Vasa

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Editor-in-Chief

Andreas Creutzig

Editors

Beatrice Amann-Vesti
Erich Minar
Pavel Poredoš
Omke Teebken

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Leukotrienes E4 – new prognostic biomarker of restenosis after endovascular treatment in patients with lower limb ischemia?

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Influence of myocardial injury after endovascular treatment on major adverse cardiovascular events in patients with critical lower limbs ischemia

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Financial incentives for smoking cessation medication in european countries from the perspective of the angiology outpatient clinics

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Knockout of lipocalin-2 is associated with an impaired outcome in the hind limb ischemia and carotid artery injury model

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Endovascular treatment of visceral arteries aneurysms – our experience

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Peripheral aneurysms – endovascular treatment

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What are the histomorphological effects of cryosclerosis?

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Objective

The aim of this poster is to demonstrate the histomorphological changes of the saphenous wall caused by cryosclerosis (endovenous cryoablation).

Background

Cryosclerosis was introduced by R. Milleret et P.J. LePivert. It should be considered among the endovenous thermal ablation procedures.

Methods

As a part of a consecutive trial, vein pieces were harvested for transmission electron microscopic evaluation during endovenous cryoablation. Two years after cryosclerosis, cryostripping was performed due to a recanalized incompetent great saphenous vein (GSV) and a vein segment was removed for photomicroscopic evaluation (Haematoxylin-eosin, Picro-sirius Red, van Gieson and immune histochemic – CD34, SMA – stains).

Results

The transmission electron microscopic analysis of the vein pieces showed endothelial damage (tapering of tissue, shrinkage, core fragmentation necrotical appearance of the cells) and thickening of the smooth muscle in the subendothelial layer and tunica media. During cryostripping performed two years after cryosclerosis, the GSV was very crusted and segmental strictures were found when the cryoprobe was introduced into the vessel lumen. The anatomical structure of the vein could not be recognized photomicroscopically because the wall was collagenised and padded by endothelium that was caused by progressive fibrosis.

Conclusion

The transmission electron microscopic examination proved that immediate ultrastructural changes were formed in the GSV. However, recanalization occurred two years after cryosclerosis, the vein wall underwent remodeling.

Remote pre-procedural ischemic stroke was the strongest risk for stroke and death associated with carotid stenting – a single center experience

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Rationale/Objective

Remote ischemic stroke is known risk factor for stroke recurrence during surgery. The aim of our study was to determine the periprocedural complication risk (within 30 days after CAS) associated with CAS (stroke, death) between patients with remote pre-procedural ischemic stroke and without it; to analyse periprocedural risk in other specific patient subgroups treated with CAS.

Methods

We conducted a retrospective review of prospectively collected data from all patients treated with protected CAS between June 20, 2008 and December 31, 2015. Remote pre-procedural ischemic stroke was defined as any-territory ischemic stroke > 6months prior to CAS.

Results

The risk of periprocedural stroke/death was 3.4-times higher in patients with remote ischemic stroke compared with patients without it (6.6 % vs 2.0 %, $p = 0.008$). Periprocedural stroke/death in symptomatic patients was non-significantly higher in patients with remote ischemic stroke compared with patients without it (7.9 % vs 3.6 %; $p = 0.206$). Asymptomatic patients with remote ischemic stroke had a 5.6-times higher periprocedural risk of stroke/death compared with asymptomatic patients without it (5.7 % vs 1.0 %; $p = 0.014$). Patients ≥ 75 years had a 3.0-times higher periprocedural risk of stroke/death compared with younger patients (8.4 % vs 2.9 %; $p = 0.015$); a non-significant increase of periprocedural stroke/death was found in both symptomatic and asymptomatic elderly patients ([11.4 % vs 4.0 %; $p = 0.078$], [6.3 % vs 2.4 %; $p = 0.124$]) respectively.

Conclusions

In our experience all patients with remote pre-procedural any territory ischemic stroke belong to risky subgroup for periprocedural stroke death after CAS. All asymptomatic patients with remote ischemic stroke should not be treated with CAS.

Evaluation of ischemia during rowing exercises in claudicants a pilot study

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Background

Physical activity is part of peripheral artery disease (PAD) treatment. An optimal activity for rehabilitation would induce a significant amount of ischemia of the lower limb but would not be limited by symptoms. Aerobic upper limb exercises can improve PAD patients, but their effect on lower limb ischemia is unknown.

