# 13th Central European Vascular Forum - CEVF
# 3rd IUA Multinational Chapter Congress

International Union of Angiology
Union Internationale d'Angiologie

## Ljubljana, Slovenia, September 19-21, 2024

# BOOK OF ABSTRACTS

# 13th Central European Vascular Forum - CEVF
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**EDITORS**

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# WELCOME ADDRESSES

## DEAR COLLEAGUES, DEAR FRIENDS!

It is our great pleasure and privilege to welcome you at the joint congress of the Central European Vascular Forum and the International Union of Angiology – Multinational Chapter, hosted by the Slovenian Society for Vascular Diseases in the captivating city of Ljubljana.

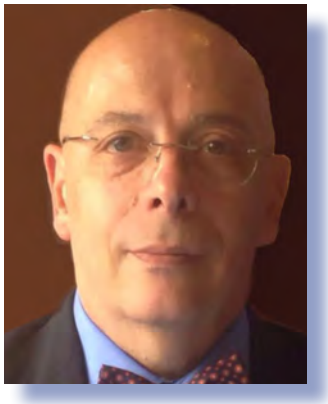
The scientific program covers all aspects of vascular medicine – from peripheral arterial disease, venous thromboembolism and insufficiency to rare vascular diseases and lymphedema, also addressing the preventive vascular medicine and the full spectrum of treatment, including vascular interventions. The distinguished speakers will present state of the art and plenary lectures, while researchers and clinicians will have the opportunity to present their work in the form of an oral presentation or poster session.

Ljubljana, the charming capital of Slovenia, is a trendy, friendly, green, and vibrant city, recognised as one of the best European tourist destinations and the perfect conference and congress city.

We eagerly anticipate your arrival and look forward to meeting you.

**Vinko Boc**
*President of the Congress*

## DEAR FRIENDS,



It is a great pleasure to announce the JOINT CONGRESS of CEVF and the IUA MULTINATIONAL CHAPTER organized by the SLOVENIAN SOCIETY FOR VASCULAR DISEASES in Ljubljana.

The scientific programme includes multidisciplinary symposia, lectures, and free paper and poster sessions on the major topics and advances in the fields of angiology, vascular and cardiovascular medicine and surgery, phlebology, lymphology, thrombo-embolic disease, and interventional techniques.

An outstanding Faculty has been assembled to provide the most up-to-date best practice guidelines on vascular topics.

I would like to invite you to join us in this project and actively contribute by providing examples of your scientific work to the Meeting. You will be able to meet many European and international specialists and discuss clinical cases, new research results, and major advances in the fields of angiology, phlebology, vascular medicine, and surgery.

I look forward to seeing you in Ljubljana!

**Pier Luigi Antignani**
*President of the Central European Vascular Forum – CEVF*

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# Oral Presentations

## CEVF Symposium: Peripheral Arterial Disease - Indicator of Polyvascular Disease

### Relationship between PAD and cerebro-vascular disease

Novo Salvatore[1]

[1]*International School of Cardiology, "Ettore Majorana" Foundation and Centre for Scientific Culture, Erice , Italy*

Atherosclerosis (ATS) is often a polyvascular disease interesting contemporaneously several arterial districts.

Most people think of these conditions as separate diseases, but really they are the same disease, just occurring in a different part of the body.

PAD involves ATS of the peripheral arteries, the arteries that supply blood to our arms and legs.

Stroke can be caused by ATS, or plaque rupture, but not all strokes are caused by ATS; a stroke can also be caused by a blood clot that starts in one part of the body, travels to the brain and gets stuck in an artery (i.e. when there is a PFO).

There are several risk factors that may influence development of ATS. As the age increase, normally, the risk for these conditions increases and if there is a family history, patients are more likely to develop heart disease, PAD and stroke.

PAD affects people mostly over the age of 65. But it also may affect younger people who have additional risk factors, such as diabetes, smoking, high blood pressure (BP), dislypidemia, in particular hypercholesterolemia, and obesity as well as inflammatory conditions.

Patients with polyvascular disease and diabetes are at the highest PAD risk. Approximately one-third of patients will die within five years of a PAD diagnosis, and 20% will experience a heart attack or stroke. Although peripheral artery disease primarily affects large arteries outside the brain, PAD is also associated with elevated cerebral vulnerabilities, including greater risks for brain injury (such as stroke), cognitive decline and dementia.

Several studies have demonstrated that PAD is associared with an increased risk of stroke, TIA, and vascular events or vascular death.

So, in patients with PAD it is very important the correction of known risk factors to slow the progression of PAD as well as to prevent cerebro-vascular and cardiac events. In particular, it is very important to stop smoking and to reach the appropiate target of Blood Pressure, glycemia and glycated haemoglobin and LDL-Cholesterol as suggested by Guidelines.

# PAD and risk for coronary artery disease

Rodica Avram

# Estimation of risk for cardiovascular events in patients with polyvascular disease

Borut Jug

# Diagnostic assesment to patients with polyvascular disease

Pier Luigi Antignani

# Conservative treatment of patients with polyvascular disease

Barbara Krevel[1]

[1]*Clinical Centre Ljubljana, Slovenia*

Numerous studies have established a clear link between polyvascular disease (PVD) and an increased risk for adverse cardiovascular events. However, despite available conservative treatment options these patients frequently remain undertreated, which might be at least partially attributed to the lack of clear therapeutic recommendations for this very high-risk subgroup of patients.

All patients with cardiovascular disease (CVD) should be encouraged to maintain a healthy lifestyle and receive guidance on dietary restrictions, smoking cessation and regular physical activity.

Considering the very high cardiovascular risk associated with PVD, utilization of intensified antithrombotic treatment strategies might seem warranted; nevertheless, the decision on appropriate antithrombotic therapy should be based on careful consideration of the expected cardiovascular risk reduction and possible haemorrhagic complications. In accordance with the results of the COMPASS study, it is reasonable to consider a combination of aspirin and low-dose rivaroxaban in patients with PVD and without significant bleeding risk, especially in those with stable lower extremity peripheral artery disease, prior lower extremity revascularisation or coexisting diabetes. Prolonged dual antiplatelet therapy (DAPT) (a combination of aspirin and P2Y12 inhibitor) may be considered in patients after acute myocardial infarction or percutaneous coronary intervention and with significant involvement of extracardial arterial beds. In stable asymptomatic PVD patients, routine long-term DAPT is not recommended due to the high risk of haemorrhagic complications associated with prolonged use of DAPT.

Lipid lowering should begin with a high-intensity statin at maximum tolerated dose, targeting a ≥50% low-density lipoprotein cholesterol (LDL-c) reduction from baseline and LDL-c < 1.4 mmol/L. Ezetimibe and PCSK-9 inhibitors should be added only in patients who do not achieve the recommended treatment goals. According to the current recommendations, lower LDL-c target (< 1.0 mmol/l) should be considered only in patients with atherosclerotic CVD, who experience two cardiovascular events (not necessarily of the same type) within 2 years.

In regard with other risk factors (diabetes and hypertension), clinicians should strictly adhere to treatment recommended by current societal guidelines. Anti-inflammatory treatment with low-dose colchicine may be considered in patients with recurrent CVD events despite optimal therapy.

Further studies with targeted inclusion of patients with PVD are needed to establish the optimal conservative management of these patients.

# Treatment of patients with polyvascular disease: Surgical options

Arkadiusz Jawien

# Young IUA Symposium: IUA Position Statements

## International Union of Angiology Position Statement on no-option chronic limb threatening ischemia

Michal Juszynski[1]

[1]*Medical University of Warsaw, Warsaw, Poland*

The incidence of peripheral artery disease (PAD) has increased over the years due to population ageing and the global epidemic of diabetes. Some patients progress to chronic limb-threatening ischemia (CLTI).

Management decisions in the patient with CLTI are derived from the clinical presentation, physical examination, and review of non-invasive vascular studies, with consideration of risk factors that impact a decision for intervention or conservative care.

The approach is tailored to each patient based upon several factors, including presence and degree of tissue loss, patient-specific vascular anatomy, availability of vascular conduits for revascularization, and comorbidities such as cardiac disease and renal insufficiency. All patients with CLTI should receive best medical therapy including the use of antithrombotic, lipid-lowering, antihypertensive, and glycemic control agents, wound infection management as well as counselling on smoking cessation, diet, exercise, and preventive foot care.

The optimal revascularization strategy is influenced by the availability of autogenous vein for open bypass surgery. Vein bypass may be preferred for average-risk patients with advanced limb threat and high complexity disease, while those with less complex anatomy, intermediate severity limb threat, or high patient risk may be favored for endovascular intervention.

Unfortunately, for some patients defined as “no-option”, the most appropriate choice could be primary amputation or palliation. In these patients, the effectiveness of innovative revascularization strategies or non-revascularization therapies (spinal cord stimulation, lumbar sympathectomy, pneumatic compression, prostanoids, and hyperbaric oxygen) has not been well established. In addition, regenerative medicine approaches (cell and gene therapies) for CLTI patients should be restricted to rigorously conducted randomized clinical trials.

In this position statement document, the authors report all conditions for the correct management of the no-option CLTI including the wound treatment and the rehabilitation. This position paper, written by members of International Union of Angiology Youth Committee and senior experts, shows an overview of therapeutical approaches for patients with CLTI and absence of 'standard' solutions for revascularization. The aim was to demonstrate the accurate management of the 'no-option' CLTI patient including the wound treatment and the rehabilitation, considering always the goal of the increase of quality of life of the patients.

# Vaccines Directed Against Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9)

Andrej Juretič[1]

[1]*Ukc Lj Kožb, Grosuplje, Slovenia*

Despite progress in primary and secondary prevention, atherosclerotic cardiovascular disease remains one of the leading causes of mortality. Long-term exposure to elevated levels of low-density lipoproteins (LDL)-cholesterol is a significant risk factor for its development. Various treatment strategies for hypercholesterolemia exist; however, their success is limited. Treatment with tested and registered humanized monoclonal antibodies against proprotein convertase subtilisin/kexin type 9 (PCSK9) is not widely available due to high costs.

One potentially effective treatment currently under preclinical and clinical investigation is the development of vaccines against PCSK9. This could ensure a long-term reduction of total and LDL-holesterol in an effective and affordable way. Preclinical research on animal models and a smaller clinical study indicate that these vaccines induce a significant, long-lasting antibody response that effectively lowers LDL- and total cholesterol levels without significant side effects. Larger clinical phases II and III studies are still needed to further elucidate the safety and efficacy of PCSK9 vaccines. In this articlee the current knowledge in the field is briefly summarized.

# IUA position statement on perioperative drug and hemostasis management in vascular surgery

Joao Rocha Neves

# IUA consensus document on vascular compression syndromes

Mario D'Oria

# Microcirculation

## The link between macro- and microcirculation and its deterioration

Mateja Kaja Ježovnik

# Involvement of microcirculation in the development of CLI

Pavel Poredos[1]

[1]*University Medical Centre Ljubljana, Ljubljana, Slovenia*

Critical limb ischemia (CLI) represents the most severe pattern of peripheral arterial disease (PAD) associated with the high risk of major amputation, cardiovascular events and death.

CLI is a consequence of advanced atherosclerosis with multilevel occlusion of peripheral arteries and deterioration of microcirculation. Microcirculation plays a critical role in tissue oxygenation and tissue survival. In physiologic conditions, patent proximal conduit arteries provide adequate blood supply of microcirculatory bed. Normal perfusion pressure provides pulsatile blood flow, vasodilation of precapillary arteries. Leucocytes and erythrocytes whose diameter is bigger than the diameter of capillaries adapt their shape and rotate during passing capillaries which decrease blood viscosity and promote blood flow and oxygen supply. In the case of significant stenosis or occlusion of proximal arteries vasoconstriction in precapillary sphincter appears, blood cells become rigid, vasomotion disappears and in advanced hypoxia, because of platelet activation and activation of coagulation, micro thrombosis appears. All these processes cause tissue ischemia and devitalization. In hypoxia also leucocytes are activated and produce proteolytic enzymes, which damage vessel wall and aggravate ischemia. Further, reduction of perfusion pressure increases haematocrit and blood viscosity in microcirculatory bed. Therefore, state of microcirculation has a crucial role in tissue oxygenation and development of CLI.

# Diagnostic procedures for detecting microangiopathy

Patric Carpentier[1]

[1]*Grenoble - Alps University, Grenoble, France*

A huge number of techniques are able to detect the many microvascular dysfunctions related to peripheral arterial, venous or microvascular diseases. However, the most useful in clinical practice are those which measure the distal perfusion pressure, most often similar to the distal systolic arterial pressure, and the direct observation of the superficial skin capillaries, through capillaroscopy, which is able to detect the capillary microangiopathy itself.
The presentation will focus on these two approaches and their complementarity that will be illustrated with the clinical model of systemic sclerosis.

# Management of diabetic microangiopathy

Pier Luigi Antignani

# Presidential Lectures

## How noninvasive investigations have modified our therapeutical approach

Pier Luigi Antignani

# Interrelationship between arterial atherosclerosis and venous disease

Pavel Poredos

# Carotid atherosclerosis is predictive of coronary atherosclerosis and events?

Novo Salvatore[1]

[1]*International School of Cardiology, "Ettore Majorana" Foundation & Centre for Scientific Culture, Erice, TP, Italy & Department PROSAMI, University of Palermo, Palermo, Italy*

We present data deriving from two personal clinical-epidemiological studies, the first one on the value of carotid ultrasound (CUS) in increasing the prediction CV risk in primary prevention and the second one demonstrating the value of CUS in predicting coronary ATS detected with coronarography (CVG) and SYNTAX score, in secondary prevention.

1st study. Background and Aim: Cardiovascular diseases (CVD) represent important causes of morbidity and mortality. Our study aimed to evaluate CV risk using the EuroSCORE, ECG and CUS for prevention in subjects aged 50-70 years, asymptomatic and without known CVD.

Methods: 1860 subjects were consecutively screened in 2016-2019 in the context of the Project "No Infarction, No Stroke" promoted by the District 2110 (Italy & Malta) of the Rotary International, in cooperation with the Division of Cardiology of the University Hospital "Paolo Giaccone" of Palermo (Head: Prof. Salvatore Novo). History of CVD, risk factors (RFs), ECG and CUS were evaluated. Intima-media thickness (IMT) was defined as wall thickness > 0.9 mm, while focal thickening ≥ 1.5 mm protruding into the lumen as asymptomatic carotid plaque (ACP).

Results: of the total of 1860 screened subjects, 393 (21.1%) had no RFs, 780 (42%) hypertension, 571 (30.7%) hypercholesterolemia, 557 (29.9%) diabetes, 474 (25.5%) smoking, 648 (34.8%) overweight, 300 (16.1%) obesity and 184 (9.9%) MetS. Carotid ATS was detected in 903 (48.5%) subjects, 821 (44.1%) had IMT and 547 (29.4%) ACP, significantly related to diabetes, hypertension and hypercholesterolemia. Atrial fibrillation was found in 29 subjects (1.6%) and Brugada pattern in one. Using EuroSCORE, 220 subjects resulted at low risk (11.8%), 1338 at moderate (71.9%), 292 at high (15.7%) and 10 at very-high risk (0.5%). Adding ACP 547 subjects (29.4%) resulted at more high risk.

Conclusions: A total of 302 (16.2%) subjects were at least at high risk/very high for CV events according to the EuroSCORE, increasing to 547 (29,4%, P < 0.001) adding ACP.

2nd study. Background and Aim: several studies have shown that the risk of CV events is higher in subjects with CUS evidence of subclinical carotid ATS. The aim of our study was to evaluate the association of CUS-ATS with the severity of coronary artery ATS (CAD) in patients with typical chest pain undergoing diagnostic CVG during hospitalization.

Methods: we studied retrospectively 1067 patients admitted to our Hospital consecutively (2004–2014) for chest pain that underwent CVG. The study of carotid ATS was performed as described previously. During the CVG we considered one, two or three vessel disease if coronary vessels had stenosis > 50%.

Results: CUS examination showed an 81% prevalence of ACPs, whereas CVG demonstrated that 12% of patients had normal coronary arteries. The detection of ACP was predominantly associated with the presence of coronary ATS in 72,8% of patients (P=0,001). In particular, the presence of ACPs with a diameter > 2,5 mm (P < 0,0001) was associated with a higher prevalence of coronary ATS. Dimensions of ACPs were significantly related with the complexity of coronary ATS as calculated by Syntax score (P < 0,0001). Moreover, bilateral ACPs was associated with coronary ATS too (P < 0,0001). Besides the detection of ACPs was strongly related with the coronary ATS itself (overall P=0,006).

Conclusions: given the significant correlation between the carotid ATS and the severity of CAD (in terms of number of involved vessels), we believe that the CUS evaluation might provide to the clinician additional information about the global CV risk of the patients and the presence of ACP may be predictive of coronary ATS and its severity.

General Conclusions: in primary prevention the detection of ACP wit CUS examination consent the reclassification of subjects in a superior category of risk, suggesting a more aggressive pharmacological therapy (LDL-C levels between < 70 and < 55 mg%). If subjects remain asymptomatic the good

correlation between carotid and coronary ATS consent to avoid more expensive (CAC) or aggressive methods (CVG) to allow an effective prevention. Of course, when the patients became symptomatic CVG became mandatory to evaluate better the coronary bed in order to perform revascularization with PCI or surgery according to the anatomy of coronary bed.

# Anticoagulant Therapy and Venous Thromboembolism

## Treatment of upper extremity DVT with DOACs

Maria Cristina Vedovati

# Extended treatment of venous thromboembolism

Paolo Prandoni[1]

[1]*Arianna Foundation on Anticoagulation, Bologna, Italy*

After discontinuing anticoagulation, the risk of recurrent venous thromboembolism (VTE) in patients suffering an episode of unprovoked or weakly provoked VTE ranges between 30 and 50%, the rate being higher in patients with primary deep-vein thrombosis (DVT). Baseline parameters that increase this risk are male sex, obesity, the carriership of thrombophilia, the proximal location of DVT, and renal failure. While the latest international guidelines suggest indefinite anticoagulation for most such patients, new scenarios are being offered by the availability of risk stratification models, which have the potential to identify patients in whom anticoagulation can be safely discontinued because of a low risk of recurrence, and those in whom extending anticoagulation is undesirable because of a high risk of bleeding. Low-dose apixaban and rivaroxaban are the mainstay of extended treatment of VTE in all patients but those who are carriers of the antiphospholipid syndrome. As an alternative, low-dose aspirin and sulodexide have been reported to decrease by 30 to 50% the risk of recurrent events without increasing the bleeding risk.

