with dyslipidemia, 18% with obesity and

HF in 15%, without differences between groups. DM2 patients were older with a mean age of 67,9±10,1 (p=0.010), with more chronic renal failure (14.3%, p=0.011), worst creatinine clearance 69.3±27.9 (p=0.006) and less use of contrast during PCI (225±84.8, p=0.009). Both groups improved LVEF after intervention (p<0.001). Symptoms recurrence occurred in 18% of patients after 2 years. Composite primary outcome was not significant higher in DM2 group (15.5% vs 22.7%, p=0.238). Angina recurrence was significant higher in DM2 group (5.80% vs 15.2%, p=0.043). Secondary outcomes were low after 2 years, without difference between groups. Right coronary artery (RCA) CTO vessel treated was an independent predictor for total symptoms recurrence after PCI (p=0.014, OR 2.86, 95% CI 1.24 to 6.60), although presence of diabetes was not (p=0.324, OR 1.53, 95% CI 0.66 to 3.53).

Conclusion
DM2 did not influence outcomes in CTO patients submitted to PCI, and its presence should not be a limiting factor in the decision of CTO revascularization.

P-17

Type A acute aortic dissection - Predictors of in-hospital mortality

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Background
Stanford Type A Acute Aortic Dissection (AAD) is the most common life-threatening disorder affecting the aorta and is associated with a high rate of in-hospital mortality, even in patients that are surgically treated. Early recognition of patients that are at increased risk of mortality is important to guide clinicians for optimal treatment.

Material and Methods
We performed a retrospective analysis of patients admitted with type A AAD in our centre in the last 10 years to determine the predictors of in-hospital mortality in this population. Association between patient characteristics and in-hospital mortality was evaluated.

Results
A total of 75 patients with acute aortic syndrome were selected and 49 (65.3%) patients with Stanford type A AAD were identified. Among these patients, 59.2% were male, with a mean age of 64±13 years. Hypertension was the most prevalent risk factor (62.5%), followed by dyslipidemia (31.3%), obesity (25%), smoking (14.6%) and previous cardiovascular disease (8.3%). At admission, the most prevalent symptoms were chest pain (64.6%), abdominal pain (22.9%) and syncope (22.9%). 33.3% of patients presented with shock, 28.6% had ischemic ECG changes and 58.3% had pericardial effusion. Median aortic diameter was 51.0mm (IQR 47-58) and the dissection extended to the abdominal aorta in 49.6% of patients

and to the supra-aortic trunks in 8.2%. 70.8% of patients underwent emergent cardiothoracic surgery, 4 patients died before surgery and 8 were not eligible due to multiple comorbidities. Total in-hospital mortality was 39.6%, with a median length of hospital stay of 9 days (IQR 2-19). Among patients that were treated surgically, 18.2% died before discharge.

In a multivariate regression analysis, independent predictors of in-hospital mortality were age (OR 1.122, 95%CI 1.003-1.255) and cardiogenic shock at admission (OR 25.914, 95%CI 1.324-507.391). Non-fatal cardiac arrest was also associated with higher mortality (p<0.001). There were no other significant differences in in-hospital mortality regarding risk factors, clinical presentation and aortic characteristics.

Conclusions
In our study, total in-hospital mortality in patients with type A AAD was 39.6%. Even in patients submitted to emergent cardiothoracic surgery, in-hospital mortality rate was 18.2%. In this group of patients, age and cardiogenic shock at admission were independent predictors of in-hospital mortality.

P-18

Bleeding or thrombosis?, the brain must not choose

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Introduction
Oral anticoagulation is the mainstay pharmacological method used to prevent embolic stroke in patients with atrial fibrillation. In the case of some patients, however, anticoagulation is not a viable option.

Clinical case
75 years old female patient, with past medical history of atrial fibrillation, hyperthyroidism, chronic kidney disease and arterial hypertension. After developing two episodes of neurological deficits, she was diagnosed with cerebral amyloid angiopathy, grade 1 in the Fazekas scale. The patient was medicated with a direct oral anticoagulant, but would benefit in suspending it in order to avoid an accelerated disease progression. She is currently waiting left atrial appendage closure.

Discussion
Oral anticoagulants have been fundamental in decreasing the rates of embolic stroke in patients with atrial fibrillation. Nevertheless, the side effects can be deleterious for some patients, in which cases left atrial appendage closure can be a suitable option.

Conclusion
Embolic stroke is detrimental for the health of our patients, sometimes with long-life consequences. In patients with cerebral amyloid angiopathy, we should choose the best option to prevent it with the lesser bleeding risk – the brain must not choose between the two.

P-19

Association of the FVIII/DD and FvW/DD indices as an indicator of severity and mortality in patients with COVID-19

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Background
There are different studies on severity and mortality indices, such as the neutrophil/lymphocyte (INL) ratio as well as the lymphocyte/C-reactive protein (ILR) ratio, which has been relevant as a serum biomarker to define severity. Cataudella et al. reported the proportional relationship of the INL with the severity of pneumonia and some adverse outcomes; Furthermore, it has been observed that it can be a predictor of mortality in intensive care units.
Due to the increase in the demand for hospital care, fast and inexpensive strategies are required to early classify patients with higher risk of death. There are biomarkers to predict the severity of COVID-19. However, the cut-off points are variable and have not been established for mortality in the Mexican population, indices where hemostatic factors are present, such as the FVIII/DD and FvW/DD ratio. Due to their low cost and availability, these markers could be useful in the classification of patients with severe disease. The usefulness of these indices in patients at high risk of dying from COVID-19 hospitalized in Mexico is still unclear. Knowing this information will favor a more efficient patient classification strategy and a better use of resources.

Objective
To determine if the factor VIII and D-dimer (FVIII/DD) indices and the von Willebrand factor (vWF/DD) index as a marker of endothelial dysfunction can be useful as a marker of poor prognosis and mortality and to identify patients with a poor prognosis in hospitalized COVID-19 cases from the National Institute of Respiratory Diseases.
Methods: A prospective, longitudinal and analytical study was carried out, in which all patients admitted to the emergency department of the National Institute of Respiratory Diseases with a diagnosis of SARS-CoV-2 infection with a confirmed PCR test were admitted; in a period of time between March and November 2020, in which clinical follow-up was carried out during their hospital stay. The hematological laboratory data were recorded to generate

the FVIII/DD and VWF/DD indices, the clinical-epidemiological data, and the discharge status of the patients.

Results
Data from 249 hospitalized patients with severe COVID-19 were analyzed, of which 67.5% were male. With one discharged from the hospital for improvement 40.8% with one death (141/249) 59.2%. The clinical characteristics (quantitative and qualitative variables) as well as laboratory characteristics are described in Table 1. The patients who died presented cyanosis and complications in the ventilatory state. The main comorbidities in the patients were diabetes (27.7%), hypertension (31.7%) and obesity (30.1%). FVIII/DD24H indices were constructed. A value >115 was established as the cut-off point for the DD/FVIII and DD/VWF index to predict mortality, which are shown in Figure 2.

P-20

KAWASAKI DISEASE - Is there an end? - Case report

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Background
Kawasaki disease is one of the most common causes of vasculitis in childhood, affecting mainly the coronary arteries, leading to the development of stenosis or aneurysms at this level. The management of the pathology is determined by possible complications at the coronary level and the risk stratification for these patients. The use of imaging methods (echocardiography, multidetector computed tomography, or even single-photon emission computed tomography) is necessary to evaluate changes and aneurysm-related complications.

Material and methods
We present the case of a 38-year-old patient who presented to the ED with the reappearance of coronary chest pain with progressive accentuation. From a detailed medical history, we learned that the patient had a known history of acute myocardial infarction with the need for drug-eluting stent implantation, non-compliant with the recommended medication. On physical examination, the patient had an influenced general state, normal-colored skin, normal BMI, BP 120/70 mmHg, HR 95/min, rhythmic cardiac sounds, without cardiac or vascular murmurs, without signs of pulmonary congestion.
The ECG showed sinus rhythm at 75 bpm, with QS and negative T waves in DI, AVL, and LVH changes.
Laboratory tests revealed hypertriglyceridemia with hypercholesterolemia (LDL-c 125 mg/dl). Transthoracic echocardiography showed a normal-sized left ventricle (LV) with regional wall motion, a moderate reduction of the anterior wall longitudinal strain and a slight reduction of the ejection fraction (48%). Mitral regurgitation was present. "Bull's Eye" type imaging

showed a low global longitudinal strain (-14%), with infarction in the anterior territory.
After evaluating the patient, with no signs of myocardial cytolysis but with persistent chest pain, coronary angiography was necessary, which revealed bivascular coronary disease, Kawasaki disease, PCI with drug-eluting stents at the level of the IVA and CxA. IVA had patent stents at the level of segments I and II (with a fusiform aneurysmal dilation between stents) and a 90% stenosis at the level of segment III.
During hospitalization, after coronary revascularization, with the following treatment: acetylsalicylic acid 75mg od, bisoprolol 2.5 mg od, ticagrelor 90mg bid, ramipril 2.5 mg od, atorvastatin 80mg and ezetimibe 10 mg od, the patient's evaluation was favorable, with remission of chest pain.