Methods

We used the DROP index of transcutaneous oxygen pressure to monitor exercise-induced regional blood flow impairment (RBFi) when walking during a treadmill test (-3.2 km/h; 10 % M slope) and during rowing tests in 6 male patients: 60.3 $\pm$ 5.1 years old, ankle-brachial index 0.63 $\pm$ 0.14, Body Mass Index 25.7 $\pm$ 3.7 kg/m². Three series of rowing exercise were planned for each patient with complete freedom of leg movements (R100) with leg movements partially blocked half distance from leg extension (R50) or with no leg movement possible (R0). A target power for rowing exercises was defined according to Cooper & Storer formula. The study was registered on the NIH base: NCT/02833597.

Results

All patients completed the protocol. Compared to maximal duration of exercise while walking (349 $\pm$ 142) rowing allowed higher exercise periods 461 $\pm$ 390, 424 $\pm$ 275 and 543 $\pm$ 421 sec for R0 R50 and R100 respectively. Average of the two legs RBFi was -24 $\pm$ -9 on treadmill, -9 $\pm$ -5, -18 $\pm$ -10 and -18 $\pm$ -8 mmHg for R0 R50 and R100 respectively ($p < 0.05$ for all).

Conclusion

Rowing allows prolonged periods of aerobic exercise as compared to treadmill while limiting the severity of leg ischemia even in patients with no specific rowing experience.

We thank "Angers Nautique" for their support.

Long-term outcomes of veno-venous bypass operations in postthrombotic syndrome

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Objective

The present study was aimed at assessing long-term results of veno-venous bypass operations in postthrombotic syndrome (PTS).

Methods

We analyzed long-term outcomes of crossover vein bypass procedures in 69 patients with unilateral postthrombotic iliac vein obstructions at periods from two to 28 years and 12 patients who underwent saphenopopliteal bypasses for femoral vein obstructions.

Results

It was validated that the decisive factor of the success of the crossover bypass procedure was a sufficient diameter of venous graft, i.e. not less than 7–8 mm. It has been determined that in 70.6% of the patients, crossover grafts have a propensity to dilate, furnishing the requisite venous blood outflow from an affected extremity. Venous hemodynamic studies of the affected extremity with the graft being open and cross-clamped revealed that crossover bypasses assume the primary role in the maintenance of venous returns. Some grafts (23.6%) undergo pathological transformations that diminish venous blood outflow and they require redo surgeries. Such operations were auspiciously performed in seven patients in a long-term period. In 15 years, cumulative patency of crossover grafts was 77%. There was cumulative clinical success in 71% of the patients. The patency rate of saphenopopliteal grafting within the period up to 12 years was 91.7%. Long-term outcomes of the procedures proved durable functioning of the grafts and improvement of regional venous hemodynamics. It was established that the grafts are capable of prolonged functioning without pathological dilatations and that there was significant improvement of reconstructive operations with the usage of distal arteriovenous fistulas.

Conclusion

Long-term results demonstrated a high efficacy of veno-venous bypass operations in PTS.

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First experience of performing hybrid operations in chronic venous obstructions of iliofemoral segments in patients with postthrombotic syndrome

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Objective

To assess the first results of hybrid operations in chronic venous obstructions of iliofemoral segments in patients with postthrombotic syndrome (PTS).

Methods

Hybrid operations (open endovenectomy from the common femoral vein (CFV) with arteriovenous fistula (AVF) creation and iliac vein stenting) were performed in 12 patients diagnosed with PTS. All of the patients were diagnosed with severe chronic venous insufficiency (CVI). The degree of manifestations of PTS was assessed by means of the Villalta scale before, and seven months after, the surgical intervention. Diagnostic methods of study included ultrasound duplex scanning (UDS), magnetic resonance and/or multispiral computed venography and contrast venography.

Results

Technical success of the procedure was 92%. The outcomes of hybrid operations after seven months were followed up in six patients. Secondary patency rates of the stented iliac veins amounted to 100%. No recurrences of venous ulcers were observed. Median Villalta scores improved from 15 to 7 ($P = .012$).

Conclusion

The first experience of hybrid operations for obstructive lesions of veins of the iliofemoral segments demonstrated their high efficacy and safety.