# Cancer-associated venous thromboembolism and thrombocytopenia

Gregor Tratar[1]

[1]*Univerity Medical Centre Ljubljana, Department of Vascular Diseases, Ljubljana, Slovenia*

Venous thromboembolism (VTE) often occurs in patients with cancer. Risk of VTE is increased because of prothrombotic state (platelet activation, increased tissue factor expression) as well as cancer treatment (surgery, central venous lines, chemotherapy). On the other hand, thrombocytopenia also frequently develops in cancer patients due to cancer itself (e.g. in haematological malignancies) or due to anti-cancer therapy. Management of cancer-associated thromboembolism (CAT) in patients with thrombocytopenia is therefore challenging because of increased risk of recurrent VTE on one hand and increased risk of bleeding on the other. Generally, use of full-dose anticoagulation is considered safe in patients with platelet count above 50 X 109/L. In patients with more pronounced thrombocytopenia however, careful assessment of VTE recurrence risk and risk of bleeding has to be made. In this paper, we review current recommendations regarding thrombocytopenia and CAT management in these patients.

# VAS Symposium: Buerger's Disease Pathophysiology: From Hypotheses to Evidence Synthesis

## Is Buerger's Disease a variant of atherosclerosis?

Takehisa Iwai

There are few immunological studies on Buerger's disease or thromboangiitis obliterans (TAO), but it is likely an immunological pathology that transitions from acute to chronic inflammation. The fact that atherosclerosis (AS) is a chronic inflammation with acquired immunity has already been accepted. From this point of view, we will review the two chronic arterial occlusions and give an outline of the treatment.

The subjects were cases in which immunological studies were performed on TAO and AS. In addition, 22 samples from 11 rats in the chronic phase at the 4th week of experimentally periodontal bacteria induced arterial thrombus were used, in which Buerger disease-like pathological findings were obtained. And 11 human cases with AS were also included. From the literature, 9 cases of TAO by Kobayashi and 8 cases by Lee were used as reference cases. And our 2 cases of TAO will be used.

Results: T cells were detected in the all cases, although there were some differences. Macrophages and lymphocytes were also found in almost all cases.

From the above, it was understood that TAO and experimental animals are pathologically characterized by chronic inflammation, just like AS. On the other hand, considering that TAO is a condition with no risk factors other than smoking, and AS also includes risk factors such as hyperlipidemia, diabetes, hypertension, and dialysis, TAO can be divided into simple and the others into complex. The most likely causes of acute inflammation are gram-negative anaerobic bacteria such as periodontal disease bacteria or Chlamydia pneumoniae. Since no infection (attachment or proliferation) is observed in pathological points, it would be more reasonable to assume that the cause is the attachment or persistence of bacterial DNA.

Conclusion: TAO currently exists as a chronic inflammatory arterial occlusive disease in young people, but the number of cases that meet the strict definition will decrease dramatically. As has been argued, its symptoms and findings can be explained by bacterial embolism caused by uptake into platelets or monocytes. The pathology is similar to AS. From the above, it is considered appropriate that TAO exists as part of AS.

# Is Buerger's Disease a rickettsial infection?

Pier Luigi Antignani

Buerger's disease (BD) is a chronic inflammatory vasculitis of unknown etiology. The infectious etiology of BD was proposed by Buerger in 1914. Furthermore, there are scattered reports insisting that BD may be related to rickettsial infection, first asserted by Goodman since 1916, followed by Giroud and other French investigators from the 1940s through the 1960s, Nicolau in the 1960s, Bartolo (1980s), and Fazeli (2010s). However, their causal relationship has hardly been accepted because rickettsial infections are known to be acute febrile, vector-borne illnesses, whereas BD is a chronic afebrile illness. Some authors hypothesize that BD patients acquired a rickettsial infection far before the onset of BD. Over years, the infected area expands to become a segment of the infected vessel. Subsequently, thrombus develops on the luminal surface of the infected endothelial cells, which produces the vascular obstructive manifestations of BD. Collectively, it is postulated that BD is a chronic infection with a member of the family Rickettsiaceae with superimposed thrombosis.

We report the experience of our group: specific seroagglutination tests were performed in 70 patients with Buerger's disease to detect possible antibodies to rickettsia, the test being repeated in 8 cases after activation by doxycycline administration over 10 days. In 21 patients a Weil-Felix test was also carried out. Tests were assessed as positive in 44 cases (62.8%): 18 times for Rickettsia Q. 18, 14 times for Rickettsia Mooseri, 13 times for Rickettsia Burnetii, 5 times for Rickettsia Conorii and 3 times for Rickettsia Prowazekii. After activation by doxycycline the antibody titre was increased 5 times, unchanged 3 times and reduced once. The Weil-Felix gave positive results in 3 of the 21 cases (14.28%), the reaction being positive to Rickettsia Prowazekii. These findings provide supplementary arguments for a possible pathogenic role of rickettsial infection in Buerger's disease and for the role of doxycycline treatment.

# Smoking and Buerger's Disease

Andrzej Szuba

Buerger's disease (thromboangiitis obliterans) affects mainly young smoking men of Asian and Eastern European origin. Typical symptoms include peripheral ischemia with severe pain and quick progression to necrosis, migratory superficial thrombophlebititis and Raynaud phenomenon. Pathophysiology of BD is not fully understood, however it is clearly related to smoking. Tobacco exposure is required for both disease initiation and progression. Possible mechanisms include immunologic dysfunction and tobacco hypersensitivity. Buerger's disease incidence worldwide is decreasing and the decrease is only weakly related to fall in tobacco consumption and cigarette smoking. Socioeconomic status and its impact on oral hygiene and better diet may also play role. However precise disease mechanisms remain obscure.

# Inflammation and immune dysregulation in Buerger's Disease

Fazeli Bahar

Inflammation of the layers of the vessel wall, inflammatory thrombus and neuritis of the involved limb are the characteristics of Buerger's Disease (BD). For these reasons, BD can be considered a type of vasculitis. However, it is more effective to manage it as a peripheral arterial disease rather than a type of vasculitis. On the other hand, immunosuppressant therapy is not typically considered for BD patients, although several auto-antibodies have been detected in BD. Notably, the footprints of infectious pathogens, including Rickettsia and oral bacteria, in the vascular lesions of BD have been reported for decades. Until recently, however, only the genome of the pathogens has been detected—not the whole pathogen. Therefore, it has been suggested that BD is a type of infectious induced autoimmunity, but this hypothesis cannot not explain the close relationship between BD and tobacco smoking. Another hypothesis holds that BD consists of a hypersensitivity to an unknown agent in tobacco, which is supported by the occurrence of thrombophlebitis migrans hours after smoking in BD patients who have given up smoking or a burning sensation in the toes of the involved limb during smoking. Yet, according to several studies, it appears that the T-cells are the main players in BD pathogenesis. The hypersensitive immune response by the T-cells (type IV) cannot explain the rapid clinical reactions of BD patients after smoking tobacco. Another hypothesis that deserves further investigation is neurogenic inflammation as the first event in BD.

# International Delphi consensus on diagnostic criteria for Buerger's disease

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Buerger's disease (BD) remains a debilitating condition and early diagnosis is paramount for its effective management. There are many published diagnostic criteria for BD, but different vascular centers utilized different criteria to diagnose BD worldwide. Therefore, we conducted an international Delphi Consensus Study to determine the gold standard diagnostic criteria for BD globally. Our study showed that none of these published diagnostic criteria have been universally accepted as a gold standard. Apart from the presence of smoking, these published diagnostic criteria have distinct differences between them, rendering the direct comparison of patient outcomes difficult. Subsequently, the expert committees from the Working Group of the VAS-European Independent Foundation in Angiology/Vascular Medicine critically reviewed the findings from the Delphi study and provided practical recommendations on the diagnostic criteria for BD, facilitating its universal use. We recommend that the 'definitive' diagnosis of BD must require the presence of three features (history of smoking, typical angiographic features and typical histopathological features) and the use of a combination of major and minor criteria for the 'suspected' diagnosis of BD. The major criterion is the history of active tobacco smoking. The five minor criteria are disease onset at age less than 45 years, ischemic involvement of the lower limbs, ischemic involvement of one or both of the upper limbs, thrombophlebitis migrans and red-blue shade of purple discoloration on edematous toes or fingers.

We recommend that a 'suspected' diagnosis of BD is confirmed in the presence of a major criterion plus four or more minor criteria. In the absence of the major criterion or in cases of fewer than four minor criteria, imaging and laboratory data could facilitate the diagnosis. Validation studies on the use of these major and minor criteria are underway.

# Unravelling the Mysteries of Peripheral Arterial Disease in Diabetes

## Specifics of PAD and optimal non-invasive diagnostics in patients with diabetes

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Calcium deposits in the form of hydroxyapatite can accumulate in both the intima and the media of arterial wall leading to the development of different clinical entities. Calcium deposits in the intima are well known feature of atherosclerosis while medial deposits represent medial arterial calcification (MAC) or Mönckeberg's sclerosis. Atherosclerotic plaque progression results in the narrowing of arterial lumen while medial calcification increases arterial stiffness and cardiac afterload, changes pulse wave velocity as well as its form, and alters hemodynamics resulting in an impaired function of the microvasculature.

Patients with diabetes not only have more extensive and more progressive atherosclerotic vascular disease, they also have higher prevalence of MAC. These two clinical entities coexist in the vast majority of patients with diabetes. Increased arterial stiffness plays an important role in PAD pathophysiology, being a limiting factor for positive arterial remodelling in atherosclerosis. Furthermore, medial calcification increases the risk of complications during vascular interventions, mitigates their outcomes and increases the risk for amputation. For that reason, medial calcification is now recognized as a strong predictor of cardiovascular morbidity and mortality in diabetic patients.
As a result of an increased arterial stiffness patients with diabetes often have increased values of ankle-brachial index (ABI), making the ABI an unreliable non-invasive diagnostic tool for this population. To properly estimate the presence and severity of PAD in patients with diabetes it is sometimes essential to use other non-invasive diagnostic techniques: toe-brachial index, transcutaneous oximetry or Doppler ultrasonography. All these techniques have their own limitations which should be taken into account during result interpretation.

# Novel antidiabetic therapy beyond glucose control: is there added value in patients with PAD?

Manfredi Rizzo

# When do endovascular procedures outperform surgery in PAD patients with diabetes?

Mariano Palena

# Rescuing the un-rescuable: the finesse of vascular surgery in peripheral artery disease in diabetes

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BACKGROUND: Diabetic patients with advanced peripheral artery disease (PAD) have an increased prevalence of heavily calcified tibio-peroneal disease and therefore an elevated risk of chronic limb-threatening ischemia and limb amputation. Strategies that optimize the success of arterial revascularization in this challenging patient population can have a substantial public health impact and improve patient outcomes.

The choice of the most effective surgical technique for revascularization of the lower limb in diabetic patients depends on patient risk, presenting symptoms, severity of limb threat, and anatomic pattern of disease. Contemporary open surgical revascularization techniques include bypass to distal or collateral arteries, hybrid procedures, and vein arterialization techniques.

RESULTS: Surgical bypass using autologous veins should be considered in patients who have no (more) endovascular options, have extensive tissue loss, and have an acceptable surgical risk. A vein bypass to the pedal arteries has become a standard procedure in the last decades. Bypass to the medial or lateral plantar artery or to the lateral tarsal artery are less often performed since these procedures have a relatively high rate of early graft occlusion. In patients lacking an adequate tibial or pedal artery, an alternative is to use the perigeniculate arteries for distal anastomosis since they are often unaffected by atherosclerotic disease. In the presence of a popliteal segment without outflow into crural vessels but with good collaterals, a bypass grafting to such an isolated popliteal segment can be performed.

In frail diabetic patients with multilevel disease, hybrid procedures should be considered as they offer the advantages of an effective open approach and the minimally invasive nature of endovascular procedures.

In patients who present without a patent target vessel for revascularization, the venous system can be used as an alternative route for oxygen delivery to ischemic tissues. Open, hybrid, and endovascular techniques for vein arterialization, have led to variable results, thus making it difficult to predict limb salvage rates in individual patients.

CONCLUSION: Open surgical techniques in patients with poor revascularization options have acceptable results and increase limb salvage rates. This could improve the outcomes in diabetic patients for whom amputation would otherwise be the only option

# Diabetic foot: multidisciplinary treatment

Claudia Riera Hernandez

# MLAVS Symposium 1: Methods of Preventing Cardiovascular and Other Complications in Patients with Peripheral Arterial Disease

## Intermittent claudication: An overview

Nicos Angelides

Sudden onset of pain in the calf while walking, may be ischemic in origin. Fontaine's classification of PAD identifies 4 stages: 1st stage: asymptomatic. 2nd stage: claudication. 3rd stage: rest pain, and 4th stage: gangrene.

Stage 1, should be suspected in individuals over 70 years old; between 50-70, in individuals with a history of smoking or diabetes mellitus; and in less than 50 years old when multiple risk factors are present. Asymptomatic PAD can be identified by measuring ankle – brachial index at rest and after exercise. In such patients it is advisable to proceed with the identification and correction of all risk factors.

Stage 2, is split into 2 stages, 2a and 2b. The 1st one is characterized by mild claudication which is defined as the presence of cramps in the lower limb when climbing or walking a certain distance which depends on the degree of arterial stenosis and on the collateral circulation. In this stage the following diagnostic investigations are indicated: Measurement of ankle-brachial index before and after exercise. Colour flow duplex sonography to reveal positive changes in the upper and lower extremities and in the aorta, and other investigations such as ECG, 3D-sono, and stress test (33% positive chance for coronary stenosis). The goals of management in mild claudication are to slow the progression of PAD, to improve walking capacity, and to prevent major cardiovascular events. The steps of management include life style modification, and regular exercise; correction of risk factors (stop smoking, control of diabetes, hypertension, hypercholesterolemia and correction of renal function abnormalities; administration of drugs (antiplatelet drugs: aspirin 75 mg, etc.). Patients with mild claudication should be re-evaluated annually. In case of worsening, a colour flow duplex ultrasonic examination is recommended. Stage 2b is defined as the presence of cramps in the lower limbs after climbing less than two flights of stairs or walking less than 200 meters. The same diagnostic procedures are used with the following differences: The walking capacity should be measured by a 6-min walking test, and the duplex ultrasonic examination should be extended to all the arterial axis of the limb up to the metatarsal arteries. The management in this stage includes correction of lifestyle and of the risk factors is essential as in mild claudication. However, physical training must be supervised at least at the beginning with an increasing warm up, a submaximal treadmill exercise, either without or with a mild slope. Vasodilating drug as well as drugs improving deformability of the red cells are used. These drugs are given in addition to those administered for the correction of risk factors as statins and Ramipril.

Severe claudication is defined as the presence of claudication occurring when climbing less than one flight of stairs or walking less than 100 m. The main investigations for severe claudication are: Extensive 3D-sono; Angio CT, MR Angiography; Transcutaneous partial pressure of oxygen TcP <40 mm Hg); Cardiac investigation, as well as sonography of the supra aortic branches. The first option of treatment in severe claudication is revascularization, either endovascular or via open surgery. In case of early deterioration especially in a diabetic smoker with intermittent rest pain or onset of cyanosis, the patient should be referred urgently to a Vascular Centre.Critical limb ischaemia should be considered when there is rest pain in the limb during night, when minimal ischemic lesions occur in diabetic patients, and when extended cutaneous lesions are present. it is important to specify the degree of collaterals and the distal run off which is defined as good, adequate or poor depending on the patency of 3,2,1, or none of the calf arteries. Newer angiographic methods are using gadolinium for the MR

Angio and iodine for the CT angio, taking into consideration the renal function. Finally, it is important to mention that prognosis of patients with CLI depends on the existing cardiovascular risk.

# Management of dyslipidemia in patients with PAD

Kosmas I. Paraskevas[1], Vasileios Papaioannou[1], Paraskevi Tsiantoula[1]
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BACKGROUND: Dyslipidemia is an established risk factor for cardiovascular diseases. We aimed to review its role in the pathogenesis of lower extremity peripheral arterial disease (PAD), as well as the effect of lipid-lowering treatment on the progression of PAD.
PATIENTS AND METHODS: The literature was reviewed for the effect of hyperlipidemia/dyslipidemia on PAD progression and the role of lipid-lowering therapy in reduction of limb and cardiovascular event rates.
RESULTS: There is evidence that dyslipidemias play a major role in the development of PAD. All patients with PAD should receive intensive lipid-lowering therapy for the reduction not only of claudication symptoms and amputation rates, but also of myocardial infarction and cardiovascular event rates.
CONCLUSION: Vascular specialists should keep in mind the pivotal role of dyslipidemia in the pathogenesis and progression of LEAD.

# General principles of prevention of cardiovascular events in patients with PAD

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Risk factor modification has been shown not only to increase pain-free and total walking distance but also decreases cardiovascular events in patients with PAD.

Smoking has probably the earliest recognized relationship with PAD. PAD can be diagnosed almost one decade earlier in smokers than in nonsmokers. Also, smoking cessation is associated with decline in incidence of IC. All patients with PAD should be advised to stop smoking coupled with a formal smoking cessation program. Nicotine replacement therapy and/or bupropion can be added to enhance cessation rates. Heated tobacco smoking is still today a controversial option for these patients.