Results
The patient's discharge was possible without the occurrence of chest pain, with treatment recommendations. The possibility of periodic echocardiographic and coronary angiographic evaluations remains doubtful for this patient due to non-compliance with treatment.
Echocardiographic evaluation should involve measuring vessel diameters using the Z-score, identifying associated structural anomalies, possible valvulopathies, and the pericardial fluid. Coronary angiography is considered the standard method for diagnosing and treating coronary aneurysms. It is important to provide antithrombotic prophylaxis to patients, and anticoagulation therapy should be considered.

In conclusion, although the cause of coronary aneurysms remains unknown, it is crucial to make a prompt diagnosis and administer intravenous immune globulin, as patients with aneurysms require lifelong cardiology follow-up.

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P-21

Contribution of unconventional antiphospholipids antibodies in the diagnosis of antiphospholipid syndrome

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Background
The diagnosis of antiphospholipid syndrome (APS) is based on clinical and biological arguments. Nevertheless, the negativity of the conventional antibodies induces a diagnostic

ambiguity. In addition, other non-conventional antiphospholipid antibodies (aPL) could explain this syndrome. In this context, we studied the contribution of anti-cardiolipin (aCL) and anti-Glycoproteine-1 (anti-M2GP1) IgA class APL as well as IgG and IgM anti-annexin V in the diagnosis of APS. Methods: Patients consulting Internal medicine department with clinical symptomatology consistent with APS associated or not with conventional positive aPL were identified over a 3-year period (2019-2021). The above mentioned non-conventional aPL were tested by ELISA (Biosystems and Euroimmun) in the Immunology Department of Mohammad Taher Maamouri hospital.

Results

Eighty patients were enrolled in the study. The mean age was 46 years [19-78], and the F/M sex ratio was 2.3. Twenty-two patients were classified as confirmed antiphospholipid syndrome (APS) (27.5%), and 58 had seronegative APS (72.5%). Seventy patients had thrombotic events (87%), and twenty had embolic manifestations (25%). Anti-M2GP1 IgA were positive in 15% of the studied patients (12 patients) and were associated with 9% of seronegative APS (5 patients). The IgA aCL were positive in only 4% (3 patients) of the study population, allowing the detection of 3% of seronegative APS. Anti-annexin V IgG and IgM were positive in 19% (15 patients) and 5% (4 patients) of the total population, respectively. Interestingly, 80% of positive IgG anti-annexin V were associated with seronegative APS, revealing it in 21% of cases (12 patients). Fifty percent of positive IgM anti-annexin V were associated exclusively with seronegative APS in 2 patients, accounting for 3% of this population. Twenty-one out of 58 seronegative APS patients (36%) had at least one unconventional aPL among those studied in our study. The distribution of unconventional aPL according to APS clinical manifestations showed a predominant association with thrombotic events (60-100%) compared to obstetric manifestations (8-30%). IgA aCL were exclusively associated with venous thrombosis (4%) in thrombotic events. IgA anti-M2GP1 were mainly associated with thrombotic events 16% vs. 5% in obstetric manifestations, with a similar association with arterial and venous thrombosis. They were more prevalent in secondary APS (71% vs. 47%). The distribution of IgG anti-annexin V was similar in thrombotic events and obstetric disorders (20%) with a slight predominance in venous lesions compared to arterial lesions (21% vs. 12%). Anti-annexin IgM was exclusively revealed in thrombotic events (6%), with a predominant association with venous embolism (6% vs. 2% in arterial thrombosis). A predominance in secondary APS (29% vs. 13%) was noted.

Conclusion

The preliminary results of this study reveal the diagnostic value of anti-M2GP1 IgA and anti-annexin IgG during seronegative APS which deserves to be confirmed by a large cohort.

P-22

Clinical and immunological profile of anti-phospholipid syndrome in the Tunisian population

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Background
The anti-phospholipid syndrome (APS) is characterized by a polymorphic clinical presentation involving thrombotic and obstetric manifestations. Its biological diagnosis is based on the persistent positivity of an anti-phospholipid autoantibody (aPL). The conventional immunological assessment includes lupus anticoagulant (LAC) and anti-cardiolipin (aCL) and/or anti-M2GP1 (IgG and IgM). The objective of this study was to investigate the clinical presentations of APS according to the immunological profiles of patients.

Methods
Over a period of two years (2020-2022), patients with confirmed APS who met the Sapporo 2006 criteria were identified. Conventional aPL including anti-ACL and anti-M2GP1 (IgG and IgM) were confirmed positive at 12 weeks using the ELISA technique (EUROIMMUN®). The LAC test was performed using a standardized hematological method.

Results
Twenty-two patients were included in the study. The mean age was 41 years, and the female-to-male ratio was 2. A thromboembolic event was present in 17 patients (77.3%) and obstetric manifestations in 7 patients (32%). APS was primary in 68% of cases (15 patients) and secondary in 31.8% of cases (7 patients). Eight patients had a positive LAC (36%). Positive aCL was of IgG type in 7 patients (22%) and of IgM type in 9 patients (41%). Positive anti-B2GP1 was of IgG class in 10 patients (45%) and of IgM class in 8 patients (36%). Some associations of autoantibodies were positive, allowing the identification of specific profiles, including the association of IgG (aCL and B2GP1) in 27.3% (6 patients) (p=10-3) (profile 1) and the association of IgM (aCL and B2GP1) in 22.7% (5 patients) (p=10-3) (profile 2). IgG aCL and anti-M2GP1 separated were similarly associated with TE manifestations (7% and 11% of cases, respectively) and obstetric manifestations (10% for both), while specific profile 1 was more prevalent in secondary APS (49%) than in primary APS (13%). Moreover, no difference was found in the distribution of IgM aCL and anti-M2GP1 types according to TE symptoms (10% and 9% of cases, respectively) and obstetric manifestations (20% for each antibody). Interestingly, specific profile 2 associating IgM aCL and IgM B2GP1 was more prevalent in obstetric cases (20% vs 7% in thrombotic events), with a slight predominance of arterial involvement compared to venous sites (10% vs 2%).

Conclusion
The preliminary results of this study reveal the diagnostic value of IgM class autoantibodies for both types of aCL and B2GP1 autoantibodies in the Tunisian population. Similarly, our study highlighted clinical profiles based on the specific immunological profiles of Tunisian patients.

P-23

Hemogram and hemostasis parameters in patients with bacterial bloodstream infection

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Background
The differential diagnosis of Gram-negative (GN) and Gram-positive (GP) bacterial bloodstream infection (BSI) is mainly based on blood culture pathogens. Hemogram, coagulation parameters and C-reactive protein (CRP) play auxiliary roles in the diagnosis and outcome of sepsis. However, it is not clear whether these parameters can help to distinguish bacterial classification or guide the choice of empirical antibiotics. The aim of this study was to investigate the differences in values of leukocyte, platelet, platelet indices (plateletcrit (PCT), mean platelet volume (MPV), platelet distribution width (PDW), platelet large cell ratio (P-LCR)), CRP, prothrombin time (PT), activated partial thromboplastin time (aPTT) and D-dimer between GN-BSI and GP-BSI.

Material and methods
We conducted a retrospective investigation of 81 blood samples (BS) with positive BSI from 37 patients admitted at emergency department of Traumatology clinic. After excluding 22 BS with multiple bacterial (N = 16) or fungal infections (N = 6), we eventually enrolled 59 BS of 30 patients, divided into GP-BSI (N = 18) and GN-BSI (N = 41). Demographic parameters, hemogram, coagulation parameters, and CRP were recorded and compared between the two groups. The Mann-Whitney test was used for group comparisons with $P < 0.05$ (MedCalc Software, Ostend, Belgium).