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Kounis syndrome – what to do if the patient needs surgery after suffering allergic vasospastic attack

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Kounis syndrome first defined in 1991 as the coincidental occurrence of acute coronary syndromes, with hypersensitivity reactions that involve the stimulation of relating and interdependent inflammatory cells. It comprises of anaphylactoid, anaphylactic and hypersensitive or allergic insults. Inflammatory mediators such as neutral proteases, platelet activating factor, histamine and aracidonic acid products are the agents of aetiology. In addition, to a variety of chemokines and cytokines released during the hypersensitive insult.¹ This syndrome, although underreported is not rare – in the small district of Achaia, Greece with a total population of 300.000, 20 cases have been reported in the period 2009–2011.²

We report the case of 55 year old man who suffered severe coronary artery vasospasm and instability with ST elevation as a result of an IV cephalosporin. The patient required a secondary major eight hour neurosurgery due to a risk of paraplegia. He was administered one gram twice daily amoxicillin/clavulanic acid 875 mg/125 mg for two weeks before the operation with no antibiotics during and one gram twice daily for two weeks after the operation. The patient showed no evidence of infection following his surgery and the operation was successful with him walking post-surgery.

As it stands, there are no clear clinical guidelines for the management of patients that require emergency, non-elective surgery following a diagnosis of Kounis syndrome. We postulate an oral pre- and post-surgical antibiotic regimen for patients that require surgery following vasospastic attack, excluding intra-surgical antibiotic administration. This postulation may provide physicians with some guidance for clinical practice.

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Aortic diameter at age 65 in men with incipient or newly diagnosed type 2 diabetes

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Objective

Type 2 diabetes mellitus has been linked to a decreased risk for abdominal aortic aneurysm (AAA) development in men.

Methods

We cross-sectionally compared aortic diameter in 691 men aged 65 years with incipient or newly diagnosed type 2 diabetes with 18,262 65-year old control men without diabetes.

Results

Men with incipient or newly diagnosed type 2 diabetes (group A) did not have smaller aortic diameter than men without (group B) 18.8 (17.4–20.8) vs. 19.0 (17.5–28.7) mm; $p = 0.43$. Prevalence of AAA was 2.5 % in group A, and 1.5 % in group B ($p = 0.010$). Groups differed concerning body mass index (BMI), smoking, presence of atherosclerotic disease, and hypertension. In logistic regression the differences concerning AAA prevalence ($p = 0.15$) were lost, whereas group A still showed higher BMI ($p < 0.001$), and prevalence of previous myocardial infarction ($p < 0.001$), peripheral arterial disease ($p = 0.001$), and hypertension ($p < 0.001$). Among men in group A, C-peptide ($r = 0.093$; $p = 0.034$), but not HbA1c ($r = 0.060$; $p = 0.24$) correlated with aortic diameter.

Conclusions

At age 65, aortic diameter and AAA prevalence did not differ between men with incipient or newly diagnosed type 2 diabetes and those without diabetes. Putative protective effects of type 2 diabetes mellitus upon AAA development probably occur later.

CHIVA strategy – the hemodynamic management of primary varicose leg ulcers: a single center prospective study

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Rationale

The hemodynamic concept of varicose veins means that varicose veins are the symptoms of a background hemodynamic disorder. In a prospective manner we studied the primary varicose ulcers' clinical and ultrasound evolution after minimally invasive ambulatory surgical correction of underlying hemodynamic disturbances with saphenous trunk preservation (CHIVA: „Cure Conservatrice et Hemodynamique de l'Insuffisance Veineuse en Ambulatoire”).

Methods

38 patients with primary varicose leg ulcers were enrolled. With duplex mapping the hemodynamic shunt type was defined and the appropriate CHIVA intervention strategy was applied in local anesthesia in ambulatory. The patients underwent clinical and ultrasound follow-up for 1 year.

Results

The most prevalent hemodynamic shunt type was shunt 1 + 2. The main CHIVA intervention was the so called CHIVA 1 strategy (escape point elimination and varicose tributary disconnection). In few cases a complementary foam sclerotherapy was performed. The ulcer healing rate was 100 % with no recurrences in the follow up period. The healing duration was on average 6 weeks. There was a significant diameter reduction (45%) of saphenous trunks. In 26 % transitory thrombophlebitis of varicose trunk/tributaries was observed with spontaneous resolution of the thrombus.

Conclusions

CHIVA strategy for varicose leg ulcers is a highly efficient, safe, well tolerated and durable treatment option even in elderly and co-morbid patients. A correct hemodynamic duplex mapping is mandatory planning this strategy.