Increased total cholesterol, low-density lipoprotein (LDL-C), triglycerides and lipoprotein (a) are considered to be independent risk factors for PAD. Elevated levels of high-density lipoprotein (HDL-C) and apolipoprotein (a-1) levels are believed to protect against the development of PAD. A recent meta-analysis of statin therapy shows that a one mmol/L reduction in LDL cholesterol level is associated with 20% reduction in major CV events regardless of initial lipid levels. According to current recommendations, all patients with PAD should maintain an LDL-C level less than 70 mg% and less than < 55 and < 40 mg% for patients with previous AMI and with polyvascular disease in multiple beds. Fibrates and/or niacin as well as omega 3 fatty acids or Icosapent ethyl, should be considered to raise high-density lipoprotein levels and lower triglyceride levels in patients who have abnormalities of these lipid fractions.

Dietary modification should be the considered a mandatory intervention to help in the control of abnormal lipid levels in patients with PAD.

Hypertension is associated with two- to threefold increased risk for PAD. The current recommended goal for blood pressure is less than 140/90 mmHg, and less than 130/80 mmHg in the presence of diabetes and renal insufficiency. Thiazides and ACE-I are considered to be the first-line agents for blood pressure control in patients with PAD. ACE-I have shown benefits beyond blood pressure control in patients with PAD as shown in the HOPE study comparing ramipril with placebo in high-risk patients. Similar benefit may be obtained with the use of Angiotensin I receptor blockers (ARB). Also, Calcium-antagonists may be good drugs to treat hypertension in these patients. The theoretical risk of worsening claudication symptoms with the use of beta-blockers was unfounded in randomized clinical trials. In particular, patients with concomitant CAD may have additional benefit from beta-blocking agents.

Diabetes increases the risk of PAD by three to four-fold over the general population. Diabetes is also associated with peripheral neuropathy and increased risk of infection, which is probably responsible for higher amputation rates. Because of these reasons, daily foot inspection, skin cleaning and appropriate footwear should be an integral part of diabetes management. Any skin lesions or ulceration should be promptly addressed in patients with diabetes and PAD.

Many studies have shown that optimum management of diabetes decreases the risk of microvascular complications, such as nephropathy and retinopathy. Current recommendations from Guidelines are to reduce glycosylated haemoglobin to less than 7%.

An elevated level of homocysteine is considered to be an independent risk factor for PAD. However, currently, use of folate and vitamin B12 for reduction of homocysteine in patients with PAD is still controversial. Exercise therapy significantly improves the exercise performance and community-based walking ability in patients with symptomatic PAD. Mechanisms for the response to exercise includes improvement in walking efficiency, endothelial function and metabolic adaptation of skeletal muscle. The formation of collaterals and increased blood flow is believed to have minimal effect, if any, in improving pain-free and total walking distance after exercise training.

Antiplatelet drugs such as acetylsalicylic acid, 100 mg/day, have shown a clear mortality benefit in patients with coronary and cerebrovascular diseases. The addition of small doses of Rivaroxaban (2.5 x 2 mg/day) should give further benefit in reducing cardiovascular events in patients with Polyvascular disease.

# Do patients with PAD need a different target level of blood pressure than those with other cardiovascular diseases?

Pavel Poredos

# Antithrombotic treatment of PAD - is aspirin still a basic antiplatelet option?

Arkadiusz Jawien

# Arterial Ultrasound Testing to Predict Future Cardiovascular Events

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Studies have indicated that presence and size of subclinical atherosclerotic plaques improve the prediction of atherosclerotic cardiovascular events (ASCVE) provided by conventional risk factors alone. However, the relative contribution of different ultrasonographic measurements is largely unknown.

Our aims were to: i) demonstrate the relative performance of maximum plaque thickness and plaque area in improving the 10-year ASCVE prediction when added to conventional risk factors in a single cohort; ii) determine whether the vascular bed of these measurements, carotid or common femoral bifurcation and the number of beds with plaques would improve prediction.

We enrolled 985 adults in the Cyprus Epidemiological Study on Atherosclerosis (CESA) (mean age±SD 58.1±10.2; female 54.6%) free of clinical atherosclerotic cardiovascular disease (ASCVD). Conventional risk factors were recorded and both carotid and both common femoral bifurcations were scanned with ultrasound. The primary endpoint was a composite of first time fatal or non-fatal ASCVE: myocardial infarction, onset of angina, coronary artery revascularisation, ischemic stroke, transient ischemic attacks, onset of claudication or critical limb ischemia.

Over a mean±SD follow-up of 13.2±3.7 years ASCVE occurred in 154 (15.6%) participants. The area under the ROC curve for prediction of ASCVE was 0.738 (95% CI 0.696 to 0.781) using conventional risk factors. It increased to 0.773 (95% CI 0.731 to 0.841), 0.770 (95% CI 0.728 to o.813) and 0.774 (95% CI 0.732 to 0.815) ($P<0.007$) by adding number of bifurcations with plaque, total plaque thickness and total plaque area respectively; net reclassification improvement was also increased by 16.1%, 16.6% and 16.6% ($P < 0.0001$) respectively.

Number of bifurcations with plaque, maximum plaque thickness or plaque area from both carotid and both common femoral bifurcations provide a better prediction of future ASCVE than measurements from a single site.

# Management of Carotid Atherosclerosis

## Treatment of dyslipidemia in patients with carotid atherosclerosis

Dimitri Philippe Mikhailidis

# Vulnerable carotid plaque - how to identify it using ultrasound

Andrew Nicolaides[1]

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It has now been recognised that in patients with asymptomatic internal carotid stenosis the degree of stenosis alone is not able to identify patients at high risk of stroke (> 3% per year).

Based on prospective cohort studies, three methods that compliment stenosis are now available that may identify those at high risk:

1. Presence of microembolic signals (>2/hour) on Transcranial Doppler (TCD) identifies a subgroup with a 7% ipsilateral annual stroke rate (no strokes after the 1st year).
2. The presence of silent embolic infarcts on CT- or MRI- brain scans identify a subgroup with a 3.6% ipsilateral annual stroke rate.
3. Plaque image analysis

(a) Juxtaluminal plaque area (JBA) > 8 mm2 in the absence of a visible fibrous cap indicates a large lipid core with a thin fibrous cap (<200 microns) or an intraluminal thrombus and identifies a subgroup with a 4.1% ipsilateral annual stroke rate.

(b) Presence of Discrete White Areas (DWA) in a hypoechoic part of a plaque is associated with neovascularisation and identifies a subgroup that has a double the risk of ipsilateral stroke between years 3 – 8 of follow-up

In a multivariate logistic regression, degree of stenosis, previous contralateral TIA, JBA and DWA were independent predictors of ipsilateral hemispheric stroke and could be used to stratify risk in 923 patients with a stenosis ≥70%.

| Annual stroke rate | N= |
|---|---|
| < 1% | 524 (56%) |
| 1-2% | 149 (16%) |
| 2-4% | 176 (19%) |
| 4-6% | 40 (4.3%) |
| > 6% | 34 (3.6%) |

A recent cross-sectional study comparing asymptomatic with symptomatic plaques has demonstrated that discordant motion is more frequent in symptomatic plaques. This needs to be tested in a prospective study. It remains to be seen whether it will be another independent predictor of increased risk.

# Asymptomatic carotid artery stenosis: revascularization or best medical therapy?

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BACKGROUND: The optimal management of asymptomatic carotid artery stenosis is controversial. Some physicians/surgeons support conservative treatment alone, whereas others support offering these patients a carotid intervention (carotid endarterectomy or carotid artery stenting)
PATIENTS AND METHODS: A review of the recent data from the literature will be performed comparing outcomes with invasive vs. conservative management of patients with asymptomatic carotid stenosis.
RESULTS: For some patient subgroups, conservative treatment is appropriate, whereas for other patient subgroups a prophylactic carotid intervention may be considered to reduce the long-term risk of stroke and death.
CONCLUSION: A "one-size-fits-all" approach for patients with asymptomatic carotid stenosis is inappropriate and unethical. All asymptomatic patients are not the same. The management of patients with asymptomatic carotid stenosis should be individualized, taking into consideration patient age/comorbidities, patient preference, patient compliance and individual patient needs and wishes.

# How to treat symptomatic carotid stenosis?

Arkadiusz Jawien

# Chronic Venous Insufficiency

## Surgery for chronic venous leg ulcers

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BACKGROUND: Chronic venous leg ulcer as an advanced stage of chronic venous insufficiency represents a significant burden for both the patient and the healthcare system. In our last retrospective cohort study of 109 patients with active ulcers treated with EVLA of superficial refluxing truncal vein we achieved healing rate of 97,5% of leg ulcers in average 3,49 months . The ulcers recurred in 12 patients and pathological perforators were present in 7 out of 12 patients (58,3%) with recurring ulcers. This finding was much higher then in our cohort of patients with first active ulcers prior the EVLA (17,9%) . Due to this observation we concluded that the pathological perforators play crucial role in the genesis of recurrent venous leg ulcers.

PATIENTS AND METHODS: We treated 12 patients with recurrent leg ulcers targeting therefore to occlude the perforators. We started with less invasive methods namely ultrasound-guided occlusion with 2% Aethoxysclerol foam. In case of failure we continued with EVLA of perforators when feasible and in the rest of non occluded perforators were sealed with Histoacryle glue under US control.

RESULTS: The rate of healed ulcers after the procedure was 85,7 % (6 patients out of 7) with an average time of 2,31 months. Healing was prolonged in patients with history of deep venous thrombosis. Complication were just minor redness and pain

CONCLUSION: In our cohort of 12 patients with recurrent leg ulcers after the prior successful surgical intervention with EVLA the presence of pathological perforators was 58,3%. That was much higher rate then the rate of pathological perforators of our cohort of 109 patients with primary venous leg ulcers treated with EVLA (17,9%) . Our observation and our treatment of pathological perforators emphasize the importance of early detection of presence of new refluxing perforators and to treat them by non-aggressive methods ultrasound-guided foam sclerotherapy, EVLA or sealing them up with cyanoacrylate glues.

# Mixed Leg Ulcers

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Mixed arterial and venous leg ulcers (MAVLU) are estimated to affect up to 26% of patients with lower extremity ulcerations. The origin of MAVLU is primarily due to chronic venous insufficiency and the ability of mixed ulcer to heal is determined mainly by the severity of the coexisting arterial insufficiency.

In contrast to patients with venous leg ulcers, patients with mixed leg ulcers are significantly older, have lower body mass index, a history of smoking, and more comorbid conditions. Ulcer pain is highly prevalent. MAVLU were associated with lower health related quality of life, greater mobility impairments, and more deficits in self-care and usual activities.

The ankle -brachial index (ABI) would be determinative of peripheral artery disease (PAD) diagnosis, especially in old patients who may not have claudication because of decreased mobility.

When the ABI value is less than 0.6, the first step should be revascularization for ulcer healing and to prevent recurrence. Conversely, when the ABI value is above 0.6 there is no consensus on the treatment sequence and procedures that should be followed. If initial treatment is successful, close follow-up is strongly recommended as recurrence of MAVLU due to revascularization failure is frequently difficult to manage. In the group with moderate arterial insufficiency, patients may be considered for venous ablative procedures when superficial venous reflux is identified, primarily to prevent ulcer recurrence after healing.

Conservative management using modified compressive therapy seems reasonable in patients with ulcers and moderate arterial disease and venous ulcer. Compression therapy with a pressure of 20–30 mmHg would be acceptable in cases with ABI index value between 0.5 and 0.8 to avoid the deterioration of the tissue vitality. Patients with ABI index values less than 0.5 should not receive compression therapy before any revascularization procedures. After arterial intervention, standard wound care and compression therapy remain crucial to wound healing and the prevention of ulcer recurrence.

# Recanalization of chronic venous occlusions

Marzia Lugli

# Tubulcus Device Compressive Therapy vs. Vacuum Assisted Closure in Venous Leg Ulcer Healing – A Comparative Analyses

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Background. Venous leg ulcers (VLUs) are still a prevalent condition in the Balkans. Compression therapy is recommended as the primary treatment to aid VLUs healing. As well, negative pressure wound therapy (NPWT) is a safe and promising method to treat hard-to-heal ulcers, including VLUs. This study aims to compare the clinical outcomes, feasibility, and costs associated in both methods. Patients and Methods. Conducted in the Emergency County Hospital Timisoara, Romania, this single-center prospective study assessed a series of parameters in patients treated for VLUs: demographic data, wound dimensions, closure period, hospitalization duration, calf circumference, treatment costs, quality of life (Chronic Venous Insufficiency Questionnaire - CIVIQ-20) and revised Venous Clinical Severity Score (r-VCSS). In order to maintain the uniformity of the study groups, only patients with venous ulcers of a maximum size of 10/4 cm were included in the study. In all the cases, wound debridement and cleaning with chlorhexidine-benzalkonium antiseptic solution was practiced first. 33 patients were treated by positive pressure compression therapy (Tubulcus - a heelless open-toed elastic compression device knitted in tubular form, Laboratoires Innothera, Arcueil, France); and 31 patients were treated by NPWT (VivanoTec Pro; Laboratorios Hartmann S.A.). Results. The demographic distribution between the two groups showed a balanced representation across gender and environment. The analysis revealed no significant differences in age, wound dimensions, closure periods, or r-VCSS scores post-treatment. However, the hospitalization period and treatment costs were significantly higher for the NPWT group (p=0.0001), compression therapy by using Tubulcus being a much cheaper method, which can be performed on an outpatient basis. A statistically significant oedema remission (p=0.0016), as well a quality of life improvement (p=0.0004) were noted in the Tubulcus group. Conclusions. Although compression therapy and NPWT revealed similar results in terms of wound healing, Tubulcus device proved superior in oedema remission, offering a cost-efficient alternative to NPWT, reducing hospitalization time and improving quality of life. These findings advocate for a more nuanced selection of treatment modalities based on patient-specific needs and healthcare economic considerations.

# Venous thromboembolism in pregnancy

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Pregnancy is an independent risk factor for venous thromboembolism (VTE) due to changes in coagulation and fibrinolysis. These are on the procoagulant side, as are changes in blood flow in the leg veins due to compression of the veins by the pregnant uterus. Some endothelial changes especially during delivery are described, too. There are in addition some other risk factors related to normal pregnancy like increased body weight, due to pregnancy-related or concomitant diseases. The incidence of VTE is about 0.1%. Venous thromboembolism could happen during the whole pregnancy, and about half of the events are observed in the six weeks postpartum. Diagnostic procedures to detect VTE start with clinical suspicion, which is probably less reliable than in nonpregnant persons. However, the VTE should be confirmed by objective methods like in nonpregnant persons. For diagnosis of deep venous thrombosis the main diagnostic procedure is compression ultrasound, and for suspected pulmonary embolism is computerized pulmonary angiography. D-dimer assessment is less reliable than in the nonpregnant population, but it could be used. In patients with pulmonary embolism risk assessment for worse outcomes should be performed using established criteria. Treatment of VTE is specific, because direct oral anticoagulant drugs and vitamin K antagonists are contraindicated, and low-molecular-weight heparin is the drug of choice during pregnancy. After delivery vitamin K antagonists could be also used. Treatment should last during the whole pregnancy and six weeks postpartum or at least three months. In some rare cases of pulmonary embolism thrombolysis could be used, too.

# New Trends in Management of Peripheral Arterial Disease

## The role of biomarkers in PAD

Mislav Vrsalovic

# Subtherapeutic low-dose combination of statins and sartans for the treatment of impaired arterial wall function

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Although current cardiovascular prevention strategies are effective, they are not yet sufficient. New targets for prevention are therefore being sought. The arterial wall could be a suitable target as it is actively involved in all phases of the atherothrombotic process – from early onset to clinical events. It is best characterised by impaired functional (endothelial function) and morphological (arterial stiffness) features. We have extensively studied the effects of subtherapeutic doses of statins and sartans on the arterial wall. These drugs have pleiotropic effects that may be different at different concentrations. In the animal studies, we found that subtherapeutic doses of statins and sartans are more effective than higher doses in improving the arterial wall, and that the combination of statin and sartan is the most effective. Among the different combinations, low-dose combination of fluvastatin and valsartan (low-flu/val) proved to be the most effective. The substantial prolonged effect was observed after discontinuation of the combination. These favourable results were replicated in different patient groups: in patients with moderate or high cardiovascular risk, in patients after myocardial infarction, in patients with type 1 and type 2 diabetes and in apparently healthy middle-aged men. The improvement in endothelial dysfunction (as measured by flow-mediated dilation) and arterial stiffness (as measured by pulse wave velocity) is in a range that, when incorporated into clinical prediction models, reduces cardiovascular risk by approximately 20-25% (on top of best medical theraphy). Low-flu/val is effective despite concomitant treatment with a statin and/or sartan (unlike than fluvastatin or valsartan). Several beneficial biochemical, molecular and genetic changes were measured during therapy, which may underlie the efficacy of low-flu/val: reduction of inflammatory markers and vascular adhesion molecules, increased expression of vasoactive genes (especially NO synthetase), increased expression of telomerase and expression of beneficial genes such as SIRT, KLOTHO, PRKAA1. Overall, low-flu/val has been shown to effectively improve impaired arterial wall function and morphology, which could have important clinical benefits. Due to its unique properties, a cyclic treatment is possible (one month of treatment followed by several months without treatment). It seems that low-flu/val could be a valuable new tool for cardiovascular prevention.

# Endocrine disorders and PAD

Gerit-Holger Schernthaner

# Gene therapy for peripheral arterial disease

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Gene therapy (GT) of peripheral arterial disease (PAD) came into the spotlight a quarter of a century ago with the 1998 Circulation article »Constitutive expression of phVEGF165 after intramuscular gene transfer promotes collateral vessel development in patients with critical limb ischemia« by Iris Baumgartner and co-workers from Jeffrey Isner's group. Although this work provided proof of principle that injection of naked plasmid DNA encoding for human vascular endothelial growth factor (VEGF) caused a transient increase in serum levels of VEGF, which promoted neovascularization and limb salvage, subsequent results of GT for PAD did meet the expectations. The 2018 Cochrane Database systematic review of GT for PAD evaluated 6 studies using VEGF-encoding genes, 4 studies using hepatocyte growth factor-encoding genes, 3 studies using fibroblast growth factor-encoding genes, 2 studies evaluating hypoxia-inducible factor 1-alpha GT, 1 study using a developmental endothelial locus-1 GT, and 1 study evaluating stromal cell-derived factor-1 GT. No clear differences were found between subjects receiving GT or placebo in amputation-free survival, major amputation, and all-cause mortality, but there was low-quality evidence suggesting improvement in complete ulcer healing with GT (odds ratio 2.16, 95% confidence interval 1.02 to 4.59; p = 0.04). It has become clear, that developing a functional, non-leaky capillary network in ischemic muscles requires coordinated expression of several genes. Various non-coding RNAs have been tested for this purpose in animal experiments.