Results
Overall, 74% patients were male and median age was 71 (23-78). Pseudomonas aeruginosa (19/41) and Methicillin Resistant Staphylococcus aureus (7/18) were the most common GN-BSI and GP-BSI in our study, respectively. The median values (interquartile range) for platelet count (x109/L) and fibrinogen (g/L) in the GN-BSI were lower than those in the GP-

BSI (218 (157-293) vs. 296 (215-450), P = 0.037; 3.9 (3.1-5.0) vs. 4.8 (4.2-5.5), P = 0.032, respectively). However, prolonged PT (%) and aPTT (s) with higher D-dimer (mg/L) were observed in GN-BSI (73 (60-86); 29.0 (26.1-34.7); (0.8 (0.6-2.6)) compared to GP-BSI (88 (63-101); 25.0 (23.8-27.39); 0.4 (0.3-0.5)) with P = 0.032; P = 0.011; P = 0.026, respectively. All platelet indices except PCT in the GN-BSI were higher than those in the GP-BSI, but not significantly.

Conclusions
Patients with GN-BSI had significantly lower platelet and fibrinogen as well as prolonged PT and aPTT with higher D-dimer compared to GP-BSI. These findings suggest that there are differences in host responses on different pathogens, but their role in distinguish bacterial BSI needs further investigation.

P-24

Venous thromboembolism in antihtrombin deficient pregnant woman despite therapeutic doses of low-molecular-weight heparin

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Background
Antithrombin (AT) deficiency is rare, but frequently associated with thromboembolic complications, especially in pregnancy. However, data on management of pregnant AT deficient women is scarce and recommendations vary widely.

Aim
To emphasize difficulties in the management of pregnant women with AT deficiency by presenting a case of a patient who experienced venous thromboembolism in the 23rd week of pregnancy despite therapeutic doses of heparin.

Methods
The patient's chart was reviewed for details of diagnosis, treatment, and outcome.

Results
A 35-year-old woman with AT deficiency (49% AT activity) had two venous thromboses before the age of 21. Her first two pregnancies ended in spontaneous abortion in the first trimester. In the 7th week of the second pregnancy she suffered superficial thrombophlebitis despite therapeutic doses of dalteparin. In the third pregnancy she received suprathera-peutic doses of dalteparin (230 IU/day/kg body weight, monthly anti-Xa peak levels slightly below the expected range of 1.0 IU/ml) Despite treatment, she suffered pulmonary embolism

and popliteal vein thrombosis at 23 weeks. At this time anti-Xa was around 0.5 IU/mL on several measurements, which is too low for a therapeutic level. It was low even though the dose was increased, which was expected because of the lack of AT. She was switched from dalteparin to argatroban, and later warfarin was reintroduced. At week 36 she was switched back to dalteparin at therapeutic doses, along with the daily substitution of AT. AT activity was maintained at 75-100%, and the anti-Xa for dalteparin was within the expected range. The planned delivery at 38 weeks was vaginal with minimal blood loss. Neonatal birthweight was adequate (3,640 g). Warfarin was reintroduced after delivery. No further thromboembolic complications occurred.

Conclusions
Heparin in AT deficient pregnant women may be ineffective due to the lack of AT activity. However, the substitution of AT throughout pregnancy is impractical, while supratherapeutic doses of heparin may increase the risk of bleeding. Second- and third-trimester vitamin K antagonists may be a viable option for these women, and substitution of AT should be limited to the peripartum period only.

P-26

A breathtaking diagnosis - Case Report

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Background
Venous thromboembolism (VTE) is the third most frequent acute cardiovascular syndrome. The aging of populations and the increasing diagnostic capacity suggest that VTE will continue to play an important role in health care systems in the future. Defining the etiology is important to define the treatment, the anticoagulation therapy duration and to prevent recurrence.
Case report: A 25-year-old male presented to the emergency room complaining of a 1-week worsening dyspnea with pleuritic chest pain and left calf pain. He was obese and sedentary. He had no cough, loss of weight, anorexia, or hemoptysis. He was tachycardic, apyretic, with normal blood pressure. Laboratory workup revealed elevated D-dimer levels; ECG showed sinus tachycardia and S1Q3T3 pattern; chest CT confirmed bilateral pulmonary embolism (PE) and lower limb venous Doppler confirmed left deep vein thrombosis. Additional study showed elevated titers of anticardiolipin-antibodies. The patient was started on anticoagulation and was discharged.

He was readmitted three weeks later complaining of worsening pleuritic chest pain, fever and marked asthenia. Radiologic study showed hepatomegaly, splenomegaly and multiple chest and abdominal adenopathies, not presents in the previous study. Infectious etiologies were

discarded, and a lymphoproliferative disease was considered as hypothesis. An excisional lymph node biopsy was performed and histologic characterization revealed metastatic adenocarcinoma with lung phenotype with PD-L1 expression and EML4(13)-ALK(20) rearrangement. The patient started treatment with alectinib and anticoagulation therapy was changed from NOAC to tinzaparin. Radiologic re-evaluation after two months of treatment showed progression of disease with liver, bone and splenic involvement. A second line therapy with carboplatin and pemetrexed failed to succeed and a new pulmonary embolism (PE) occurred on antithrombotic therapy. A third line therapy with lorlatinib was tried but the patient's clinical condition deteriorated, culminating in the patient's death 7 months after diagnosis.

Discussion

Cancer is a well-know risk factor for VTE and PE is common in lung cancer patients, especially those with adenocarcinoma phenotype. However, the relation between PE and lung cancer is poorly known. PE is normally diagnosed within the first months of cancer diagnosis and rarely anticipates it. In those occurring before the diagnosis, the patients have significantly shorter mean survival time, since diagnosis of PE is more common in III-IV cancer stages and interactions between tumor cells and coagulation system seem to contribute to disease progression.

This young adult patient, without signs or symptoms of lung cancer presented a diagnostic challenge. In this age group, inherited clotting factors, post-operative states or trauma are more likely to be the etiology of PE.

Even among neoplastic diseases, lymphoproliferative was first considered given the age and the clinical presentation, emphasizing the importance of histological diagnosis. In this case, tumor mutation - EML4/ALK rearrangement – and obesity may have contributed to an earlier presentation of PE, while chemotherapy regimen, particularly carboplatin, may have contributed to its recurrence.

Conclusion

Apparently unprovoked VTE may be the presenting sign of an underlying occult cancer and should be considered even in young adults since early diagnosis may impact the survival time of the patient.

P-27

Home Treatment of Patients with Pulmonary Embolism: A Single Centre 10-year Experience from Ljubljana Registry

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Background
Current guidelines suggest careful risk stratification using structured clinical approach when selecting patients with pulmonary embolism (PE) for home treatment. However, it is not clear, how these recommendations are followed in everyday clinical practice. The aim of our study was to assess whether patients referred to our outpatient venous thromboembolism (VTE) clinic are in fact risk stratified according to guidelines prior to referral and what is the real-life course of the disease in patients treated at home.

Materials and Methods
We included patients with confirmed PE referred to our outpatient VTE clinic between 2010 in 2019. Data were obtained from a prospective anticoagulation management registry (Ljubljana Registry). Patients were stratified into low- or high-risk group using Simplified Pulmonary Embolism Index and/or signs of right ventricular strain. We compared 30-day mortality, overall mortality and rates of recurrent thromboembolism or major bleeding between low- and high-risk patients.
RESULTS: Among 278 patients, 90 (32.4%) and 188 (67.6%) were retroactively classified as high- or low-risk, respectively. 30-day mortality was low in both groups: 1.1% in high- risk group and 0% in low-risk group. However, overall mortality rate was higher in the high- risk than in the low-risk group (12.1 vs. 0.9/100 patient-years, respectively, $p<0.001$). Rates of recurrent thromboembolism and major bleeding were similar for high- and low- risk groups.

Conclusions
We conclude that in real-life clinical practice, a significant proportion of high-risk PE patients are referred to outpatient management. However, with careful and dedicated management, early mortality is low even in high-risk patients.

P-28

Management of therapeutic plasma exchange (TPE) in a patient with Goodpasture Syndrome (Anti-GBM disease)

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The term therapeutic apheresis is used to describe the removal process of pathological substances such as cells, pathogenic antibodies, immune complexes or inflammatory mediators from the patient by an extracorporeal procedure in order to “purify” the blood. In addition to conventional medical therapies, TPE has become an important adjuvant treatment option to immunosuppressive agents for primary and secondary renal diseases being associated with faster recovery and symptomatic resolution as well as improved prognosis.