Lipid lowering by GT has implications not only for prevention of coronary artery disease, but also for prevention of PAD. Silencing the gene for proprotein convertase subtilisin/kexin type 9 (PCSK9) by inclisiran, a small interfering ribonucleic acid (siRNA) conjugated to N-acetylgalactosamine, is already in clinical use. Experimentally, permanent silencing of PCSK9 has been attempted by clustered regularly interspaced short palindromic repeats (CRISPR) genome editing, and more recently by base editing resulting in a single base pair substitution, avoiding any double-stranded DNA breaks. Additional promising experimental targets for GT of dyslipidemia are the gene for angiopoietin like 3 (ANGPTL3) and the gene for apolipoprotein C3 (APOC3).

In conclusion, GT is showing promise in primary and secondary prevention of PAD, but has not yet reached clinical utility.

# New Trends in Management of Venous Thromboembolism

## Chronic thromboembolic pulmonary hypertension

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Chronic thromboembolic pulmonary hypertension (CTEPH) is an important cause of pulmonary hypertension with unique management strategy. It is a rare disease, with estimated incidence 2-6 per milion inhabitants per year and prevalence 26-38 cases per milion.

It usually occurs as a late sequel of acute pulmonary embolism or/and it evolves in patients with risk factors for CTEPH(without known pulmonary embolism), such as splenectomy, cancer, chronic inflammatory disease, hipercoagulable states, presence of surgical shunts or pacemaker leads. Patients usually present with symptoms of exertional dyspnea, decline in physical fitness level, fatigue, syncope and chest pain. The unspecific symptoms of this rare disease are often causing a delay in diagnosing CTEPH, many times months or even years pass. At least three months of anticoagulant treatment is needed before setting the diagnosis, using several diagnostic tools, particularly VQ scan, CT pulmonary angiography, echocardiography and right heart catheterisation.

If left untreated CTEPH causes right heart failure, which is the main cause of death in patients with CTEPH. The pressures in pulmonary circulation rise not only due to obstructions of pulmonary arteries with fibrotic clots, but can also be related to associated microvasculopathy as a result of shear stress on the pulmonary artery wall.

Aproximately two thirds of the patients can be treated with a surgical procedure called pulmonary endarterectomy. It is a complex and extensive surgical procedure including deep hypothermia, long lasting extracorporeal circulation, and transient complete circulatory arrest. While pulmonary endarterectomy is performed when the chronic thrombi lie relatively centrally, the preferred procedure for more distally located thrombi is baloon pulmonary angioplasty. Repeated dilatations of pumonary artery stenoses can effectively diminish the pulmonary artery pressures and improve the function of the right ventricle. When the vasculopathy of small pulmonary arteries is prominent, the patients with CTEPH can also be treated with pulmonary vasodilatators, namely riociguat and treprostinil. The patients with CTEPH need lifelong anticoagulant treatment independent of the treatment strategy. In severe cases supporting treatment of right heart failure and long term treatment with oxygen is suitable. With improving surgical and interventional treatment tehniques, the treatment of CTEPH with lung transplantation is the thing of the past.

# New perspectives for prevention of the post-thrombotic syndrome

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While on conventional anticoagulation, up to 50% of patients with one or more episodes of proximal deep vein thrombosis (DVT) can develop post-thrombotic (PTS) manifestations. The potential strategies for PTS prevention are the treatment of acute DVT with catheter-directed thrombolysis (CDT), the use of elastic compression stockings (ECS) and that of the direct oral anticoagulants (DOAC) in place of vitamin K antagonists (VKA) for the initial and long-term treatment of DVT. Based on the results of three randomized clinical trials, CDT cannot be recommended on a routine basis because of its invasiveness, the associated risk of major bleedings and the uncertainty about its efficacy. According to the results of a placebo-controlled randomized clinical trial, ECS are no longer recommended for PTS prevention on a routine basis. However, based on the results of a recent subanalysis of a prospective cohort study, patients with residual vein thrombosis and/or popliteal valve reflux at three months are likely to benefit from ECS for at least six months. Finally, following the demonstration that the inadequacy of VKA therapy plays a key role in the PTS development, several retrospective and prospective studies have shown that the use of DOACs for the initial and long-term treatment of DVT in place of VKAs reduces the risk of PTS by approximately 50%. In conclusion, the availability of DOACs and the potential of ECS in selected patients with proximal DVT are expected to play a key role for decreasing the rate and the severity of PTS in the forthcoming years.

# Highlights and controversies in the 2024 international guidelines on VTE

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Prevention and Management of Venous Thromboembolism: International Consensus Statement (Guidelines According to Scientific Evidence).
This is the 6th revision of this document, published in the February issue of this year in International Angiology. It provides a clear and concise summary of the evidence regarding the efficacy or harm of various methods available to prevent and manage venous thromboembolism (VTE) and provides recommendations based on such evidence. It is distributed by the European Venous Foundation, and it can be downloaded free of charge from the EVF website.
The Evidence is presented for the following outcomes: asymptomatic DVT at screening, symptomatic DVT or PE, fatal PE, overall mortality and development of the post-thrombotic syndrome (PTS) when available.

The decision to use asymptomatic DVT as well as symptomatic DVT or PE is a subjective one based on the following arguments: The relationship between asymptomatic and symptomatic VTE including PE has been known for some time. Reduction in the incidence of asymptomatic DVT has been shown to be associated with a reduction of symptomatic DVT and PE. Large studies that were powered to study efficacy on fatal PE have demonstrated that reduction in silent DVT is accompanied by reduction in clinical DVT, clinical PE and fatal PE.

Additional arguments: Regulatory authorities have recognized asymptomatic proximal DVT as a valid endpoint of clinical trials and drug evaluation. Relatively few PE occur in patients with symptomatic DVT. The majority of PE including fatal PE occur in patients with asymptomatic DVT. Thus, asymptomatic DVT is an important stage of thromboembolic disease that has not yet manifested itself.

The following updates will be presented: Validated Risk Assessment Tools, Compression after DVT controversy, Isolated calf DVT controversy, Validated Bleeding Risk Tools, The shift to Mechanical and Aspiration Thrombectomy, Dissemination of the Guidelines and Patient Education.

# Challenges in Management of Patients with Chronic Limb-threatening Ischemia

## Which clinical staging system is most useful in patients with CLTI?

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Critical limb ischemia (CLI) is considered the most severe pattern of peripheral artery disease. It is defined by the presence of chronic (>2 wk) ischemic rest pain, ulceration or gangrene attributable to objectively proven occlusion of peripheral arterial vessels. It is associated with a high risk of major amputation, cardiovascular events and death.

Among patients with known PAD, incidence of CLI estimated to be between 11% and 20%.4

It was estimated 1-y mortality rate of 25%-35% and 1-y rate of amputation up to 30% among patients presenting with CLI.1-4 Lower rates of mortality and amputation have been reported in patients undergoing revascularization.4

Among vascular specialists, the Fontaine and Rutherford classification systems are most commonly used to categorize severity of CLI. Current nomenclature has evolved from the previous commonly used term of CLI to chronic limb-threatening ischemia (CLTI) which reflects the chronic nature of this condition and its potentially limb-threatening nature with associated risk for amputation and to distinguish it from ALI. In fact, CLTI is responsible for most major and minor limb amputations related to PAD.3,4

In recent years, a clinical staging system for patients with CLTI that incorporates the wound extent, degree of ischemia, and severity of foot infection has been proposed. The WiFi (wound, ischemia, and foot infection) classification estimates risk of lower extremity amputation according to wound extent, severity of ischemia, and presence of foot infection and has been shown to correlate with clinical outcomes, including time to wound healing, amputation rate, and amputation-free survival.

Hemodynamic parameters have been also considered in the definition to ensure that the ulceration, gangrene, or rest pain are caused by peripheral arterial disease and that most would be expected to require a major amputation within the next 6–12 months in the absence of a significant hemodynamic improvement. To achieve this hemodynamic picture, it was suggested to use either absolute ankle pressure < 50–70 mmHg or Systolic Toe Pressure ≤ 30–50 mmHg or TcPO2 ≤ 30–50 mmHg. From a hemodynamic viewpoint there is no consensus and most of the existing classifications are not based upon evidence.1 Anyway, patients with a systolic toe pressure below 30 mmHg must be revascularized whenever possible. However other patients with clinically suspected CLTI and higher values for instance above 30 mmHg must be evaluated and treated in specialized vascular units and revascularization has to be discussed on a case by case basis, taking into account other data such as the WiFi classification for ulcers.

In conclusion, many useful but at times contradictory definitions of CLTI have been suggested. Only a few have taken into account evidence, and none have been validated prospectively. CLTI registry to prospectively validate, or not, the definitions of CLTI are desirable.

# Cardiovascular risk of patients with CLTI

Maroriella Catalano

# Frailty assessment in patients with CLTI

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Frailty is a complex age-related clinical state with a decline in physiological capacity resulting in an increased susceptibility to stressors. Frailty independently predicts both short and long-term all-cause mortality and other disability in patients with peripheral arterial disease (PAD). Confirmation of frailty status facilitates risk stratification of patients with PAD. There are several types of frailty and validated assessment tools. Currently, an agreed international consensus on the most practical and efficient frailty assessment tool for patients with PAD is lacking and urgently needed. This will ensure a better goal-focused clinical care and allow harmonisation of global research data collection for better understanding of frailty and its clinical impact. This session will describe the definitions of different types of frailty and several selected frailty assessment tools, and highlights the clinical impact of frailty among patients with PAD and its management.

# Revascularization of CLTI – endo or surgical?

Oliver Schlager

# BAD and SAD-MAC: a new scenario and new strategies for patients with CLTI

Andrea Casini

# Care of the patient with CLTI undergoing vascular interventions

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Chronic limb-threatening ischemia (CLTI) is a clinical diagnosis with objectively confirmed atherosclerotic peripheral arterial disease (PAD), leading to varying degrees of ischemia and presenting as ischemic rest pain and/or tissue loss, such as ulceration or gangrene. Hemodynamic parameters usually associated with CLTI are an ankle-brachial index (ABI) <0,4 absolute ankle perfusion pressure below 50 mmHg, toe pressure below 30 mmHg or transcutaneous oximetry (TcPO2) less than 30 mmHg. The following article will cover the topics of CLTI prognosis and risk factor treatment as well as approach to revascularisation procedure with peri-/postprocedural treatment especially regarding antithrombotic regimen to improve vessel patency.

# ESVM Symposium: Navigating PAD: 2024 Guidelines

## PAD: Understanding epidemiology and diagnosis

Oliver Schlager

# Optimizing medical treatments for PAD

Lucia Mazzolai

# Optimizing Interventional Treatment of Peripheral Arterial Disease

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Lower limb arteries' revascularization is recommended in those patients with peripheral arterial disease (PAD) who suffer chronic limb-threatening ischemia (CLTI) or disabling intermittent claudication (IC) that does not respond to the supervised or structured home-based exercise training. Revascularization methods include endovascular procedures, open surgery, or a combination of both. A decision on the type of revascularization is usually made by a multidisciplinary vascular team and is based on the location and morphology of the lesion and the patient's risk assessment.

Aorto-iliac lesions are mainly treated endovascularly. Balloon angioplasty with or without stenting for the external iliac artery and primary stenting for the common iliac artery provide good long-term patency. In more complex lesions, the endovascular treatment has lower short-term morbidity and mortality, while open surgery offers better early and midterm primary patency. However, both methods have similar secondary patency. Open surgery is therefore reserved for extensive obstructions or failed endovascular treatments. Hybrid revascularization is suitable for occlusion of common femoral or profunda femoris artery requiring endarterectomy alongside the endovascular therapy for inflow/outflow disease.

For femoropopliteal lesions, endovascular therapy is preferred especially in high-risk surgical patients. Balloon angioplasty with drug-eluting balloons should be the first-choice treatment, and stent should be implanted only in bail-out situations. In patients with severe IC, endovascular revascularization of below-the-knee arteries along with the femoropopliteal segment should be considered in the same intervention if the outflow is significantly impaired. An open bypass surgery may be considered if an autologous vein is available, patient's surgical risk is low, and lesions are complex. If endovascular therapy is chosen, landing zones for potential bypass grafts should be preserved.

In infra-popliteal lesions, endovascular therapy is often the first choice. Drug-eluting balloons and bare-metal stent implantation have shown no superiority over plain balloon angioplasty in this arterial bed, although drug-eluting stents may be used for relatively short proximal lesions.

In CLTI, revascularization should be attempted as soon as possible. These patients commonly present with multilevel disease. Eliminating inflow obstructions when treating downstream lesions is recommended. When CLTI leaves no viable arterial revascularization options, transcatheter arterialization of deep veins may be considered.

# Optimizing treatment of carotid disease

Juraj Madarič

# Joint Symposium CEVF-SIMV: Superficial Venous Thrombosis

## From varicose veins to venous thromboembolic disease

Mateja Kaja Ježovnik

# Superficial venous thrombosis in atypical locations

Ana Spirkoska[1]

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Superficial vein thrombosis (SVT) is an inflammation of the venous wall with subsequent secondary thrombus formation. In majority of cases it affects the superficial venous system of the lower extremities.

SVT, which appears in functionally and structurally normal veins, without varicose changes, is a heterogenous group of disease in which the inflammatory and thrombotic processes are differently express.

Trousseau's syndrome is a rare variant of venous thrombosis that is characterized by recurrent, migratory thrombosis in superficial veins and in uncommon sites, such as upper extremities, trunk, and chest wall. Superficial migratory thrombophlebitis is associated with systemic diseases like hypertension, Buerger syndrome/thrombophlebitis obliterans, hypercoagulable conditions like protein C, S deficiencies, lupus anticoagulant, factor XII deficiency, inflammatory bowel disease, Behcet disease and cancer.

Mondor disease describes a syndrome of sclerosing superficial thrombophlebitis of the veins of the anterior thoracic wall. The most commonly involved vessel is the superior epigastric vein producing a palpable cord in the inferior outer quadrant of the breast. It has often been linked to local trauma, including repetition injury as a tight brassiere, strenuous exercise in the case of bodybuilders, or direct injury associated with surgery. Other causes include direct damage to the veins, stagnation of blood, or extrinsic pressure on veins, cosmetic mammoplasty, mastectomy, and breast-conserving surgery for breast cancer and after core needle biopsy.

SVT, which appears in functionally and structurally normal veins, without varicose changes is heterogenous group of disease in which different etiopathogenetic mechanisms are present.

Beside diagnose of superficial venous thrombosis using ultrasound, more extensive diagnostic procedures in order to looking for systemic procoagulant state are often needed, since underlying disease are important for the treatment of SVT in atypical location.

# Superficial venous thrombosis of a healthy vein

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Superficial venous thrombosis (SVT) is an inflammatory and thrombotic process of a superficial vein. Although is a relatively common event, it is not a benign disease as several underlying disease may be the causative factors. Varicose veins are the primary risk factor for lower-limb SVT as they can be found up to 90% of cases. However, the onset of SVT in a healthy vein is a situation that must be thoroughly investigated since it can be the expression of a serious pathology. Indeed, the first description of a superficial thrombosis in history has been made by Armand Trousseau on a healthy vein as a complication of a visceral malignancy. Also, SVT on a healthy vein may occur in thrombophilia, systemic vasculitis, collagenoses, haematologic disease and infection. Specific forms of SVT on healthy vein are the "migrans" SVT and the Mondor's disease. Migrans SVT is often seen in patients with Büerger's disease and Behçet's disease while in Mondor's disease, the thrombosed veins are in the anterolateral chest wall and they are usually related to breast cancer; in other cases of Mondor's disease, the SVT can also occur in subcutaneous penile veins. Therefore, accurate diagnostic work up is necessary to prevent sequelae and costs related to the disease. Ultimately, medical treatment does not differentiate between SVT on a healthy vein and SVT on a varicose vein.

# How to treat superficial venous thrombosis of varicose veins?

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BACKGROUND: Superficial venous thrombosis (SVT) is not a benign and rare disease, although the actual incidence is underestimated. The main risk factor is the presence of varicose veins. At the time of diagnosis of SVT up to 18 % of patients already have a deep venous thrombosis (DVT) and 6.7% a pulmonary embolism (PE).

METHODS:The aim of our work was to analyze the literature and guidelines to determine exactly the best therapy for preventing complications and to identify grey zones and open questions about SVT treatment.

RESULTS: SVTs that extend beyond 5 cm and 3 cm from the saphenophemoral junction (SFJ) or saphenopopliteal junction (SPJ) require treatment. Ultrasound is necessary as the sole clinical evaluation may underestimate the extent of SVT and the possible involvement of deep circulation.

If SFJ/SPJ are involved, it is recommended to treat with anticoagulant therapy at full dose for 3 months, although further randomized studies are needed. The therapy includes the use of fondaparinux 2.5 mg for 45 days or rivaroxaban 10 mg for 45 days. Low molecular weight heparins (LMWH) are an alternative, although there is no reliable data on the exact dosage whether prophylactic or intermediate. The use of elastic stockings is suggested in addition to medical therapy. The use of NSAIDs seems to be useful for symptomatology but there is no reliable data on the prevention of complications.

CONCLUSION: All cases of SVT to be treated must be identified by evaluating the extent of thrombosis, distance from the SFJ/SPJ and excluding DVT. Anticoagulant therapy with fondaparinux 2.5 mg for 45 days is the gold standard. Alternatives are rivaroxaban 10 mg for 45 days or LMWH prophylactic/intermediate dose. The use of elastic stockings can be considered as a combination therapy, in the early stages of the disease. NSAID's are useful. Surgery is an option but after at least three months of the acute event. Further studies are needed to determine the appropriate dosage of LMWH, evaluate the effectiveness of the next anticoagulants (Factor XI inhibitory).

# The Crucial Role of Exercise in Managing Peripheral Artery Disease

Lucia Mazzolai

# MLAVS Symposium 2: Ruptured Abdominal Aortic Aneurysm

## Pathophysiology and development of a ruptured AAA

Pier Luigi Antignani

# Diagnosis and perioperative management of a ruptured aaa

Nicos Angelides

The pathognomonic symptoms of a ruptured AAA, are: (a) abdominal pain or backache, (b) deteriorating hypotension, and (c) the presence of pulsatile abdominal mass. All three, are present in 75% of the cases. However, clinical diagnosis of a ruptured AAA may be difficult or even missed at the onset of symptoms at 20% of the cases. Such atypical presentation often leads to a wrong preoperative management, which delays surgical treatment, and results in poor survival. In such cases the patient should immediately receive thoracoabdominal CT Angiography in order to come to a proper diagnosis and optimize the proper preoperative plan. Most surgeons have the tendency to transfuse such patients intensively, in order to improve hypotension. However, any significant elevation of blood pressure will increase blood loss, setting the patient in a vicious circle. Restriction of IV fluid in any case of ruptured AAA, can control haemorrhage in a better way, provided that the patient remains conscious and able to talk and move. Such restriction of fluids leads to a reduction in systolic blood pressure down to 60 or 70 mm Hg, which can control temporarily the internal bleeding, and will give time to prepare open or endovascular procedure in a better way. A way to avoid the cardiovascular collapse, is to proceed under local anaesthesia to an urgent CT angiogram in order to evaluate the patient's anatomy, and to control excessive haemorrhage by introducing a supra-coeliac aortic balloon through a 14F sheath. Such device is placed when the patient is of high risk or when the case is complicated with cardiovascular collapse.

Till the introduction of the endovascular surgery, open surgery was the only treatment for such aneurismal pathology of the aorta. EVAR, has swapped away the monopoly of open surgery and created a lot of controversial issues, which were mostly solved via well-organized trials, reaching a vascular and endovascular consensus. Elective surgery for AAA is performed with a less than 3% operative mortality. On the contrary, open surgery for ruptured AAA caries an operative mortality around 40%. The principles of EVAR seems to be particularly attractive in cases of ruptured AAA. The major advantages of this procedure vs. open surgery, are the avoidance of laparotomy and of general anaesthesia in most of the cases. Other advantages of EVAR are the following: EVAR, has a lesser operative mortality, avoids many of the problems which are associated with open surgery, and is less traumatic, especially for high risk patients. The disadvantages of EVAR are: (a) The large inventory of devices, which must be on hand. (b) The urgency, which is associated with rupture, and (c) the requirement of an endovascular team on call, with access to the appropriate facilities for EVAR. A variety of commercially made grafts have been employed. Most of these are of the modular bifurcation type. Initially, endovascular techniques were used to treat ruptured AAA in high risk patients only, who were unfit for open repair. Sometimes, patients with known cold AAAs may experience significant delay from been referred to surgery. Inevitably, some of these patients will have a rupture whilst waiting, and therefore strategies should aim at reducing any unreasonable delay. On the other hand, patients undergoing EVAR repair for a ruptured AAA, may experience after operation a persisting peri-aneurysmal haematoma, which may lead to an abdominal compartment syndrome. Such patients need to be evaluated for the presence of endoleaks. Endoleaks type I (leakage from the proximal or distal attachment site) as well as endoleaks type III (defects between components in modular grafts), may need endovascular or even open repair. Endoleaks type II (present of persistent flow in the aneurismal sac through patent branch vessels) may be considered as more benign, as the process of exclusion of the aneurismal sac by the endograft, usually will result in an early closure of lumbar arteries or inferior mesenteric artery. Personally, I believe that patient's fitness and the proper technological means are the key for a successful EVAR, in cases with ruptured Abdominal Aortic Aneurysm.

# Urgent Abdominal Aortic Aneurysms: Present Challenges for Management

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BACKGROUND: Ruptured AAA continues to be a leading cause of death in our western societies. New development s on endovascular technology, better pre-hospital admission with permissive hypotension and fluid restriction plus rapid transfer to a major referral center seem to have contributed to reduced early mortality.

National registries provide useful information from daily practice enabling a more thorough and independent review and monitoring of results of mansamente followed in the specific country.

Data from 1, 000 consecutiva patients entered the registry will be analysed

PATIENTS AND METHODS: 205 patients (20.5%) were treated nationally because of urgent repair of ruptured AAA . Protocol for management for pre-hospital admission including permissive hypotension, fluid restriction, careful preparation and selection for method of treatment was based upon clinical and imaging from CTA scan either locally or at the referral center. Endovascular planning including use of endovascular clamping were carefully and thoroughly analysed by the vascular team. Post-operative care including monitoring and strategy for Abdominal Compartment Syndrome was cerfully covered.

RESULTS: Overall mortality in Urgent cases was 34% compared to 2.7% on elective patients; mortality in the urgent group was 28.8% with EVAR comparing favourably with Open Surgical Repair 44% ($p<.024$). Supra-renal clamping endo or open, presence of post-operative myocardial infarct, need for hemodiafiltration for renal dysfunction. full blown ACS and respiratory failure were significantly associated with higher mortality. And Institutional low-volume output < 15 cases yearly was also significantly associated with higher mortality.

CONCLUSION: Our data confirm that a full-blown strategy for endovascular management in ruptured AAA is associated with a significant reduction on early <30 day mortality.

Higher volume-output >15 cases per year seem to be associated with lower early mortality, thus confirming the value of a centralisation policy for management of these patients.

# Evaluation of endoleaks and their management

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Endoleaks is a not an infrequent finding following endovascular aortic repair (EVAR) for abdominal aortic aneurysms. They require careful evaluation and management to prevent adverse outcomes such as aneurysm expansion and rupture. Although they are well described throughout the years, there are areas which still need to be addressed regarding their management.

Over the years and the advancements in endograft technology, type I (3%) and type III (2-3%) endoleaks, the risk of development appears to remain low especially with the new endografts, however it is still a concern for endografts that they were placed over a decade ago. In addition, the continuous development of new endografts, including fenestrated, branched and physician modified devices (PMEGs) for the treatment of the pararenal and juxtarenal aneurysms, pushes the boundaries of treatment that requires very careful follow up in order to detect these endoleaks early. Type II endoleaks appear in up to 10% of the endovascular aortic repairs. The incidence of rupture in these patients is as low as 0.9%. Compared to type I and III endoleaks, type II endoleaks does not require treatment, unless they meet certain criteria of sac expansion. However, it is well known that failure of sac regression is related to increased mortality and morbidity. Type II endoleaks might play a role in sac regression failure. Thus, addressing type II endoleaks early, even simultaneously with the initial EVAR, has been proposed and may have a role. Overall, for type II endoleaks ultimate management still remains a dilemma.

Endovascular abdominal aortic repair is the first line treatment for the majority of the AAAs worldwide and endoleaks are part of it. Careful follow up is the cornerstone of preventing complications of endoleaks. Older endografts, newer endografts addressing pararenal and juxtarenal aneurysms, and PMEGs, deserve closer follow up. For this, patient modified follow-up protocols including ultrasound, CTA and biological markers like D-Dimers are important.

# Oral Abstract Presentations

## Assessment of endovascular treatment in splenic artery aneurysm

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BACKGROUND: Splenic artery aneurysms are the most common visceral artery aneurysms (60% of cases), occurring in 0.1-2% of the population. The risk of rupture is 2%, with a mortality rate of 10-25%, and it increases in patients with portal hypertension and during pregnancy. These aneurysms are usually asymptomatic and are often detected incidentally during CT or ultrasound examinations, being more common in women. Still, according to some, vascular surgery is a good option for treatment - splenic artery occlusion shouldn't cause ischemia due to sufficient collateral circulation. We think that full preservation of the spleen and her function is a better solution. The aim of this study is to evaluate the endovascular treatment of splenic aneurysms in our patients.

PATIENTS AND METHODS: From 2011 to 2023, in our Department 56 patients were treated (46 women and 10 men) aged 23-57 years with endovascular therapy. All patients had splenic artery abnormalities detected during abdominal imaging, performed due to nonspecific pain or the presence of another disease. 42 patients had single aneurysms, while 14 had multiple aneurysms (ranging from 2 to 5). All patients were treated with embolization coils; additionally, 12 required self-expanding stents, and 5 also received liquid embolic material.

RESULTS: All aneurysms were successfully excluded from circulation during the initial procedure. During follow-up periods ranging from 1 to 112 months, standard examinations such as Duplex-Doppler, angio-MR, or angiography were performed. Recanalization of the aneurysm sac was observed in 10 cases, necessitating repeat embolization procedures. 1 patient required 3 procedures. Occlusion of 4 implanted stents was noted, with 3 cases being asymptomatic due to well-developed collateral circulation. 4 patients developed areas of impaired perfusion within the splenic parenchyma and in 1 case, a splenectomy was necessary.

CONCLUSION:

1. Splenic artery aneurysms should be treated to prevent rupture while maintaining vascular patency.
2. Endovascular treatment, due to its minimal invasiveness and safety, should be considered as the gold standard.
3. The use of appropriate techniques should be individual and is essential to achieve good results.

# Results of one year follow-up of patients after EVAR in UMC Ljubljana

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BACKGROUND: Endovascular abdominal aortic aneurysm repair (EVAR) is commonly used to treat abdominal aortic aneurysm (AAA). In our department the outcomes after 30 days, 1 year and later in all the patients after EVAR have been followed systematically since 2023.

PATIENTS AND METHODS: All the patients after EVAR hospitalized in our department from January 2023 till May 2024 have been included in our analysis. Our aim is to follow the outcomes in patients after EVAR during hospitalization, after 30 days, 1 year and later.

RESULTS: This analysis included 107 patients after EVAR (elective and urgent) since 1st January 2023, 87 men and 20 women (mean age 74,4 +/- 5,2). The mean AAA diameter was 58 +/- 7 mm. We analysed the duration of hospitalization in elective and urgent patients (5,6 +/- 2,9 days vs 16,2 +/- 8,2 days). 50 % of patients after EVAR had haematoma on puncture site. 69 patients already had CTA after EVAR till the end of April 2024; there were 23 endoleaks detected (endoleak type 2 in 21 patients, endoleak type 1 in one patient and endoleak type 3 in one patient).

CONCLUSIONS: Since January 2023 up till now 107 patients have been treated with EVAR in our centre. The presence of endoleaks type 1, 2 and 3 and other complications are comparable with the data from other registries

# Direct ischemic postconditioning after eversion carotid endarterectomy in prevention of periprocedural hyperperfusion

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BACKGROUND: Ischemic reperfusion (IR) injury plays a critical role in adverse neurological outcomes following carotid endarterectomy (CEA). In this context, we continue to investigate a novel surgical technique called ischemic postconditioning (IPCT), which is designed to mitigate the effects of IR injury. The primary objective of our study was to evaluate the effects of IPCT on neurological outcomes in patients at high risk of IR injury after CEA.

PATIENTS AND METHODS: This is an observational case-control investigation conducted from December 2015 to June 2024. It involved 788 patients identified as “high-risk reperfusion” candidates, divided equally into two groups: those undergoing IPCT and those who did not receive IPCT. The classification of high risk for IR injury after CEA was based on several criteria, including severe internal carotid artery (ICA) stenosis (>90%), severe bilateral ICA stenosis (>80%), severe ICA stenosis (>80%) with contralateral ICA occlusion, and severe ICA stenosis with a recent history of transient ischemic attack (TIA) or stroke. The extent of carotid stenosis before CEA was assessed through multidetector CT angiography. The IPCT procedure was implemented by executing six cycles of alternating 30 seconds of reperfusion (achieved by declamping the ICA) and 30 seconds of ischemia (through reclamping the ICA) immediately following the completion of the initial CEA.

RESULTS: The cumulative incidence of intrahospital postoperative TIA/stroke was significantly higher in the non-IPCT group compared to the IPCT group (5.6% vs. 0.7%; OR 0.078; 95% CI 0.011 - 0.611; $p < 0.004$). Throughout the follow-up period, there were no reported TIAs, strokes, or neurological mortality in either patient group.

CONCLUSION: In our study, IPCT significantly reduced the incidence of postoperative cerebral ischemic events after CEA in patients at high risk of IR injury following CEA.

# Importance of early periferal vascular US scanning for the treatment strategy of pulmonal embolism

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BACKGROUND: To determine the best treatment of pulmonary embolism, it is essential to use the results of chest CT scan and PESI score. The decission of the treatment options ( anticoagulation or lysis ) is based on these data and the clinical condition of the patient. If the patient is in a very serious, life-threatening condition the immediate lysis therapy is essential, however sometimes it has not given adequate results.

PATIENTS AND METHODS: Our hypothesis is that when an old, unlysable thrombus fragment cause acut life threatening PE, the standard systemic lysis is just waste of time and cause further risk for the patient because of the delay. For these cases the solution has to be the mechanical removal of the embolus either with catheter or surgical way as a first choice.

In order not to waste valuable time with "unnecessary" lysis therapy, an early search for the source of the embolus, the structure and the location of the remaining thrombus with a detailed ultrasound scan of the lower exterimities could help.

RESULTS: In this talk we would like to presents our experience with some cases.

CONCLUSION: Our suggestion is to be the part of the PE diagnostic/therapeutic algorithm the early peripheral venous ultrasound examination as well, where these special cases could be named as "Pulmonal Embolism from unlysable thrombus" with the recommedation of early mechanical intervention as a first choice.

# Vascular Ehlers Danlos syndrome in Croatia

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BACKGROUND: Vascular Ehlers-Danlos syndrome (vEDS) is caused by mutations in the COL3A1 gene. The clinical course is marked by life-threatening complications in early adulthood, such as rupture and/or dissection of medium-sized arteries, intestinal perforation, and uterine perforation. We report our clinical experience with vEDS at a tertiary clinical centre in Croatia.
PATIENTS AND METHODS: We conducted a retrospective analysis of patients with genetically confirmed vEDS. Demographic data, family history, genetic mutations, major complications, and celiprolol intake were collected from hospital medical records.
RESULTS: Since December 2017, nine patients (seven adults and two children) with genetically confirmed vEDS have been treated at the University Hospital Centre Zagreb. The median follow-up period was 37 months (range 1 - 78 months). The mean age at genetic confirmation was 34 years (range 3 - 66 years). Of the nine patients, six were first-degree relatives from two different families. vEDS investigation in children was initiated by a clinical geneticist based on the presence of minor criteria and first-degree relatives who suffered or died from events suspected to be secondary to vEDS. Among adults, three were index cases, while the others were tested as family members. Before diagnosis, three adult patients experienced major arterial complications (rupture or dissection of a medium-sized artery, carotid-cavernous fistula), and one patient experienced spontaneous perforation of the sigmoid. Genetic analysis confirmed a pathogenic or likely pathogenic missense variant in eight patients and a splice-site variant in the COL3A1 gene in one patient. All adult patients, except one recently diagnosed, were treated with celiprolol at a mean tolerated dose of 300 mg per day (range 200–400 mg). The most severe course was observed in a young male patient with a novel heterozygous splice donor variant; after four years of follow-up, he experienced a fatal rupture of the left renal artery. The other patients did not experience life-threatening complications during follow-up.
CONCLUSION: Awareness of the major and minor criteria of vEDS is crucial for early and accurate diagnosis. Management should be conducted in specialized hospital centres with an interdisciplinary approach and close collaboration with geneticists.

# Association of Biomarker of Cerebral Injury – NSE and Cerebral Oximetry with Neurological Changes During Carotid Endarterectomy Performed in Awake Patients

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BACKGROUND: The aim of this pilot investigation was to determine if a raised serum NSE (neuron-specific enolase) level or a decrease in rSO2 following carotid revascularization with CEA (carotid endarterectomy) could be used to detect neurological instability in CEA patients. We hypothesised that increased serum NSE levels during CEA would be linked to neurological symptoms after surgery.

PATIENTS AND METHODS: A total of 64 consecutive CEAs were prospectively evaluated in 60 patients who underwent the procedure under LA (local anaesthesia) during an 18-month period. The cerebral oximeter was used to measure cerebral oxygen saturation (rSO2) before and after cross-clamping, along with the serum concentration of NSE. Selective shunting was performed when neurological changes occurred, regardless of rSO2.

RESULTS: The neurological symptoms that occurred after clamping correlated with a less pronounced decrease in the serum level of NSE (P = .026) during the 12-hour timeframe after the procedure. The cut-off of 13.1% of NSE decrease was determined to be optimal for identifying patients with neurological symptoms. There was no correlation between rSO2 decline and neurological symptoms (P = .675). Two (3.1%) perioperative strokes occurred.

CONCLUSION: Awake neuromonitoring has been found to be a sensitive and direct evaluation method for brain tissue perfusion and is specific to CEA under LA. Although there was a favorable correlation between CEA and a change in serum NSE, serum NSE monitoring was not practicable due to postponed statistically significant change (12 hours after the procedure).

# Venous Trombosis and Cancer

Benilde Cosmi

# Venous Thromboembolism

## Mesenteric venous thrombosis

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Mesenteric venous thrombosis is part of splanchnic vein thrombosis (SVT), an unusual site venous thromboembolism (VTE), which includes portal, mesenteric, or splenic vein thrombosis, and the Budd-Chiari syndrome.1-3

The management of SVT remains challenging and often empirical with limited evidence from observational studies and few small randomized trials.