We report a 68-year-old male, with personal history of ischemic heart disease, benign prostatic hyperplasia (BPH) and cardiovascular risk factors (highBP, dyslipidemia and obesity), referred to the emergency room(ER) because of sudden decreased urine output and analytic changes in renal function (creatinine 12.25mg/dL and urea321mg/dL). At ER admission, patient presented hemoptoic sputum and long-term LUTs. A urinary catheter was placed due to initial suspicion of obstructive nephropathy with possible pre-renal involvement. Despite maintained diuresis, there was no improvement in renal function, so study was extended, which showed erythrocyturia and anti-GBM antibodies with high titre. Analytical study during admission Hb 11.2g/dL, Creatinine 14.5mg/dL, Urea 332mg/dL, CRP 3.64mg/dL, urine protein-creatinine (UPC) 4,576g/g, ANCAs negative antibodies and positive anti-GBM antibodies with titre of 629U/mL. Renal ultrasound showed an increase in the reflectivity of the parenchyma that could translate nephropathy and chestCT scan revealed increased density areas, with a ground-glass appearance, involving mainly the right upper and lower lobes, compatible with alveolar hemorrhage.

An Anti-GBM disease diagnosis was made, started hemodialysis to improve the uremic environment and daily TPE with albumin/plasma replacement as well as corticoids and cyclophosphamide. On D4 anti-GBM antibody titre reduced to 115U/mL but clinically worse with respiratory failure and hemoptysis with a need to escalate O2 to 12L/min. Diagnosis of alveolar hemorrhage by BFO was confirmed and patient was transferred to ICU. During this time had a progressive clinical improvement, with reduction of O2 supply, however also had a gradual fall in Hb (9>8.6>8.1g/dL) and platelet count (250000>176000>126000/µL). On D8, due to satisfactory evolution and continued reduction in anti-GBM titers (44U/mL), TPE schedule was switch to alternate days.
TPE was postponed on D11 given the platelet value of 22000/µL, at this moment anti-GBM antibody titre 77U/mL was increasing. After transfusional support and therapeutic review, TPE was resumed to control immune progression. The patient has been controlled from a clinical and analytical point of view, but in need of permanent dialysis support.

Early implementation of TPE is essential to delay anti-GBM nephritis development, in combination with cyclophosphamide and corticosteroids. Several case series have shown that most patients with an initial presentation with creatine > 5.7mg/dL normally do not recover renal function due to irreversible glomerular damage. However, in context of diffuse alveolar hemorrhage, there is always a clinical benefit. Currently there is some difficulty in defining an optimal strategy for TPE duration as well as transfusional management. Further studies are needed to better understand the immunopathogenic mechanisms of the Anti-GBM disease and to redefine and refine targets in order to improve treatments, especially in patients with poor prognosis.

P-29

Splanchnic Vein Thrombosis: A typical presentation and evolution

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In 1997, a 23yo woman was referred to the Hematology consultation due to severe microcytic anemia, mild thrombocytosis and a 6-month-long discomfort in her upper left abdominal quadrant. She was diagnosed with severe iron deficiency anemia and started on iron replacement therapy, with a subsequent resolution of the anemia. Due to persistent mild thrombocytosis (max 600G/L), she underwent an abdominal ultrasound, which revealed a 20cm splenomegaly. The patient was submitted to a bone marrow (BM) evaluation: BM aspirate and cytogenetics were normal and the BM biopsy was hypercellular with slightly increased megakaryocyte proliferation. Thus, the patient was diagnosed with a myeloproliferative neoplasm (MPN), NOS. In 1999, the patient moved to another city and was lost to follow-up.
In 2002, the patient was admitted to the emergency department of our hospital due to fatigue, jaundice, diarrhea and hematemesis. She was diagnosed with acute hepatic failure due to Budd-Chiari syndrome and underwent a liver transplant. Thrombophilia study revealed only heterozygous Factor V Leiden, and apart from taking an estrogen anticonceptional pill, no other thrombotic risk factors were identified. Her previous medical history and diagnosis of MPN were not noted. She was on anticoagulation therapy with UFH followed by LMWH during the admission only.
In 2021, the patient, now 47yo, was again referred to the Hematology consultation due to sporadic mild thrombocytosis (max 450G/L) and 21cm splenomegaly. JAK2 mutation analysis was positive for V617F mutation. BM evaluation: BM aspirate was dry tap; BM biopsy showed grade 3 reticulin fibrosis and the patient was thus diagnosed with Primary Myelofibrosis (MF). A review of the 1997 BM biopsy showed abnormalities in megakaryopoiesis, grade 1 reticulin and other changes compatible with prefibrotic MF. Thus, given her medical history, one can presume that the JAK2 V617F+ MPN was already present at the time of the

Budd-Chiari syndrome.
This case is remarkable in many ways. First, the MPN presented at a very young age, which is atypical in this group of malignancies. Second, the Budd-Chiari syndrome was most likely a result of a combination of multiple thrombotic risk factors: estrogen anticonceptional pill, heterozygous Factor V Leiden and, probably, JAK2 V617F mutation. After the liver transplant, the patient became pregnant twice without antithrombotic therapy and without any record of thrombotic complications. Given the very high risk of recurrent splanchnic vein thrombosis (SVT) in patients with JAK2 V617F+ MPNs, it is equally remarkable that the patient remained more than 20 years without any other thrombotic event.
At the moment, the patient is on anticoagulant therapy with apixaban 5mg bid, which was started after excluding esophageal varices. According to the most recent guidelines, SVT in patients with MPN is an indication to start anticoagulation with warfarin. However, recent data show that DOACs are safe and equally effective as warfarin. In this case, the patient did not want to start warfarin due to the dietary restrictions and the need for frequent INR evaluation. Apixaban was chosen because it is the DOAC with the lowest risk of gastrointestinal bleeding.

P-30

Thrombophilia and pulmonary thromboembolism: A case report

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Introduction
Pulmonary thromboembolism is the most feared manifestation of venous thromboembolism and has a non-specific clinical presentation, making the diagnosis challenging. It occurs as a consequence of inherited acquired or environmental risk factors. Thrombophilic disorders can be identified in half of patients with venous thrombosis. Factors such as young age, absence of a precipitating factor, recurrence and family history, make the diagnosis of thrombophilic disorders increasingly probable.

Case presentation
A 44-year-old non-smoker male, with peripheral venous disease of the lower limbs and no other relevant personal or family pathological history, presented with dyspnea, fatigue and pleuritic chest pain since two days ago. The patient did not take any regular medication and there was no history of immobilization or recent surgery. On clinical examination, the patient appeared agitated, hypotensive (97/69 mmHg), normocardic (78 bpm), oxygen saturation in room air 93% and globally decreased breath sounds on pulmonary auscultation. No signs of deep vein thrombosis (DVT) were observed. Laboratory tests revealed leukocytes 13 x 10ML, neutrophils 11.1 x 10ML, D-dimers 124420 ng/dL, C-reactive protein 150.7 mg/L, NT-proB-

NP 145 pg/mL (reference value < 133 pg/mL) and troponin I 14.0 pg/mL (reference value < 19.8 pg/mL). Arterial blood gas analysis (with patient in room air) showed pH 7.43, pO2 66 mmHg, pCO2 43 mmHg, HCO3- 28 mmol/L, and O2 saturation 93.6%. The electrocardiogram showed sinus rhythm at a rate of 79 bpm. It was decided to perform computed tomography pulmonary angiography, which showed pulmonary condensation at the bases with associated air bronchogram and evidence of pulmonary thromboembolism predominantly affecting the pulmonary arteries, segmental and subsegmental branches, predominantly of the left basal pyramid. Bedside transthoracic echocardiography showed non-dilated ventricles with preserved systolic function, with a thin and collapsible inferior vena cava. Doppler ultrasound of the lower limbs excluded DVT. According to the simplified PESI score, the patient's clinical probability of mortality risk and severity of complications was intermediate-low. Treatment was initiated with supplementary oxygen, subcutaneous enoxaparin 1 mg/kg and analgesic therapy. The possibility of pneumonia was assumed, so empirical antibiotic therapy was started with Piperacillin/Tazobactam, with regression of inflammatory parameters. Further investigation revealed low levels of vitamin B12 and hyperhomocysteinemia. Treatment with cyanocobalamin was started, with correction of hypovitaminosis. Investigation of thrombophilia revealed the patient to be homozygous for the MTHFR C677T gene and heterozygous for factor G20210A. The patient was discharged home on the 21st day medicated with rivaroxaban 20 mg once a day.