Risk factors for SVT are: liver cirrhosis, solid cancer, myeloproliferative neoplasms, surgery/trauma, inflammatory diseases (e.g. IBD), abdominal infections, rare autoimmune/hematologic diseases (e.g. Behcet, Paroxysmal Nocturnal Hemoglobinuria), thrombophilia.3

All SVT have in common high 30-day mortality up to 20% and it seems to be difficult to diagnose SVT early because of their rarity and their wide spectrum of unspecific symptoms. SVT is primarily diagnosed by sonography and/or computed tomography.

Anticoagulant therapy is the first line of treatment for splanchnic vein thrombosis because it improves significantly recanalization rates and stops the progress of thrombosis.2-4

Low-molecular-weight heparin, vitamin K antagonists, as well as direct-acting oral anticoagulants (DOAC) are possible anticoagulants, but it is noteworthy to be aware that all recommendations supporting the off-label use of anticoagulants are based on poor evidence and consist predominantly of case series, observational or studies with small case numbers.

Before treatment is started, careful individual assessment of the bleeding risk is recommended, especially in patients with liver cirrhosis and patients with solid or hematologic cancer. Most common risk factors for bleeding include esophageal varices, low platelet count, severe liver or renal failure, and concomitant therapies.

Several observational studies have shown that early initiation of anticoagulation is associated with better vessel recanalization, which can reduce the occurrence of portal-hypertension-related complications.3 Thus, anticoagulant therapy in patients with acute splanchnic vein thrombosis should be started early after diagnosis, if there is no active bleeding, to avoid the extension of the clot and promote vessel recanalization. If esophageal varices are present, implementation of adequate prophylaxis such as nonselective β-blockers or endoscopic variceal band ligation is recommended and full anticoagulation should be started after complete endoscopic variceal eradication is obtained, if required.

Heparins represent the mainstay of treatment during the acute phase of disease. Due to its very short half-life and to the possibility to measure the anticoagulant effect with the activated partial thromboplastin time, unfractionated heparin is preferred in patients at very high bleeding risk, patients who are potentially candidates for surgery (e.g., for bowel infarction), and in patients with severe renal insufficiency.2-4

LMWH is administered as a stand-alone drug or followed by oral anticoagulants for the majority of patients. Administration of LMWH alone for the first weeks/months of treatment is preferred in patients with solid cancer, in particular gastrointestinal cancer, and in patients at high bleeding risk (e.g., patients with thrombocytopenia) thanks to the possibility to use individualized dose reductions (e.g., 50% dose reduction for platelet count between 30 and 50 x 103/□L) and prophylactic doses for platelet count between 20 and 30 x 103/□L).4

For all other patients, a switch to vitamin K antagonists is generally suggested, with a therapeutic international normalized ratio (INR) range between 2.0 and 3.0.

Recently, the DOACs have become a possible alternative to vitamin K antagonists. Despite limited available evidence, a recent guidance document from the International Society on Thrombosis and

Haemostasis (ISTH) has suggested the DOACs as the first line treatment for patients with nonmalignant and noncirrhotic splanchnic vein thrombosis.4

In cancer- associated thrombosis, LMWH or DOACs are preferred over vitamin K antagonists, because of their greater efficacy. LMWH should be preferred over the DOACs for patients with solid cancer at high bleeding risk (e.g., luminal gastrointestinal or genitourinary cancers) or in patients receiving ongoing treatments which might potentiate or reduce the effect of the DOACs.3-5

In cirrhosis-associated splanchnic vein thrombosis, the recent guidance of the ISTH suggests starting therapy with LMWH and to consider a switch to oral agents (either vitamin K antagonists or DOACs) only if not contraindicated by severe liver dysfunction.3,4

Similar therapeutic strategies have been recently suggested for patients with symptomatic and patients with incidentally detected splanchnic vein thrombosis since several studies found no difference in recurrence rates between the two groups.4 This topic however, is still controversial .5

Local or systemic thrombolysis is usually proposed to a limited number of patients with thrombus progression or worsening clinical conditions despite adequate anticoagulation or with bowel infarction.4,5

Anticoagulation should be given for a minimum of 3 to 6 months and continued indefinitely in patients at low bleeding risk with recurrent thrombosis, permanent risk factors, or unprovoked events.

When choosing a suitable anticoagulation, the individual risk of bleeding and thrombosis must be weighted very carefully in the follow up. In cases of bleeding, bowel infarction, or other complications, the optimal therapy should be determined on a case-by-case basis by an experienced multidisciplinary team involving a surgeon. Besides anticoagulation, there are therapeutic options including thrombectomy, balloon angioplasty, stenting, transjugular placement of an intrahepatic portosystemic shunt, liver transplantation, and ischemic bowel resection.

# Invasive treatment of deep venous thrombosis – when and how?

Oliver Schlager

# Antiphospholipid syndrome

Aleš Ambrožič

# New strategies in treatment of pulmonary embolism

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Pulmonary embolism (PE) represents a major cause of cardiovascular morbidity and mortality. Over the last few years, there has been an increase in the incidence of PE, while simultaneously the mortality rates associated with PE have been declining. The improved survival rates in PE are likely to result from better availability of more precise diagnostic methods, better adherence to the guidelines, and use of the new enhanced therapeutic options.

Since hemodynamic compromise is the principal cause of poor outcome in patients with acute PE, early identification of patients at risk and appropriate risk stratification of patients with PE are essential for further management and can direct the use of more invasive treatment strategies. Anticoagulation therapy is the cornerstone of treatment for acute PE, while for hemodynamically unstable patients, systemic thrombolysis is the recommended treatment of choice. However systemic thrombolysis comes with a cost of increased risk of major bleeding, including possibly fatal intracranial bleeding. Interventional catheter-based therapies with mechanical thrombectomy or catheter-directed thrombolysis with very low doses of thrombolytic offer the possibility for this bleeding risk to be minimized, while sufficient recanalization of pulmonary arteries allows for hemodynamic stabilization of the patient and improves the patient's symptoms. The decision when to use interventional procedures over pharmacologic treatment is still a matter of debate, especially in the intermediate high-risk group of PE patients. Ongoing studies comparing one interventional method against another, and catheter-based therapies against anticoagulation are ongoing. While the results of these studies are eagerly awaited, implementations of local hospital protocols for optimal PE treatment with consultations between multidisciplinary specialists in the so-called pulmonary embolism response team are suggested.

# Thrombophilia

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Thrombophilia may be defined as a hereditary or acquired abnormality in a haemostatic system with a shift to prothrombotic condition resulting in a tendency for thrombosis (mostly venous). Various thrombophilias differ in a prevalence in various populations as well as in clinical significance – they may be associated with considerably different risks of first lifetime or recurrent venous thromboembolism. Of hereditary thrombophilias, the most prevalent is factor F Leiden (FVL), followed by prothrombin gene mutation G20210A – both of them, if heterozygous are only of moderate significance. Of acquired thrombophilias, the most important is antiphospholipid syndrome (APS), an autoimmune condition with variable significance, the riskiest variant being so called triple positive APS. Only some thrombophilias are considered strong (major): antithrombin deficiency, combined hereditary thrombophilias, homozygous FVL or prothrombin G20210A, antiphospholipid syndrome, homozygous deficiency of protein C or protein S.

Thrombophilia testing is a controversial issue and in the practice, it is often ordered incorrectly. There is general consensus that testing should be performed only if it has an impact on patient´s management. However, there are no uniform guidelines for thrombophilia testing available and, moreover, the adherence to the guidelines is poor. There are also many variables affecting thrombophilia assays. To optimize thrombophilia testing, more education is needed as well as the close cooperation of clinicians and laboratory staff.

# Calf venous thrombosis

Maria Cristina Vedovati

# Session of Slovenian Society for Vascular Diseases

## Significant variation in low-molecular-weight heparin plasma concentration measured with anti-Xa assays with or without exogenous antithrombin

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Background: Low-molecular-weight heparin (LMWH) plasma activity can be determined using an anti-Xa assay. This is an automated assay that is well established in clinical practice, but poorly standardized. Therefore, the anti-Xa results vary greatly between the different reagents used. The reason for the variations could be antithrombin (AT) and dextran sulfate (DS), which are added to some but not all reagents. Therefore, the influence of exogenous AT and DS on the anti-Xa results was investigated in an in-vitro study. Methods: Plasma samples with different AT activities (0, 14, 27, 50, 68 and 81%) were prepared from the normal pool and AT-deficient plasma and spiked with different concentrations of LMWH dalteparin (0, 0.3, 0.5, 0.7, 1.0 and 1.5 IU/mL). In all 36 plasma samples prepared in this way, anti-Xa was measured with four different anti-Xa assay variants using coagulation factor Xa with or without dextran sulfate (DS+ or DS-), with or without addition of exogenous AT (AT+ or AT-) and specific factor Xa substrate (all Hyphen Biomed, France). All other assay conditions (incubation times, source of factor Xa, etc.) were the same for all four assay variants. Results: Dunn's post-hoc analysis showed that both AT+ assay variants (AT+/DS+ and AT+/DS-) gave similar results regardless of AT activity or LMWH concentration. Similar results were also obtained when comparing the two AT- assay variants (AT-/DS+ and AT-/DS-). However, there was a significant difference in anti-Xa levels between AT+ and AT- assays at all but the highest AT activity (Figure 1). Anti-Xa levels were decreasing with decreasing of AT activity in all assay variants, however the decrease was more prominent for the AT- assay variants. We could not confirm that DS has an effect on anti-Xa results.
Conclusions: The addition of exogenous AT leads to significantly higher anti-Xa values, while we could not confirm any influence of DS. The choice of anti-Xa assay could have an impact on clinical decision making, but this needs to be confirmed with ex-vivo samples.

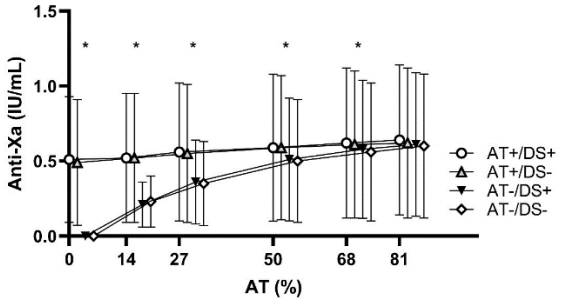


Figure 1. Anti-Xa levels (means±SD) obtained with all assay variants.
* post-hoc $p < 0.05$ for AT+ compared to AT- assay variants

# Efficacy and durability of multilayer flow modulators in aortic aneurysms

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BACKGROUND: Endovascular aneurysm repair (EVAR) is an established treatment of aortic aneurysms in favourable anatomical conditions. Treatment of other areas is complex and demanding endovascularly or with open surgery. Multilayer flow modulators (MFM) were developed to treat aorta in areas where standard EVAR or thoracic endovascular aortic repair (TEVAR) is not feasible. Implantation is simple, arterial coverage by the device should not compromise the flow in arteries. The aim of our study was determining long-term efficacy and durability of MFM in the treatment of aortic aneurysms.

PATIENTS AND METHODS: Our study included 16 male and one female patient, treated in a 91 months period (starting in March 2011); the follow-up extended to March 2023. Mean age of patients was 68 years, none of patients was suitable for EVAR, TEVAR or open surgical management. The data collection was concluded in May 2023; median follow-up was 25 months (range 7-76).

RESULTS: MFM was successfully implanted in all patients, with no 30-day mortality observed. By the end of the follow-up period, five patients were alive. Three patients died due to aortic rupture at 9-, 40-, and 51-months post-implantation. Most additional procedures were performed due to Type 1a endoleak, with one occurring within the first month and four occurring after that. During follow-up, we observed occlusion of two superior mesenteric arteries, one renal artery, one subclavian artery, and the celiac trunk. Only the renal artery occlusion was symptomatic. No cases of paraplegia were detected. Mean aneurysmal flow volume was reduced in most patients (64.5%); however, this did not correspond to a reduction in mean volume or mean diameter, which increased in 59% and 88.2% of patients, respectively.

CONCLUSIONS: MFM are simple and safe to implant in patients with aortic aneurysms, however long-term results did not confirm efficacy and durability of the procedure in majority of patients. Further studies will be needed to highlight reasons for our results.

# Peripheral arterial occlusive disease and perioperative risk

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Surgical procedures represent a risk for different complications which may appear during the perioperative period. Cardiac ischemic events and vascular complications are the most important causes of increased morbidity and mortality and they are much more frequent in patients with manifest cardiovascular disease. This is particularly seen in patients with peripheral arterial occlusive disease (PAD), which represents advanced atherosclerosis frequently accompanied by the presence of coronary artery disease. Therefore, patients with PAD need careful preoperative examination, including estimation of the presence of other co-existing atherosclerotic diseases. The perioperative risk of cardiac complications should be calculated by Apgar score. In patients with unstable coronary syndrome myocardial revascularization should be performed, whereas in other coronary patients a pharmacotherapy should be intensified before operative procedures. The latter includes beta-adrenergic receptor blockers, statin therapy, which significantly improves postoperative outcome and antiplatelet drugs, which do not significantly increase major bleeding complications but significantly reduce cardiovascular thromboembolic events. Postoperative strategy for prevention of complications should be focused particularly on identification of myocardial infarction which is frequently asymptomatic. Therefore, serial postoperative measurements of troponin levels allow close monitoring of postoperative myocardial damage and help to implement strategic choices for the treatment of postoperative adverse cardiac events.

# Wearing or no wearing high heel? Or: Can foot and muscoloskeletal disorder be a risk factor for chronic venous disease?

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The appearance and progression of chronic vein disorders depend on different risk factors, such as genetics, female sex, hormones, obesity with a sedentary lifestyle. Another important factor is occupational and prolonged time standing or sitting without moving the ancle. Because of that can increase venous reflux and with that the oedema of the lower leg. Ambulatory venous hypertension is dominantly associated with reflux and less with obstruction. In daily practice is often underestimated angle of ankle at patients with chronic venous insufficiency. A lot of study show that static disorders of the foot and musculoskeletal disorders of the calf can be an important risk factors that negatively affects chronic venous disorders by increasing the reflux in the vein. Plantar flexion and dorsiflexion are reported as maximal angular deviations of the sole of the foot from the 'neutral' position, defined as 90° on a 0–180° scale, that is perpendicular to the body. Normal range of ankle motion at the ankle is approximately 57 +/− 2°, which in patients with active ulceration is decreased to only 21 +/− 4°. Prospective randomized controlled trials which were done on dry land with compression therapy and in a thermal aquatic environment can change transmural pressure by increasing external venous pressure. Correction of static disorders of the feet and the effect of active stretching training on lower limb will improve symptoms and signs due to the chronic venous disorders by improvement of foot pump efficacy. This highlighted the importance of proper ankle joint mobilization to maintain the efficacy of the valvulo-muscular calf pump which can be disrupted also with wearing high heel or shoes which are without the heel. With increase an ankle range of motion improved ejection fraction and with that significant improve venous symptomatology and the signs. The evidence suggests that exercise may improve also wound healing, quality of life, and physical functioning in adults with venous leg ulcers.

# Correlation of QISS MRA, CTA and DSA for PAD assessement

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BACKGROUND: Cross sectional imaging methods as computer tomography angiography (CTA) and magnetic resonance angiography (MRA) represent widely used methods for assessment of peripheral arteries in patients with critical chronic limb ischemia or claudication. They are of utmost value in treatment planning, but each has it's own limitations. Vascular calcification represent the most common limitation in CTA, but doesn't have an impact in MRA. In last decade new non-contrast enhanced MRA methods have emerged. The QISS (Quiescent-Interval Single-Shot) sequence being one of them.
In our study we have compared CTA and MRA images of pelvic, femoro-popliteal and below the knee arteries with DSA of respective segments. Our aim was to discern weather MRA better corelates with DSA in heavily calcified arteries.
PATIENTS AND METHODS: In a retrospective study, we included 25 patients who underwent an MRA examination of the lower limbs between April 2022 and April 2024. Of these patients, 13 also had a CTA examination, and 19 had a DSA examination. The average age of the patients was 67±12 years (32-86 years), there were 20 men.12 patients (48%) had chronic critical ischemia, mediocalcinosis was present in 7 patients (28%).
RESULTS: 444 segments were evaluated on MRA examination, 229 on CTA examination and 149 on DSA examination. Segments with artifacts were excluded from the analysis and therefore the assessment was not possible.
There was moderate agreement between MRA and CTA ($\kappa$=0.41, P<0.001, number of valid cases 156), moderate agreement between MRA and DSA ($\kappa$=0.49, P<0.001, number of valid cases 121), also moderate agreement between CTA and DSA ($\kappa$=0.57, P<0.001, n. of valid cases 39).
We then limited our analysis to the bellow the knee arteries only. There was moderate agreement between MRA and CTA ($\kappa$=0.42, P<0.001, n. of valid cases 50) and significant agreement between MRA and DSA ($\kappa$=0.61, P<0.001, n. of valid cases 72). Between CTA and DSA was fair agreement ($\kappa$=0.32), but statistically nonsignificant (P=0.084), the number of valid cases was small (16).
CONCLUSION: In our study we have confirmed that QISS MRA represents promising tool in evaluation of peripheral arteries, regardless of severity of vessel wall calcification, especially in bellow the knee arteries.

# Early versus delayed carotid endarterectomy after acute neurological deficit

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BACKGROUND:The aim of this study was to investigate the safety of early carotid endarterectomy (CEA) in relation to the delayed CEA after acute ischemic neurological events (TIA / CVI).
PATIENTS AND METHODS: A total of 157 patients in the prospective study followed 30 days postoperatively. Group I or early CEA, had 50 patients operated from 3 to 14 days after TIA / CVI event. Group II or delayed CEA, had 107 patients operated from 15 to 180 days after the TIA / CVI. Accompanied by the general and specific procedural morbidity and mortality in 30-day postoperative folow up. The significance level was 0.05.
RESULTS:The mean age was 66.72 years with 66.2% of males. In Group I is the average time to intervention was 9.5 days, and in group II 72.22 days. The groups were homogeneous in relation to risk factors and co-morbidities. Group I had 54% of unstable atherosclerotic plaques compared with group II, where it was 31.8% ($\chi 2 = 7.084$; $p < 0.01$). In the group I TIA had 50% of respondents, while in group II CVI was 68.2% ($\chi 2 = 4.825$; $p < 0.05$). CVI to 1 cm in size were significantly more frequent in the group I, a CVI to 2 cm in group II ($\chi 2 = 6.913$; $p < 0.05$). CVI rate in the group I was 2.0%, and in group II was 2.8% ($F = 0.083$, $p > 0.05$). Postoperative myocardial infarction (MI) in the group I is 2.0%, and in group II was 1.9%. Specific surgical morbidity rate in the group I and 4.0% in the group II 3.7%. In group I total morbidity was 6.0% in group II 7.5%, the difference was not statistically significant ($F = 0.921$; $p > 0.05$). Mortality in both groups was not. CVI/IM/death rate in group I was 4.0% in group II was 4.7% ($F = 0.122$; $p > 0.05$). Hyperlipidemia is a significant risk factor for CVI/IM/death ($\chi 2 = 4.083$; $p < 0.05$). Improving mRS in the group I had 52% and in group II 31.8% of patients ($\chi 2 = 5.903$; $p < 0.01$).
CONCLUSION:Early CEA is as safe as the delayed CEA in respect incidence of perioperative morbidity and mortality.

# Arm ischemia after arteriovenous vascular access construction – individual approach

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BACKGROUND: The radiocephalic arteriovenous fistula (AVF) is the gold standard of vascular access. Even the preferred vascular access can cause severe complications in specific populations. Distal arm ischemia in patients with diabetes mellitus and generalised atherosclerosis is a significant and debilitating complication. Surgical interventions to reduce its consequences are DRAL, DRIL, PAI, and bandages, but RUDI reduction surgery or AVF inflow elongation can be used in some exceptional cases.
PATIENTS AND METHODS: We treated a patient with chronic kidney disease and diabetes mellitus with severe atherosclerosis. We primarily constructed a radiocephalic AVF with distal side-to-side anastomosis. After a few months, distal arm ischemia developed, which was resolved with a DRAL procedure. After a transient improvement, ischemia worsened again. We closed the proximal venous drainage of distal AVF and performed the proximalisation of the arteriovenous anastomosis to the axillar region (PAI-type procedure). We also removed the DRAL clip with total lumen restoration. Because the condition did not improve despite the intervention, we decided to ligate the main proximal outflow veins distal to the primary anastomosis. Necrotic lesions of the fingers were surgically debrided, and the patient underwent hyperbaric therapy.
RESULTS: The control angiography showed a well-functioning AVF after PAI reconstruction, persistent complete occlusion of the radial artery distally to the primary anastomosis and occlusion of the ulnar artery in the distal third of the forearm. With the ligation of the proximal draining veins distal to the primary anastomosis, we ensured indirect blood supply to the hand through the veins distal to the side-to-side anastomosis. We achieved sufficient wound healing, cessation of ischemic pain, and a gradual improvement in the hand's functionality while preserving an AVF.
CONCLUSION: Guideline-recommended procedures for distal arm ischemia are the basis for treating arterial flow disorders following the construction of an AVF. However, a successful resolution requires an individual and multimodal approach in a dedicated centre with many interventions and experiences. According to available data, our case report is a unique procedure with successful results using standard PAI procedure and indirect hand perfusion combined with hyperbaric therapy.

# Clinical and laboratory heterogeneity of antithrombin deficiency: The need for personalized management

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BACKGROUND: Antithrombin deficiency (ATD) is a heterogeneous disorder, which makes the treatment of these patients challenging. The aim of this study was to describe the clinical and laboratory characteristics of genetic variants in patients with ATD treated at our medical centre. PATIENTS AND METHODS: 46 adult patients (36 families) with known ATD were included in the study. The type of ATD was characterized by measuring antithrombin (AT) activity and antigen. The presence of genetic variant was examined by Sanger sequencing and multiplex ligation-dependent probe amplification. Clinical data were collected from the hospital information system. RESULTS: A genetic variant was identified in 94% of the families. Twenty patients had quantitative (type 1) ATD: 5 different genetic nonsense variants, 3 genetic missense variants and whole gene deletion. Variants causing qualitative (type 2) ATD, namely AT Padua I, AT Basel, AT Denver and AT Budapest III, were detected in 24 patients. In addition, 2 patients were carriers of transient ATD (AT Dublin). Patients with type 1 ATD developed their first thrombotic event at a younger age, experienced more thrombotic events and had a higher chance of recurrent venous thromboembolism compared to those with type 2 ATD. Patients with type 1 ATD had a significantly higher incidence of venous thrombosis, while arterial thrombosis was more associated with type 2 deficiency. No significant differences were found between type 1 and type 2 ATD with regard to prevalence of pulmonary embolism, thrombophlebitis or pregnancy complications. Patients with type 1 ATD had significantly lower AT activity, although the difference was clinically irrelevant. Clinical and laboratory presentation differed between the specific variants of type 1 and type 2 ATD. Patients with AT Dublin had normal AT activity, but their clinical phenotype was similar to that of type 2 ATD. It was not possible to differentiate between patients with 0 – 1 thrombotic event and those with recurrent events on the basis of AT activity. CONCLUSION: The type of ATD influenced the risk and localization of thrombotic events, which should be considered when treating these patients.

# Peri-operative myocardial infarction/injury after peripheral artery disease revascularization

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Use of serial high-sensitivity troponin assay enables the diagnosis of peri-operative myocardial infarction/injury (PMI) which proved to be a valuable peri-operative prognostic marker. An absolute increase of post-operative high-sensitivity cardiac troponin T or I in more than the upper limit of normal above pre-operative concentration was associated with important increase in 30-day and long-term mortality and cardiovascular events. In patients after vascular revascularization the incidence of PMI is approximately 20% which is higher than after non-cardiac surgery in general. Only a minority of patients with PMI after vascular revascularization have clinical symptoms or ECG changes suggestive of myocardial ischemia. Therefore, active surveillance is mandatory to promptly address their residual atherosclerotic risk.

# Poster Presentations

## Severely symptomatic postrombotic syndrome - fighting the impossible?

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BACKGROUND: Despite advances in the primary and secondary prevention of DVT, DVT affects 1 to 3 of 1000 people in the general population annually. Well-designed prospective studies with long-term follow-up (ie, ≥12 months) report that 20% to 50% of patients with DVT develop PTS sequelae. In most cases, PTS develops within a few months to a few years after symptomatic DVT.

However, some studies have reported that the cumulative incidence of PTS continues to increase, even 10 to 20 years after DVT diagnosis. About 5% to 10% of patients develop severe PTS, which may include venous ulcers. Schulman et al. have shown that the probability of developing a venous ulcer over 10 years after DVT was almost 5%.

Although the pathogenesis of PTS is complex and has not been fully characterized, venous hypertension appears to play a central role.

PATIENTS AND METHODS: The literature on whether PTS development is predominantly the consequence of outflow obstruction, venous valvular reflux, or both, is conflicting; which may reflect, in part, the limited ability to quantify venous obstruction and reflux. Prandoni found that PTS developed more frequently in patients who had persistent venous obstruction within the first 6 months after an episode of acute proximal DVT.

When PTS develops despite early and adequate treatment of DVT, or original episode of DVT was not recognised and treated properly, late complications can be a part of clinical picture. Pelvic or central (IVC) vein severe stenosis or occlusion is often found in the background.

RESULTS: Open surgical bypass and reconstruction of deep veins are feasible, although quite invasive procedures with significant morbidity risks, highly varied patency rates, and limited evidence in literature. In recent years, endovenous recanalization/stenting became a viable option of tretament in severely symptomatic patients. Dedicated venous stents represent an important factor in technical succes and patency of recanalization procedures.

CONCLUSION: Literature overview upon central venous recanalization and stenting, and presentation of two complicated cases from our practice is the aim of our presentation.

# Pedal bypass in the diabetic patient

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In diabetic patients with foot ulcers, it is important to consider peripheral arterial involvement and guide diagnostics accordingly. Stenosis or occlusions of the tibial arteries in diabetic patients are a common phenomenon. The foot arteries are frequently patent, making an important point for treatment considerations. The rapid development of endovascular medicine has, in recent years, led to preferred use of this approach in the treatment of tibial arteries in the patient with chronic critical ischemia of the limb. Lower extremity bypasses in diabetic patients are not without risk. They carry a higher risk of postoperative complications and cardiovascular events in comparison to endovascular therapy. However bypass surgery also offers several advantages, including longer primary patency rates and lower rates of reintervention. Despite the rising popularity of the endovascular approach, surgical vascular bypass, also known as pedal bypass when performed on the foot, remains an important form of revascularization and can sometimes be considered as the primary treatment option. Our case description shows a diabetic patient with chronic limb threatening ischemia, where endovascular and surgical treatment have been combined for the benefit of the limb preservation.

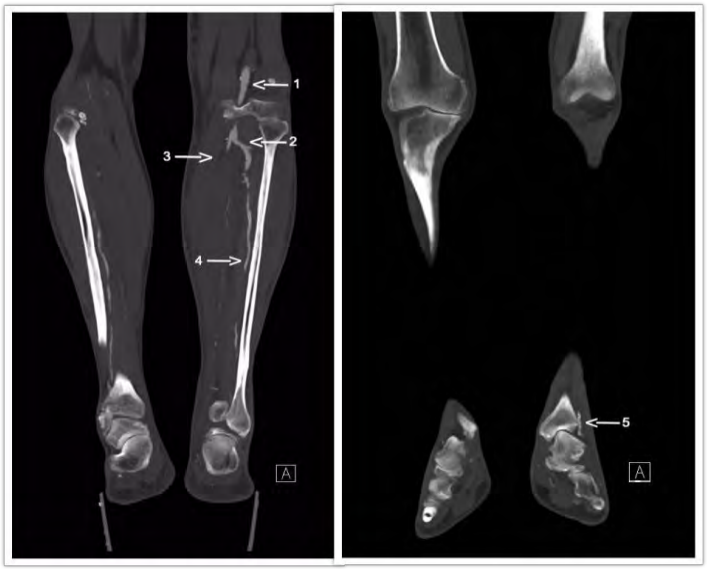


Figure 1. Occlusion of tibial arteries shortly below division. Dorsalis pedis artery is patent. Arrow 1 – popliteal artery, arrow 2 – tibioperoneal trunk, below occluded tibialis anterior artery, arrow 3 – occluded tibialis posterior artery, arrow 4 – peroneal artery, arrow 5 – dorsalis pedis artery.

# Hyperbaric oxygen promotes wound healing and reduces the risk of amputation

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BACKGROUND: The aim of this pilot study was to determine the benefits of hyperbaric oxygen (HBO) therapy for chronic wounds in patients with chronic limb-threatening ischemia (CLTI).
PATIENTS AND METHODS: The study was performed as a retrospective cohort study, with five patients with CLTI included. Patients were treated with HBO after endovascular treatment (EVT).
RESULTS: Of five patients with CLTI, three had diabetes, while two did not. Following EVT, three patients underwent toe-level amputations, and two required debridement of necrotic tissue. HBO therapy administered post-EVT enhanced wound healing, eliminating the need for further amputations in all five patients.
CONCLUSIONS: Treatment of chronic wounds in patients with CLTI requires a multidisciplinary approach. HBO therapy can be used as an adjunctive therapy to the standard therapy modality, as it can increase the healing rate of wounds and reduce the number of amputations.

# Thoracic aorta and coronary artery calcification in patients referred to myocardial perfusion scintigraphy

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BACKGROUND: Myocardial perfusion imaging (MPI) is a well-established non-invasive imaging technique for the diagnosis of coronary artery disease (CAD). MPI may detect obstructive CAD but fail to discover subclinical atherosclerosis. With advances in technology, low-dose computer tomography (CT) for attenuation correction has become an important part of nuclear cardiology. CT imaging in MPI allows for visualization of thoracic aorta calcification (TAC) and coronary artery calcification (CAC). The aim of the study was to evaluate the prevalence of TAC and CAC in patients referred to MPI.

PATIENTS AND METHODS: Clinical characteristics, MPI results, and prevalence of CAC and TAC were collected from 90 consecutive patients with an intermediate likelihood of CAD and without previously known atherosclerosis who were admitted to MPI.

RESULTS: Out of 90 patients, 32 (35,6%) had ischemia, 58 (64,4%) patients had normal MPI. 63,3% of all patients had calcification on low-dose CT (75% with ischemia vs. 57% with normal MPI, p=0,09). The majority of patients with CAC had concomitant TAC. In more than a quarter of patients, only TAC was present. More patients with ischemic MPI had CAC than patients with normal MPI (53,1% vs. 25,8%, p=0,01). Patients with normal MPI and TAC or CAC were older (71,1 ± 7,6 years vs. 56,5 ± 9,2 years, p< 0,001) and had more arterial hypertension (78,9% vs. 52%, p=0,03) than patients without calcification. Patients with normal MPI and only TAC had more arterial hypertension than patients with CAC (94,4% vs. 60%, p=0,01).

CONCLUSIONS: The combination of myocardial perfusion, CAC, and TAC from a single MPI scan may have a complementary role in the management of patients with an intermediate risk of CAD. In addition to improving risk estimation, reporting visually estimated calcification may influence patient management decisions.

# Endovascular treatment of a huge high-flow renal arteriovenous malformation

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BACKGROUND: Renal arteriovenous anomalies are rare, with a prevalence of less than 0.04%. They are characterized by an abnormal vascular connection that usually bypasses the capillary bed. 70% of such pathologies are acquired arteriovenous fistulas (AVF), while 30% are congenital or idiopathic arteriovenous malformations (AVM). AVFs are usually caused by renal interventions, trauma or neoplastic processes. Although often asymptomatic, AVF and AVM can cause hypertension, heart failure, hematuria, and renal insufficiency. Historically treated with open surgery, endovascular techniques are now preferred for their minimal invasiveness and renal function preservation.
CASE PRESENTATION: In July 2023, a 69-year-old woman with arrhythmia, tachycardia, mild ankle edema and increasing fatigue was admitted to a local hospital. Right kidney color Doppler ultrasound confirmed the presence of a huge AVM with a blood flow of 9 liters per minute and a dilated, 35 millimeters in diameter right renal vein. In September 2023, an attempt to embolize the AVM failed as the Amplatzer Vascular Plug II migrated to the pulmonary circulation and was later removed. Due to those technical issues, the patient was admitted to our Department. Complete embolization was achieved by implanting two Amplatzer Type II Vascular Plugs, various embolization coils, histoacryl glue and lipiodol (Figure 1). Right subclavian artery endovascular access was closed with 2 PROGLIDE-PROSTYLE systems. In this place, control angiography revealed a significant stenosis which was treated with Bentley BeGraft and Cook Zilver stents. The patient was discharged on the third postoperative day, all her symptoms resolved and she reported eventual recovery. In December 2023 the patient was operated on due to a 40x58mm pseudoaneurysm at the right femoral access site.
CONCLUSION: In conclusion, renal AVMs should be included as a potential alternative diagnosis for various symptoms, such as hematuria and hypertension resistant to medication. Endovascular embolization is a less-invasive, safer, and more effective option than open surgery, but it has a risk of complications like renal infarction and pulmonary embolism. Success requires fully occluding the shunted vessel, preventing embolic material migration and preserving normal arterial branches. It depends on selecting adequate techniques and embolic materials individually, based on etiology and precise vascular anatomy assessment.

# Brachiocephalic AV-fistula - only the last resort for native AV-fistula

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BACKGROUND: Brachiobasilic arteriovenous (AV) fistulas are rarely used for hemodialysis vascular access since their puncture area is limited to the elbow. The brachiocephalic AV-fistula was traditionally considered the gold standard in patients when constructing a radiocephalic AV-fistula on the forearm was impossible.
PATIENTS AND METHODS: Despite being the gold standard for vascular access on the upper arm, brachiocephalic AV-fistula has frequent and severe complications. In our reference vascular access centre at General Hospital Trbovlje, we perform more than 20 large-scale reconstructions of brachiocephalic AV-fistulas annually. We observe at least one of the classic three complications in all patients with brachiocephalic AV-fistula: stenosis of the cephalic arch, aneurysmal transformation of the vein in the distal half of the upper arm, and flow rate over 2000 ml/min.
RESULTS: Reconstruction of a brachiocephalic AV-fistula is usually a two/three-step procedure. The basis of the reconstruction is ensuring drainage through the arch of the cephalic vein, which requires the insertion of a stent graft (sized 8x60 to 10x120 mm). In the second session, we close the brachiocephalic AV anastomosis and perform an aneurysmoraphy. The reduction of vascular access flow is linked to this intervention with the PAVA procedure – inserting a 20-30 cm long 5 mm PTFE-graft between the trunk of the cephalic vein and the brachial artery axillary or, more often, with the RUDI procedure, using a 6 mm PTFE-graft inserted between the trunk of the cephalic vein and the radial artery at the wrist area. When using the median antebrachial vein for the RUDI procedure, we construct an additional radio-cephalic AV-anastomosis distally following the stent graft insertion and, after maturation, close the primary AV-anastomosis, do the aneurysmoraphy of the cephalic vein and connect it to the median antebrachial vein.
CONCLUSION: Distal AV-fistula is a vascular access with better longevity, a longer punction area, and fewer complications, which are characteristic of the brachiocephalic AV-fistula. Before constructing a brachiocephalic AV-fistula, we recommend an examination in a dedicated vascular access centre. AV-fistula construction can be successful even in the case of morphologically small arteries and veins.

# Treatment with ticagrelor leads to higher plasma concentrations of rosuvastatin in patients receiving both drugs

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BACKGROUND: Ticagrelor and rosuvastatin are often prescribed together to patients who have suffered an atherothrombotic event. Rosuvastatin is mainly excreted unchanged in the urine and bile. However, hepatocyte membrane transporter proteins, BCRP and OATP, significantly influence the pharmacokinetics of rosuvastatin. Ticagrelor inhibits both BCRP and OATP, which may affect rosuvastatin exposure. The aim of this study was to compare rosuvastatin plasma concentrations in patients receiving different antiplatelet drugs.