Discussion

This case illustrates the importance of screening for thrombophilia in patients with venous thromboembolism at a young age and in the absence of a precipitating factor. In these cases, the diagnosis of thrombophilia influences the choice of long-term anticoagulant agent.

P-31

Thrombosis pre and postdiagnosis of essential thrombocytemia: Implication in survival

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Background

Thrombosis may precede or present after the diagnosis of Essential Thrombocythemia (ET), conditioning the patients' survival.

Objective: To analyze the number of thromboses before and after the diagnosis of ET and to assess its impact on survival.

Material and methods
Retrospective study of patients with ET diagnosed between the years 2000 and 2022 inclusive.
Demographic, clinical and biological variables were collected at diagnosis as well as the presence of thrombosis prior to or after this diagnosis. We analyzed the overall survival of patients with thrombosis prior to the diagnosis of ET or after the diagnosis.

Results
We evaluated 198 patients, 117 women (59%) and 81 men (41%) with an average age of 66.01 (± 15.66).
Regarding the driver mutation, 150 patients (75%) had Jak2, 31 (16%) CALR, 9 (5%) MPL, and 8 (4 %) were triple negative.
Before ET diagnosis, 36 (18%) had had a thrombosis and 17 (9%) a thrombosis after diagnosis.
54 (27%) patients died during the study period. The following table expresses the total survival.
Previous Thrombosis:
No: 162; Exitus: 43 (27%); Mean value (IC95%): 188 (156,43 ; 219,57); p-value: 0,642
Yes: 36; Exitus: 11 (31%); Mean value (IC95%): 220 (56,25 ; 383,76).
Posterior Thrombosis:
No:181; Exitus: 42 (23%); Mean value (IC95%): 199 (155,53 ; 242,468); p-value: 0,004
Yes:17; Exitus: 12 (71%); Mean value (IC95%): 115 (64,61 ; 168,39)

Conclusions
Thrombosis after the diagnosis of essential thrombocythemia decreases survival (p 0.004). However, thrombosis prior to the diagnosis of essential thrombocythemia does not modify survival.

P-36

A “massy” situation: giant cardiac myxoma as cause of cerebrovascular accident

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Background
Cardiac myxomas are the most common primary intracardiac tumors. Although myxomas are histologically benign, they are potentially dangerous due to the risk of systemic and cerebral embolism, with some studies estimating this risk to be as high as 30% to 40%.

Case description
A 67-year-old diabetic patient was admitted to the emergency department with sudden onset of dysarthria and central facial paralysis. He was then diagnosed with ischemic cerebrovascular accident due to occlusion of the middle cerebral artery. The patient undergone endovascular therapy, successful, with symptom resolution (NIHSS scale 0). His auscultation revealed an early diastolic sound followed by a diastolic murmur grade II/VI. An echocardiogram was requested, revealing a giant, mobile, globular mass in the left atrium, pedunculated and adjacent to the interatrial septum, with heterogeneous echogenicity and protruding into the left ventricular inflow in diastole . Contrast study was performed revealing contrast perfusion within the mass, suggestive of cardiac myxoma . The patient was proposed for cardiac surgery and a large, globular mass was extracted, then confirmed to be a cardiac myxoma.

Conclusion
This case highlights the role of echocardiography in the etiologic investigation of ischemic cerebrovascular accidents, as it facilitates the prompt identification of cardiac masses (e.g., myxomas) as potential sources of ischemic embolization. In the setting of cardiac myxomas, larger tumor size and irregular tumor surface morphology are associated with increased risk of embolism, and surgical therapy confers the best outcome.

P-39

Low Molecular Weight Heparin Resistance and Dabigatran Non Response in a patient presenting with provoked Pulmonary Embolism

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Background
Unfractionated heparin (UFH), low molecular weight heparin (LMWH), coumarin derivatives and direct oral anticoagulants (DOAC) are indicated for the treatment of Pulmonary Embolism (PE). While heparin resistance is a known entity, LMWH resistance and lack of response to DOACs are not well documented, as anti-factor Xa activity and serum DOAC levels are not routinely tested.

Material and Methods
We report a challenging clinical case of pulmonary embolism complicated with LMWH resistance, UFH resistance and possible non-response to Dabigatran.

Results

A 64-year-old man was admitted for chest trauma after falling from a height of 1.5 meters, with fracture of the 2nd to 8th left ribs, fracture of the scapula and hemothorax. Due to the development of severe respiratory failure on day 4 (D4) he was admitted to the intensive care unit and underwent a new thoracic computed tomography scan (CT scan) which revealed a peripheral pulmonary embolism (multiple repletion defects mainly involving the left lower lobe pulmonary artery). The same day he started LMWH (enoxaparin 1mg/kg/12h).

Given the lack of improvement in respiratory failure, which culminated in orotracheal intubation, the patient repeated the chest CT on D10, which showed PE progression even under anticoagulation with LMWH at a therapeutic dose. Treatment failure was assumed, and the patient immediately started UFH infusion while serum levels of antithrombin (AT) were assessed. AT assay revealed an AT deficiency of 34%. On D12, UFH was suspended (maximum UFH dose was 52800 UI/24h), without ever reaching therapeutic levels of activated partial thromboplastin time (aPTT), and infusion of Argatroban was initiated, with good aPTT response.

After clinical improvement, switching to Dabigatran 150mg/12h was attempted on D20, but failed to achieve therapeutic serum levels 4h and 6h after the first intake (4h=46.9 ng/mL ; 6h=34.1ng/mL). Dabigatran was then discontinued and Argatroban infusion restarted. A switch to Acenocoumarol (coumarin derivative) was attempted on D24, achieving a therapeutic INR on D28 (INR 2.1).

On D32 INR dropped to 1.6 and, since the patient had AT levels of 56%, he restarted enoxaparin 1.1mg/Kg/12h simultaneously with Acenocoumarol, but therapeutic levels of anti-factor Xa were never reached (maximum anti-factor Xa 0.29 IU/mL 4h after LMWH administration).

Conclusion

It is concluded that resistance to LMWH or DOAC should be considered in hospitalized patients with recurrence or worsening of thrombotic events under anticoagulant therapy with these drugs. LMWH and DOAC have predictable pharmacokinetics without the need for continuous monitoring, therefore the lack of evidence in the literature of resistance to therapy, resulting in high levels of residual factor Xa activity or low serum DOAC levels.

P-40

Early Mortality Risk Assessment in Pulmonary Embolism: The Role of D-Dimer Levels as a Distinctive Marker

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Introduction
D-dimers are fibrin degradation products, resulting from coagulation cascade activation.
Their use is usually as a dichotomic interpretation, in the context of suspected pulmonary embolism (PE), due to their high sensitivity value.
Parallelly, after PE diagnosis, the `Classification of pulmonary embolism and the risk of early (in-hospital or 30 day) death score` subdivides patients into four categories – High; Intermediate-high; Intermediate-low; Low risk - using clinical (Hypotension), laboratorial (NT-proBNP and troponin) and imagiologic criteria (right ventricle dilatation or dysfunction).
The distinction between low and intermediate risk categories is highly relevant for clinical practice, with therapeutic, need for hospitalization and prognosis implications. Being that the study of laboratorial biomarkers which can contribute for a more accurate risk classification is of the higher importance.

Material and methods
Single center cross-sectional study comprising 175 patients admitted to the emergency department due to PE with a low or intermediate gravity and mortality classification. Statistical analysis of the data was performed using Independent-Samples T Test and ROC curve analysis.

Results
From the total population (n=175), 65,7% were classified as having intermediate early death risk (n=115). There weren't significant statistic differences between the two groups related to past PE history (p=.087) or prevalence of Chronic Obstructive Pulmonary Disease (p=.215).
In comparison, the intermediate class group had a majority of older (72,3 vs 58,2 years; p<.05) and female patients (66,1% vs 43,9%; p<.05), and had more frequently I-troponin and Brain Natriuretic Peptide (BNP) elevation at admission (81,3 vs 3,9%; p<.05) and 84,6 vs 20,0%; p <.05, respectively).
Patients in the intermediate risk class presented with a higher D-dimer value (11.414 vs 6.498 ng/mL; p=.001) when compared with patient within the low-risk class.
For a defined D-dimers cut-off value of 5142 ng/mL), it was established a sensitivity of 70,2% and specificity of 67,3% for the differentiation between low and intermediate early death risk categories (AUC 0,699; CI 0,608 – 0,791).