PATIENTS AND METHODS: We included 79 consecutive patients after myocardial infarction who were treated with rosuvastatin and an antiplatelet agent (ticagrelor, prasugrel or clopidogrel). The choice of antiplatelet agent was at the discretion of the treating physician. Data on associated medical conditions and lifestyle factors were collected for statistical analysis.

Blood samples were collected from patients on rosuvastatin at trough (approximately 24 hours after taking the last dose). Plasma extracted from these samples was used to quantify rosuvastatin concentrations by LC-MS/MS. Patient groups were compared using non-parametric Mann-Whitney test to assess differences in rosuvastatin concentrations between patients receiving ticagrelor and patients receiving prasugrel or clopidogrel, and between patients receiving prasugrel and clopidogrel.

RESULTS: The rosuvastatin concentration of the 79 patients receiving rosuvastatin varied considerably: The median concentration was 7.7 ng/mL (4.9 – 12.3 ng/mL, Q1 – Q3). Of these patients, 45 (57%) were concurrently prescribed ticagrelor, 10 (13 %) clopidogrel and 24 (30%) prasugrel. Rosuvastatin plasma concentrations were significantly higher in patients receiving ticagrelor than in those taking prasugrel or clopidogrel (9.7, 6.9 – 26.7 vs. 4.9, 2.7– 9.2 ng/mL). No significant differences in rosuvastatin concentrations were observed between patients receiving prasugrel and clopidogrel (4.6, 2.2 – 9.0 vs. 5.1, 4.0 – 10.4 ng/mL).

CONCLUSION: Our study showed significantly higher rosuvastatin plasma levels in post-myocardial infarction patients taking ticagrelor compared to patients receiving prasugrel or clopidogrel. We thus confirmed previous findings suggesting that ticagrelor may potentiate the effect of rosuvastatin. A better insight into this interaction will help to optimize patient therapy and safety in the treatment of atherothrombosis.

# Effect of peripheral vascular rehabilitation with $CO_2$ on microcirculation and healing of chronic wounds

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BACKGROUND: Diseases related to microcirculation and vascular diseases are often the result of chronic disorders of normal blood circulation. $CO_2$ causes blood vessels to dilate, resulting in increased blood flow, greater delivery of $O_2$, and an increase in $O_2$.The main role of vasodilatation is to increase blood flow to the body's tissues when it is most needed, as described by the Bohr effect, which is an adaptation of oxygen release in tissues with low oxygen concentrations in the capillaries, where $CO_2$ lowers the pH of the blood. When the pH of the blood decreases, the binding capacity of hemoglobin also decreases and remains bonded with oxygen. With the study, we carried out at the Novo Mesto General Hospital; we aim to demonstrate how peripheral vascular rehabilitation with $CO_2$ affects microcirculation. The study was conducted on a female patient with bilateral chronic wounds.

PATIENTS AND METHODS: Every fifth PVR therapy out of a total of twenty was recorded with TIVITA®system and NIRS before and after the therapy. We also measured local body temperature and VAS score. WITH TIVITA, four parameters were regularly measured with the system, namely Oxygenation $StO_2$ (%), Tissue Hemoglobin index– THI, NIR Perfusion Index, and Tissue Water Index - TWI. We also measured NIRS, which continuously monitors regional tissue oxygenation.

RESULTS: TIVITA measurements showed an improvement in microcirculation after the first therapies. Measurements were taken before, during, and after the therapy in the area of the left and right shin and foot every fifth therapy. By measurements with NIRS, we detected a minor improvement in tissue oxygenation before, during, and after the therapy.

CONCLUSION: According to the study we conducted, peripheral vascular rehabilitation with $CO_2$ is a useful method for improving the functioning of microcirculation. The patient in our study experienced a reduction in pain, and her chronic wound became smaller and shallower. Microcirculation plays a key role in homeostatic and defensive conditions during tissue damage and inflammation. Other roles include the protective role of the microcirculation, the impairment of the microcirculation and the possibility of being the missing link in the chain of events leading to chronic wounds and vascular disease.

# Takayasu's arteritis initially presented with cerebral infarction

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Takayasu's arteritis is a chronic inflammation (vasculitis) of medium and large vessels. The most involved vessel is the aorta and its primary branches. The incidence of the disease ranges from 0.3 to 3.3 million per year. It is primarily seen in young women.

Granulomatous inflammation of vascular media, and mononuclear infiltration that results in arterial wall thickening with stenosis, occlusion and aneurysmal dilation is characteristic of this arteritis.

Chronic inflammation causes progressive arterial occlusion that leads to reduced blood flow with end-organ ischemia, arm or leg claudications, and diminished or absent peripheral pulses.

Stroke is one of the common complications but it is rarely the initial presentation.

We describe a case of Takayasu's arteritis in a 38-year-old woman who presented with syncope, dizziness, non-fluent aphasia and right-sided hemiparesis without any significant history.

From laboratory findings only non-specific inflammatory markers such as erythrocyte sedimentation rate (ESR) were elevated. CT imaging angiogram studies and digital subtraction angiography revealed left middle cerebral artery territory infarct with occlusion of common carotid arteries, bilateral bifurcation, proximal parts of the left internal carotid artery, and the right internal carotid artery. She was diagnosed with Takayasu's arteritis and was prescribed steroids and NSAIL therapy on which she gradually recovered and was discharged from hospital.

Young patients who present with stroke should be investigated for Takayasu’s arteritis, it can lead to earlier treatment and prevention of further life-threatening complications.

# Hybrid vascular procedures at University Medical Centre Maribor

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BACKGROUND: Hybrid operations are relatively new in the world of vascular surgery, especially from the point of view of the used technology and technique, which has changed significantly since its beginnings in the 70s of the last century. In our institution, the hybrid procedure is also considered a novelty, which, like the rest of the world, has proven to be extremely useful, especially in vascular patients with a multilevel problem.
PATIENTS AND METHODS: Retrospective analysis of 60 patients undergoing hybrid surgery at the Department of Vascular Surgery at the University Medical Centre Maribor between 2020 and 2022.
RESULTS: Of the 60 patients, 12 (20%) were women and 48 (80%) were men. The gender ratio was 4:1. The average age of the patients was 69 years, the oldest patient was 87 years old, the youngest was 39 years old. The average length of stay in hospital was 8.4 days, the longest length of stay was 31 days, and the shortest length of stay was 3 days. In 37 (57%) patients, the indication for the procedure was chronic critical ischemia, in 17 (29%) patients intermittent claudication, in 4 (7%) patients aneurysm, in 3 (5%) patients fistula thrombosis, in 1 (2% ) the patient has an artery injury. The most frequently operated limb was the left in 32 (53%). The surgical part of the intervention consisted of TEA in 18 (30%) patients bypass, in 13 (22%) patients embolectomy, in 5 (8%) patients profundoplasty and in 1 (2%) patient thrombectomy. The endovascular part of the procedure consisted of DSA in 28 (47%) patients, PTA in 12 (20%) patients and stenting in 20 (33%) patients.
CONCLUSION: Hybrid operations represent a new way of treating complex vascular patients with high success rates, where cooperation between the vascular surgeon, radiologist and anesthesiologist is important.

# Acute limb ischemia caused by popliteal artery entrapment syndrome

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A 27-year-old athletic male patient without previous comorbidities presented with acute right lower extremity ischemia. Clinically the limb was viable without signs of immediate threat (Rutherford Class I). On the right lower extremity only the femoral pulse was palpable. Computer tomography angiography (CTA) showed acute thrombotic occlusion of the right popliteal artery, which extended distally to the tibioperoneal trunk and the proximal part of anterior tibial, posterior tibial and fibular arteries. At first, local catheter-directed intra-arterial thrombolysis was attempted, but was not successful. During the procedure digital subtraction angiography (DSA) revealed impingement of the proximal part of the popliteal artery, suggesting popliteal artery entrapment syndrome (PAES) (Figure 1). Consequently, magnetic resonance imaging (MRI) was performed, confirming the diagnosis of PAES type II. After consultation with cardiovascular and plastic and reconstructive surgery popliteal artery thrombectomy was performed and the entrapped popliteal artery was released. The patient's symptoms improved after the procedure.

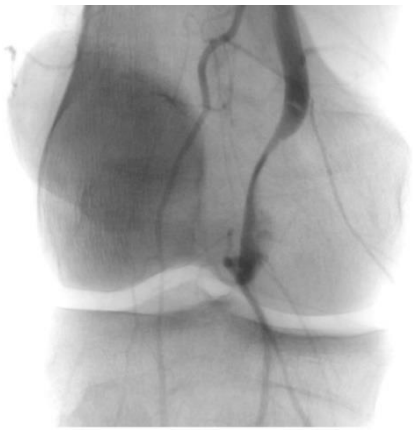

Figure 1: Digital subtraction angiography of the right lower extremity showing proximal impingement and distal occlusion of the right popliteal artery, caused by popliteal artery entrapment syndrome type II.

PAES is a rare cause of lower extremity ischemia. It may be congenital or acquired and is caused by external compression of the popliteal artery, most commonly by the medial head of the gastrocnemius muscle. Patients are usually young, physically active and the majority are male. Symptoms can range from exertion induced intermittent claudication to acute limb ischemia. PAES is often diagnosed late since patients are usually young, without classical risk factors for atherosclerotic vascular disease and may have a normal examination at rest. When PAES is suspected, available diagnostic tests include exercise ankle-brachial index measurement and vascular imaging modalities with provocation maneuvers, such as provocation duplex ultrasonography, MRI, CTA, or DSA. The advantage of MRI and CTA is that they can show the local anatomical relationship of the popliteal artery with nearby musculotendinous structures. Surgery with release of the popliteal artery remains the gold standard of PEAS treatment in symptomatic patients.

# Surgical treatment of endarteritis of iliofemoral region with use of selective perfusion of left lower limb during a prolonged vascular reconstruction – a case report

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Surgical treatment of septic endaretritis of iliofemoral region can result in prolonged ischemia to the lower extremities. Distal perfusion of the limb can improve earlly postoperative outcome.
We present a case of a 35-year-old woman who was diagnosed with septic endarteritis of the right iliofemoral region as a consequence of residual wire fragments from a prior endovascular procedure. During the intervention the entire iliofemoralarterial segment was replaced with homograft due to complete destruction of native arterial walls. Because of the extent of the replacement and predicted duration of the procedure we used selective distal perfusion of her right leg to minimise the possibility of ischemia and reperfusion injury to the tissues that is ususally followed by a compartment syndrome. The patient recovered fully.
This case highlights the importance of a multidisciplinary approach when it comes to treatment of rare and complex cases.

# Case report: Native aortic valve thrombosis: what's behind?

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Native aortic valve thrombosis is an exceptionally rare and serious condition characterized by the formation of a thrombus on the native aortic valve. It presents a significant clinical challenge and can lead to severe complications, including heart failure or cardiogenic shock due to a heart attack or aortic valve dysfunction, neurological issues such as stroke, and peripheral embolisms affecting the arteries of the arms, legs, kidneys, and other organs.

Given the numerous potential causes of peripheral embolism, thrombosis of the native aortic valve is an extremely rare source. Due to its low incidence, there is limited data on its etiology, treatment, complications, and clinical outcomes, with most information derived from individual case reports. It is imperative to identify the underlying cause, which frequently poses a significant clinical challenge.

We present the case of a 55-year-old patient with a pronounced prothrombogenic condition, which manifested as venous thromboembolism and thrombosis of the native aortic valve. This condition led to repeated embolism into the central nervous system and peripheral arteries of the arms and legs. The underlying cause of the prothrombogenic state was a newly diagnosed lung carcinoma.

# Risk-Benefit Ratio

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BACKGROUND: All drugs produce a range of therapeutic and adverse effects. A risk-benefit (R-B) ratio is the ratio of risk to its potential benefits. A drug should only be prescribed when the benefits outweigh the risks.

In the late 1990s, regulatory agencies pressured pharmaceutical companies to perform R-B evaluations. The European Committee for Proprietary Medicinal Products recommended methods for evaluating risks in post-marketing settings. The European Medicines Agency initiated the Benefit-Risk Action Team (BRAT). The FDA guided the R-B evaluation.

PATIENTS AND METHODS: Risk is the probability of physical, psychological, social, or economic harm occurring because of participating in a research study. The benefit is the potential of the research treatment to alleviate a condition or treat a disease. Blinding is the process whereby the participant does not know whether he/she is receiving an active agent. Double blinding is a process whereby neither the investigator nor the participant knows which agent the participant receives.

The BRAT framework

The BRAT involves performing BR evaluation in a structured, transparent, and consistent way. It helps inform stakeholders to make BR decisions and communicate the decisions and rationales for the decisions, increasing the transparency of the whole process.

RESULTS: In the Randomized Evaluation of Long-Term Anticoagulant Therapy trial, 110-mg and 150-mg doses of dabigatran were compared against warfarin in patients with nonvalvular AF. Both doses were non-inferior to warfarin (primary efficacy endpoint of stroke or systemic embolic event); the 150-mg dose was superior to warfarin and the 110-mg dose. The 110-mg dose was superior to warfarin (less bleeding), and the 150-mg dose was similar to warfarin (similar bleeding). The 150-mg dose reduced the risk of disabling stroke, excluding hemorrhage of more than 110 mg. The favorable benefit-risk balance for 150 mg over 110 mg led the FDA to approve the higher dose.

Donanemab

FDA advisory panel endorsed Alzeimer’s drug, donanemab, which slowed cognitive and functional decline for people in the early stages since the benefits outweighed the potential risks.

CONCLUSION: Physicians' core mission is to ensure that products are safe and effective. Regularly applying a BR assessment could help increase acceptance of these methods.

# Cancer Associated Thrombosis

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BACKGROUND: Cancer-associated thrombosis (CAT) presents a multifaceted challenge in oncology, impacting both morbidity and mortality rates. Patients with cancer face an elevated risk of thrombotic events due to various tumor-related and treatment-related factors. CAT encompasses both venous and arterial thrombotic events, excluding other thrombosis causes such as trauma or surgery. Understanding CAT is crucial for clinicians to manage and mitigate its complications in cancer patients effectively. Despite advancements in cancer treatment, CAT remains a significant concern, highlighting the need for continued research and improved therapeutic strategies.

PATIENTS AND METHODS: It involves intricate interactions between cancer cells, the coagulation system, and the vascular endothelium. Cancer cells produce procoagulant factors, such as tissue factors, promoting thrombus formation and propagation. Moreover, cancer-induced inflammation and endothelial dysfunction contribute to a hypercoagulable state. Tumor cells release tissue factor, promoting activation of the extrinsic pathway of coagulation. Cancer cells express procoagulant microparticles and cytokines, further stimulating thrombus formation. Interactions between cancer cells and the host immune system induce a proinflammatory and prothrombotic microenvironment.

RESULTS: Prevention of CAT: Reducing the risk of thrombotic events in cancer patients, particularly those undergoing surgery or receiving chemotherapy, is important. Prophylactic anticoagulation with LMWH and mechanical prophylaxis with intermittent pneumatic compression devices in patients with contraindications to pharmacological prophylaxis is beneficial

Management of CAT: Treatment of CAT aims to prevent thrombus propagation, reduce the risk of recurrence, and alleviate symptoms. Anticoagulation therapy with LMWH is the cornerstone of treatment, offering superior efficacy and safety compared to vitamin K antagonists in cancer patients. Supportive measures such as pain management, compression therapy, and hydration may also address symptoms and improve patient outcomes. Thrombolytic therapy is usually reserved for life-threatening VTEs such as a pulmonary embolism. Thromboprophylaxis in patients with clinically active malignancy, DOACs, fondaparinux, and warfarin should be considered.

CONCLUSION: CAT represents intricate interactions between cancer cells, the coagulation system, and the vascular endothelium and is a significant clinical challenge in management in these patients, necessitating both prevention and treatment. Patients with clinically active malignancy would benefit from thromboprophylaxis. Anticoagulation with unfractionated heparin or low molecular weight heparin in hospitalized cancer patients should be given.

# D-dimer

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BACKGROUND: D-dimer (DD) is a fibrin degradation product, a small protein fragment in the blood after a blood clot is degraded by fibrinolysis. DD concentration is determined in a lab to diagnose or exclude thrombosis. DD assays vary widely concerning the antibody used, capture method, instrumentation required, and calibration standard.
We reviewed the published literature on DD.
What is DD?
DD is produced when plasmin, an enzyme activated through the fibrinolytic pathway, cleaves fibrin to break down clots. DD consists of two covalently bound fibrin D domains cross-linked by factor XIII when the clot was formed. This fragment forms epitopes targeted by monoclonal antibodies in DD assays to confirm that the coagulation cascade is generating thrombin.
PATIENTS AND METHODS: DD is not usually detectable in blood; it is produced when blood clots break down. The presence of DD in the blood or urine may indicate the development of a clot.
RESULTS: Reference Range of DD
A normal DD is considered less than 0.50. A positive DD is 0.50 or greater.
DD measurement is a very important step in VTE diagnosis, as it allows clinicians to rule out the disease in around 30% of outpatients with suspected DVT or PE. However, the test is less useful in elderly patients > 50 years.
Conditions causing elevated DD
The following conditions can cause an elevated DD: pregnancy, smoking, physical trauma, cancer, and infections.
False-negative results
Aspirin, clopidogrel, ticagrelor, and statins can produce false negative results.
Laboratory testing of DD
The DD Test is often conducted in an emergency room. Low or normal DD levels indicate the person probably has no clotting disorder. Higher than normal D-dimer levels indicate a clotting disorder. The D-dimer test cannot show where the clot is located or what type of clotting disorder the person has.
CONCLUSION: DD is produced when plasmin cleaves fibrin to break down clots. DD is valuable for blood clot detection. High DD levels can indicate DVT or PE, but the presence of DD cannot tell the clot's location. Pregnancy, cancer, and old age cause elevated DD. Aspirin and statins give false negative results.

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