Conclusions

The study suggests that patients with intermediate early death risk present higher D-dimer values when compared with low-risk patients.
As such, D-dimer value quantification and interpretation can be an important contribute to an early risk stratification in addition to the usual classification.

P-42

Etiologies of thromboembolic events: A cross-sectional study

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Background
Venous thromboembolism is the third most frequent cardiovascular syndrome. It manifests mainly as deep venous thrombosis (DVT) of the lower limbs or pulmonary thromboembolism (PE). The etiology of these events can be acquired or hereditary, and the same patient can have multiple causes. Knowledge of its etiology is relevant for the patient's management, since in some cases patients will need long-term hypocoagulation.

Material and methods
We conducted an analysis of patients with venous thromboembolic events (VTE) that were referred to outcare appointments of Internal Medicine over the past 27 months, between 2021 and 2023.

Results
A total of 38 patients were identified, 24 females and 14 males. The predominant age group was 50-59 years old (28.9%), but their age varied from 22 to 86 years old. 70% of these patients were referred after hospitalization for the VTE, 13.3% were sent after seeking the emergency department, 10% by the attending physician, and only 6.7% by another specialty. Thromboembolic events were diverse: 12 patients were referred due to PE, 8 due to DVT, 8 due to PE/DVT, 2 due to renal vein thrombosis, 2 with central retinal vein occlusion, 2 due to paradoxical embolism, 1 due to lacunar brain injury, and 1 due to splenic vein thrombosis.
We studied exhaustively 36 patients for VTE, while in 2 patients no study was carried considering their functional status and comorbidities. Thus, we researched possible hereditary causes of thrombophilia (factor V Leiden mutation, prothrombin G20210A mutation, protein C, S, and antithrombin factor deficit), as well as acquired, such as antiphospholipid antibody measurement and screening for active neoplasm, using upper and lower endoscopy, thoraco-abdominopelvic CT scan, and tumor markers, mainly PSA and alpha-fetoprotein.

We couldn't identify the cause of the VTE in 52.8% of the patients, however, 47.4% of them had a mutation in the MTHFR gene without associated hyperhomocysteinemia. In the other 47.2% of patients we identified a hereditary cause, an acquired cause or a combination of both. Thus, 27,8% of the cases were attributed to an acquired cause (40% with antiphospholipid syndrome, 20% due to taking contraceptives, 10% due to a lower limb fracture, 10% due to hyperhomocysteinemia, 10% due to an active neoplasm, 10% due to severe peripheral venous insufficiency and class III obesity); 22.2% of the patients had a hereditary cause (MTHFR gene mutation with hyperhomocysteinemia); 8.3% of patients had a combination of both (a third with MTHFR gene mutation with hyperhomocysteinemia and severe peripheral venous insufficiency, a third with factor V mutation and severe SARS-CoV2 infection and another third with May-Turner syndrome and contraceptive use).

Conclusions
By conducting this study, we can conclude that each patient fulfills at least one of the criteria of Virchow triad, such as alterations of the blood flow, endothelial injury, or a state of hypercoagulability. By detecting these changes earlier, we could possibly prevent a first episode of VTE and its long-term consequences, such as post-thrombotic syndrome, that impacts severely the quality of life of our patients.

P-47

Cryptogenic stroke: Who to blame?

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Cryptogenic stroke represents 30-40% of ischemic stroke events. According to Trial of Org 10172 in Acute Stroke (TOAST), it's defined as a stroke not caused by large artery atherosclerosis, cardioembolism or small vessel occlusion; is also defined as a stroke of undetermined etiology due to two or more causes being identified, negative or incomplete evaluation. Because approximately 1/4 of stroke survivors will likely have another stroke event, pursuing the mechanism is important in order to choose adequate therapy and lower the likelihood of recurrence.

We report the case of a 38 year-old woman who went to the emergency department (ED) with an history of two months of expressive aphasia and loss of sensibility at the right hemiface since the previous day. She had a prior head computed tomography (CT) and magnetic resonance imaging (MRI) which reported a recent hypodensity in cortico-subcortical posterosuperior left parietal topography and multiple scattered infracentimeter lesions reflecting chronic microvascular etiology. Blood tests at the ED showed thrombocytosis without signs of anemia or infection. Head CT revealed absence of new focal lesions, showing chronic evolution of the previously mentioned main ischemic lesion. The patient was admitted for

surveillance and etiologic investigation. From the study performed, she had a normal lipid profile, normal hemoglobin A1c, adequate thyroid function and no iron or vitaminic deficits. She also had a normal coagulation study with normal values of factor V, antithrombin III, protein S and C, and homocysteine. Other factors like Factor V Leiden, methylenetetrahydrofolate reductase polymorphisms, plasminogen activator inhibitor 1 4G polymorphism and Prothrombin G20210A are in progress. Antinuclear, anti-neutrophil cytoplasmic, anti-myeloperoxidase, anti-double stranded DNA and antiphospholipid antibodies were negative. Protein electrophoresis was normal, as well as complement levels. Serologies for viral hepatitis, human immunodeficiency virus and treponema pallidum were negative. She had a positive JAK2 V617F mutation test; the myelogram was diagnostic for essential thrombocythaemia (ET). She did a head CT angiography that excluded carotid stenosis, intracranial aneurysms or arteriovenous malformations, findings corroborated by a head MRI angiography. A twenty-four-hour holter monitoring was normal. The transthoracic echocardiogram suggested the existence of a right-to-left shunt at rest and transesophageal echocardiography with saline contrast injection confirmed the presence of patent foramen ovale (PFO). She was discharged under therapeutic hypocoagulation, anti-aggregation and hydroxyurea, maintaining outpatient follow-up.

This case is an example of a young woman with a cryptogenic stroke since she was at least two major causes for the event: ET and PFO. Hematologic disorders are unusual causes of acute cerebrovascular accidents, with a prevalence between 0% and 7%. PFO is an interatrial communication present in >25% of the adult population that can serve as a conduit for paradoxical embolization; with the use of contrast echocardiography, a strong association with cryptogenic stroke has become evident in younger patients. The evaluation of cryptogenic stroke requires a systematic evaluation of potential etiologies. Risk of recurrency is high, so defining the cause of the underlying event is crucial for the early institution of appropriate treatment and prevention.

P-50

Perioperative management of direct oral anticoagulants in trauma patients

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Background
The increased use of direct oral anticoagulants (DOACs) as prophylaxis in atrial fibrillation (AF) patients causes new problems in emergent surgery. The recommended period for postponing surgery after taking DOACs relays on pharmacokinetic calculations using elimination

half-lives after DOACs interruption. It is between 1 to 5 days, depending on drug in use and expected risk of bleeding. However, the recommendation is not supported by clinical outcome. The aim of this study was to compare the recommended withdrawal period of DOACs according to the currently valid guidelines and to drug concentrations in patients scheduled for emergent surgery.

Materials and methods

Eighteen patients receiving DOACs due to AF for at least 3 months, scheduled for emergent surgery at the Traumatology Clinic, Sestre milosrdnice University Hospital Centre were recruited in the study. Data related to prescribed DOACs, age, gender, ICD-10 diagnosis and time of last DOAC use were collected from medical records. Requested laboratory analyses prior to surgery included complete blood count, assessment of kidney function, coagulation status and determination of DOACs concentration. The creatinine concentration and the estimated glomerular filtration rate (eGFR) was determined in serum samples using the eGFR_CKD-EPI method. Dabigatran concentrations were measured in plasma samples using the Innovance DTI chromogenic assay whereas rivaroxaban and apixaban were measured using the Innovance Heparin assay on BCSXP coagulation analyser (all Siemens Healthineers, Marburg, Germany). Plasma DOAC concentrations were categorized as negative and positive according to a threshold of ≥30 ng/mL as a clinically relevant concentration. The time to surgery was analysed in relation to drug concentration and eGFR. P <0.05 was considered statistically significant. Statistical analysis was performed using MedCalc for Windows, version19.0.3(MedCalc, Belgium).

Results

Study subjects were mainly females (61%) with median age 81(62-92), scheduled for surgery, predominantly due to hip fractures. The most common type of DOAC in use was apixaban (n=10) and rivaroxaban (n=7) whereas dabigatran (n=1) was less represented. Median time of DOAC withdrawal prior to surgery was 2,5 days for the factor Xa inhibitors and 4 days for patient on dabigatran. Considering DOAC type, no statistically significant differences were found in day when surgery was performed (p=0.767). Nevertheless, for an eGFR <60mL kg1.73 m2 median time to surgery was 3.5 days in patients with drug concentration above threshold, whereas it was 2 days in patients with drug concentration below the threshold, independently on drug in use. When eGFR was >60 mL kg 1.73 m2 median time to surgery was 2 days in both, patients with and without drug concentration above the threshold. In majority patients (n=12) surgery was performed in neuraxial anaesthesia. The postoperative course without complications was recorded in 17 patients, while one patient died.

Conclusion

This study offers real-world data on perioperative management of DOACs in high-risk patients scheduled for emergent surgery. Guideline-guided time of drug withdrawal until surgery has been shown as a good practice, although DOACs concentration and expected risk of bleeding should be considered. However, to provide the best possible care, further research and tools are needed to harmonize and guide decisions in emergency patients.

P-54

Dual antiplatelet therapy duration in patients with acute coronary syndrome treated with percutaneous coronary intervention: how do we make decisions?

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Background
International guidelines recommend at least 12 months of dual antiplatelet therapy (DAPT) in patients with acute coronary syndromes (ACS), with the possibility of extension beyond 12 months in patients with low bleeding risk. However, the selection of patients who benefit the most from DAPT extension is often a topic of debate among clinicians. The use of clinical and technical aspects associated with increased thrombotic risk, as well as risk scores (e.g. DAPT score; Academic Research Consortium for High Bleeding Risk (ARC-HBR) criteria) may be considered for decisions. We aimed to assess how DAPT duration is managed in real-world clinical practice.

Material and methods
Single-center retrospective study including consecutive patients admitted for ACS at a tertiary center, from 2016 to 2018. All patients were evaluated at 1-year follow-up regarding the decision on extended treatment (ET) or standard treatment (ST). For those undergoing percutaneous coronary intervention (PCI), clinical and technical aspects associated with increased thrombotic risk, as well as 2 recommended risk scores (DAPT score and ARC-HBR score) were evaluated. Patients under anticoagulation were excluded.

Results
A total of 423 patients were included - mean age was 63±14 years, 70% (n=297) were male and clinical presentation was STEMI in 54% (n=229). Overall, 5% (n=22) underwent CABG, 91% (n=384) underwent PCI, and 4% (n=17) medical therapy, and from the whole population, 35% (n=147) remained on ET.
For PCI-treated patients, the mean DAPT score was 1,7±1,0 and 43% (n=166) patients had high-bleeding risk according to ARC-HBR criteria. Thirty-three percent of PCI patients (n=126) were under ET.
DAPT score, age, polyvascular disease, multivessel disease, presence of more than 3 stents, and previous myocardial infarction were individual predictors of ET – table 1. Moreover, all patients who had stent thrombosis remained on ET. On the other hand, high bleeding risk according to ARC-HBR, and anemia were predictors for ST.

After multivariate logistic regression, only polyvascular disease remained significantly associated with ET (OR 3.193 [1.003; 10.165]; p=0.049) and anemia with ST (OR 0.378 [0.166; 0.861]; p=0.021).

Conclusion
In this real-world ACS population, 30% of patients continued DAPT for longer than 1 year. For those undergoing PCI, besides stent thrombosis, and after adjusting for multiple clinical and technical aspects associated with increased thrombotic risk, only polyvascular disease was a predictor of longer DAPT, while anemia was a predictor of standard therapy. The optimal duration of DAPT following PCI is still up for debate and a perfect tool is yet to come.

P-59

The Mechanisms of platelet activation in Inflammation

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Background
Although the platelets' role in hemostasis is well established, their contribution to the inflammatory response remains poorly understood. This is particularly true for the complex interactions between inflammatory factors and platelet agonists.
Aims: This study aims to determine the effects of inflammatory factors such as lipopolysaccharide (LPS) on their own and in combination with platelet agonists.

Methods
The platelets from healthy donors are exposed to well-defined agonists, including ADP, PAR-1 agonist, TRAP, epinephrine, and serotonin alone or in combination with LPS to achieve a high level of platelet activation in an in vitro environment. The resulting changes in platelet function will be analyzed using flow cytometry to measure the expression levels of activation markers.

Results
Low concentrations of different individual agonists did not lead to significant platelet activation according to CD62P expression levels. PAR-1 agonist at 0.5μM concentration resulted in 7.3% ±4.2% (P=0.3365) CD62P expression in comparison with the control tube with no agonist present (3.06% ± 2.3%). 5μM epinephrine agonist led to 15.8% ± 14.26% CD62P expression by platelets in contrast to no-agonist condition (P= 0.4594). The presence of 1μg/ml LPS agonist showed the lack of significant effects with 4.5%± 3.5% in CD62P expression (P=0.9999) similar to the control levels observed with no agonist.

However, the combinations of agonists resulted in platelet activation and in some cases a remarkable synergy. The mixture of 1µg/ml LPS and 0.5µM PAR-1 led to 17.37% ± 5.6% (P=0.3305), 1µg/ml LPS and 5µM epinephrine caused 31.83% ± 4.4% (P=0.0045) and also, the combination of 5µM Epi and 0.5µM PAR-1 led to 73% ± 9.8% (P=<0.0001) CD62P expression by platelets.
The combination of LPS, PAR-1, and epinephrine with the same concentrations reached 66.8% ± 7.8% (P= <0.0001) CD62P expression, which is a strong platelet activation.

Summary
In conclusion, the preliminary results from this study using in vitro conditions showed that a combination of agonists resulted in significant platelet activation. However, a similar process should be examined during in vivo conditions that could be evaluated in further study.

P-65

Reversal of dabigatran with idarucizumab in a patient with acute kidney injury. A case report.

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Background
Dabigatran is an oral direct thrombin inhibitor indicated for prevention of stroke and systemic embolism in nonvalvular atrial fibrillation, treatment and prevention of deep vein thrombosis and pulmonary embolism, and prevention of venous thromboembolic events in surgical patients. Idarucizumab is a reversible antibody fragment which binds dabigatran to reverse its anticoagulant effect. Renal impairment is frequently associated to high concentrations of dabigatran, affecting the efficacy of standard dose of idarucizumab.

Material and methods
We describe a clinical case of an 89-years-old man admitted to the emergency department, with gross hematuria and acute kidney injury. He was under anticoagulation with dabigatran 110mg bid due to atrial fibrillation and CHAMDSMVASc 4. He had a prior history of right nephrectomy and bladder cancer. Laboratory evaluation showed hemoglobin 8,7g/dL, platelets 174x109/L, creatinine clearance 22ml/min/1,73m2, with abnormal coagulation tests: aPTT 98,1" (N:24,2-36,4), PT 24,9" (N:10,1-13,6), dabigatran concentration 494ng/ml (peak:52-275). After siphoning and fluid replacement therapy, hemoglobin levels continued to fall and the patient became hypotensive. Idarucizumab (5g) was administered and two packed red blood cells were transfused.

Results
The patient remained hemodynamically stable after idarucizumab administration. 48 hours after admission, as it was intended to perform a nephrostomy, coagulation evaluation was performed: aPTT 52,0", TP 15,9"and dabigatran concentration 109ng/ml. Sequential dabigatran serum levels were then obtained and, approximately 96 hours after idarucizumab administration, dabigatran concentration was 58ng/ml. Antibiotic therapy was given, resulting in kidney function normalization. Surgical intervention was postponed to after discharge.

Conclusion
This clinical case shows the importance of clinical awareness to possible late rebound of dabigatran levels after administration of idarucizumab, in patients with impaired kidney function.

P-67

Pulmonary embolism: Should we think of percutaneous catheter-directed treatment as an alternative to systemic thrombolytic therapy in high bleeding risk patients? A retrospective observational study

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Background
Acute pulmonary embolism (PE) is part of the third most frequent acute cardiovascular syndrome. Reperfusion therapy with systemic thrombolysis is the treatment of choice in patients with high-risk PE and the rescue therapy in patients who evolve to hemodynamic deterioration under anticoagulation treatment. Surgical embolectomy and percutaneous catheter-directed treatment (CDT) are recommended in patients whom thrombolysis is contraindicated or has failed.

Material and methods
An observational retrospective study was conducted in our center considering patients with the diagnosis of PE at the emergency department from January 2015 to December 2017. Data regarding sociodemographic characteristics, clinical presentation, medical background, and therapeutic decisions were collected. Additionally, follow-up until December 2019 was performed to evaluate long term outcomes.

Results
240 patients presented the diagnosis of PE. The mean age was 69 (SD ± 17) years with 66% of females. The most prevalent comorbidities among these patients were cardiovascular risk factors, with hypertension being the most expressive one (55%) and active neoplasm (17%). Nearly a third of the patients (29%) were classified has having a high-risk or interme-

diate-high risk PE. All patients early started on anticoagulation. Reperfusion treatment was performed in nine patients (4%), with systemic thrombolysis being the treatment of choice, representing 26% of the patients with high-risk PE. Surgical embolectomy and percutaneous CDT are not available in our center and were not performed. The intra-hospital mortality rate was 10%, mean age of 77 (SD ± 11) years. Of these patients, 48% presented high or intermediate-high risk PE on admission. This represents a mortality rate of 11% among high-risk patients and 20% among intermediate-high risk PE patients, significantly different from 5.2% among low or intermediate-low risk PE patients ($p<0.05$). 29 patients (12%) died during the follow-up period. 24% of the patients reported persisting symptoms and functional limitation since the event. Chronic thromboembolic pulmonary hypertension was documented in 13% of the patients.

Conclusions
The treatment of PE remained the same for several years, with focus on hypocoagulation and systemic thrombolysis. However, the most recent literature has described the experience of some centers using percutaneous catheter-directed treatment under the PE response team (PERT) model with enthusiastic results. Despite these recommendations, only 26% of high-risk PE patients were managed with systemic thrombolytic therapy at our hospital. Among the 35 patients with intermediate-high risk PE, all were on anticoagulation with no further therapeutic interventions, even those with clinical deterioration and death. Only 3 of these patients had formal contraindication to the procedure. The reluctance to use thrombolytic therapy even in the absence of contraindications might be explained by a perceived increased risk of bleeding in patients with active malignancies, advanced age, or multiple comorbidities. Percutaneous CDT has been proposed as an alternative to thrombolysis in patients with a perceived increased risk of bleeding, showing minimal major bleeding and improvement in right ventricular function. The creation of a PERT model in our center and similar centers could improve the identification of patients with the greatest benefit in referral for percutaneous CDT.

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Management of anticoagulation in gastrointestinal bleeding – a case report

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Anticoagulant therapy is indicated in highly prevalent cardiac pathologies, such as atrial fibrillation (FA), and pretend to reduce thrombotic risk associated to these pathologies. However, as a possible side effect, they cause bleeding with a high rate of morbidity and mortality, with gastrointestinal bleeding being one of the most relevant. These hemorrhages occur more frequently with direct oral anticoagulants (DOAC) than warfarin, except for apixaban and are also related to the dose, so reduced dose may reduce risk. These hemorrhages reflect

any underlying gastrointestinal pathology, namely malignant neoplasm, diverticular disease, gastritis, peptic ulcer, esophagitis and angiectasia. Sometimes bleeding episodes are the first manifestation of these diseases. Thrombotic and bleeding risk management in these patients is very complex.

Method

We present a clinical case of a patient under anticoagulation with recurrent gastrointestinal bleeding, followed at immunohemotherapy consultation.

Results

A 77-year-old male patient went to the emergency department due to extreme tiredness and melena. He had a personal history of atrial fibrillation medicated with rivaroxaban, heart failure with preserved ejection fraction, arterial hypertension, diabetes mellitus, neuroendocrine tumor of the colon underwent surgery. Analytically, hemoglobin (Hb) was 5.6 g/dl and had absolute iron deficiency, with CHA2DS2–VASc 6 points and HAS-BLED 3 points. He had transfusion support (TS) with 2 units of erythrocyte concentrate (UCE) and 1 g of iron carboxymaltose (ICM). He interrupted the anticoagulation and started a proton pump inhibitor. During this period, he underwent upper digestive and videocapsule endoscopy, which documented congestive and eroded gastric folds and ileal angiectasia, respectively. Restarted rivaroxaban two weeks later. On reassessment at our consultation, he was more tired than usual, referring darker stools. It was documented decrease in Hb, without the TS need. He switched to dabigatran at a reduced dose (110mg bid) because of high bleeding risk. About 2 months later, he had a new drop in hemoglobin, requiring 1 UCE and iron deficiency, which was corrected with CMF. The anticoagulation is interrupted again for 2 weeks, he switched to warfarin and a cardiology consultation is requested to assess the hypothesis of closure of the auricular appendix. Due to INR lability, switched to apixaban. Currently, the patient is waiting for closure of the auricular appendix and evaluates his hemoglobin weekly. When he starts to feel more tired, with significant hemoglobin drop to values close to the transfusion need, he interrupts apixaban. The kinetics of iron, folic acid and vitamin B12 are frequently evaluated in order to avoid deficiencies. The patient manages to maintain anticoagulation for about 3 to 4 weeks with no TS need and recovers hemoglobin levels in approximately 7 to 10 days.

Conclusion

The management of anticoagulation in patients with high thrombotic and hemorrhagic risks is a huge challenge. It should be performed individually and in multidisciplinary teams to optimize anticoagulant therapy, reducing bleeding episodes and improving quality of life, reducing symptoms and transfusional support need. It is also important to diagnose pathology underlying the gastrointestinal bleeding to be treated.

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Eicosapentaenoic acid significantly enhances the activity of various antiplatelet drugs in vitro

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Background
Several studies have approved that the consumption of the omega-3 fatty acid eicosapentaenoic acid (EPA, 20:5Μ3) from a variety of foods and supplements could reduce cardiovascular events. The combination of EPA with the antiplatelet drugs aspirin (ASA), an inhibitor of cyclooxygenase-1 (COX-1), ticagrelor, an inhibitor of the receptor P2Y12, vorapaxar, an inhibitor of the PAR-1 receptor, was evaluated against in vitro platelet aggregation induced by several agonists.

Materials and Methods
Platelet-rich plasma (PRP) was prepared from the whole blood of apparently healthy people. Platelets were pre-incubated at 37 °C for 10 min with the fatty acid EPA followed by 1 min of incubation separately with the antiplatelet drugs ASA, ticagrelor, and vorapaxar. Light transmittance aggregometry was performed in PRP in the presence of the agonists arachidonic acid (AA, 300 μM), ADP (6 μΜ), and thrombin receptor activating peptide-6 (TRAP-6, 10 μΜ), an agonist of the PAR-1 receptor.

Results
We evaluated the dose effect of EPA and the antiplatelet drugs, and then we tested the combination of EPA with each of the previously mentioned drugs on the aggregation of platelets. Platelet activation with AA: EPA and ASA exhibited 22.5±3.5 % and 11.50±7.5 %, inhibition at concentrations of 125 μMand 25 μMrespectively. The combination of EPA (125 μΜ) with ASA (25 μΜ) exhibited 92.6±9.5 % (n=5) inhibition ($p<0.001$ compared with ASA). Activation of platelets with ADP (6 μΜ): EPA and ticagrelor exhibited 22.5±9.5 % and 21.3±13.0 % inhibition at concentrations of 125 μMand 0.125 μMrespectively. The combination of EPA (125 μΜ) and ticagrelor (0.125 μΜ) exhibited 66.7±3.7 % (n=4) inhibition ($p\leq0.001$ compared with ticagrelor). Activation of platelets induced by TRAP-6 (10 μΜ): EPA and vorapaxar exhibited 17.9±7.6 % and 24.7±0.9 % inhibition at concentrations of 75 μMand 0.25 μMrespectively. The combination of EPA (75 μΜ) with vorapaxar (0.25 μΜ) exhibited 79.3±2.4 % (n=4) inhibition ($p\leq0.004$ compared with vorapaxar).

Conclusions
EPA strongly enhances the inhibitory effects of ASA, ticagrelor, and vorapaxar on platelet aggregation induced, respectively, by AA-, ADP-, and TRAP-6 platelet aggregation. The importance of these findings needs further clarification.

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