Angiosarcoma associated with dacron vascular prosthesis following aortic reconstruction

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Background

Primary malignancies of vasculature are rare and often diagnosed late resulting in poor prognosis. The majority of cases described have been de novo presentations but there are case reports in the literature of angiosarcoma arising in the setting of vascular grafting¹. Given the rarity of these clinical cases, is it purely coincidence or is there a causative relationship such as a foreign body reaction leading to dysplastic changes within the vessel wall?

Methods

We report on a case of a 74-year-old male who presented many years following EVAR for an infrarenal aortic aneurysm followed by open repair with bifurcated Dacron graft. Following a period of clinical deterioration a workup CT abdomen demonstrated a large right pelvic mass for which a biopsy revealed angiosarcoma. The patient continued to deteriorate and was subsequently palliated.

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Results

A prolonged inflammatory response to the Dacron material may lead to metaplasia, which can lead to dysplasia and finally to malignant change. The sequence of genetic changes driving mutation, inactivation and deletions may be caused by a prolonged inflammatory phase in a genetically susceptible patient cohort.

Conclusion

The majority of primary arterial tumours are de novo. However, there have been case reports of tumours arising in the setting of Dacron grafts. A prolonged inflammatory response to the Dacron material may lead to metaplasia, which can lead to dysplasia and finally to malignant change. With the recent uptake of endovascular stent graft repair being offered to patients at a much younger age and older patients living longer, more cases of arterial tumours may present.

The outcomes of portal vein thrombosis of patients with abdominal infection, a 5-year retrospective study

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Aim

To explore the outcomes of portal vein thrombosis (PVT) patients with intra-abdominal infections with or without anticoagulation.

Method

This five year retrospective study from 2011 to 2016 analysed clinical information collected from blue-letter referrals followed up under vascular medicine clinic. With ethics approval, we analysed demographics, co-morbidities, investigations, therapeutics, and outcomes. In total 35 PVT patients records were screened and 19 patients were noted to have PVT with intra-abdominal infection. Mean and range was calculated for demographic data and 2 groups with and without anticoagulation were analysed for outcomes

Results

19 patients (54.3%) of 35 patients with PVT and infection were analysed. Demographics included a mean age of 59.6 years (range: 30–79 years), 14 males, 5 females, 12 Chinese, 2 Malays, 2 Indians, and 3 Others. Anticoagulation therapy was used in 11, with 6 receiving low molecular weight heparin (LMWH), and 5 receiving a combination of LMWH and warfarin. The remaining 8 patients were not treated with anticoagulation.

		Anticoagulation (11) [57.9%]	No anticoagulation (8) [42.1%]
Thrombosis at diagnosis	Complete	7 (63.6%)	5 (62.5%)
	Partial	4 (36.4%)	3 (37.5%)
Outcome	Complete resolution	5 (45.5%)	2 (25.0%)
	Partial resolution	1 (9.09%)	0 (0.00%)
	No resolution	5 (45.5%)	6 (75.0%)
	Bleeding	2 (18.2%)	0 (0.00%)
	Recurrence	0 (0.00%)	2 (25.0%)
	Death	0 (0.00%)	2 (25.0%)

Conclusion

With anticoagulation therapy, complete and partial PVT resolution was higher along with higher bleeding risk. Mortality rates and recurrence in patients who received anticoagulation therapy were lower compared to those who did not receive anticoagulation.

The outcomes of portal vein thrombosis of patients with primary and secondary hepatocellular carcinoma, a 5-year retrospective study

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Aim

To explore the outcomes of resolution versus bleeding of portal vein thrombosis (PVT) against the use of anticoagulation in patients with primary and secondary liver malignancy.

Method

With ethics approval, we conducted a five year (2011–2016) retrospective study. A bank of clinical information was collected from inpatient referrals that were followed up in a vascular medicine clinic. Mean and range for demographics, co-morbidities, investigations, therapeutics, and outcomes were analysed in PVT patients with primary or secondary malignancy. They were further analysed in 2-groups – those who received anticoagulation, and those who did not.

Results

13 (6 males, 7 females) PVT patients with malignancy out of total of 35 patients with PVT were analysed. Demographics included a mean age of 66.7 years (range: 47–91 years), 11 Chinese, 1 Malay, and 1 Other. 6 received anticoagulation therapy, with 5 receiving low molecular weight heparin (LMWH), and 1 receiving a combination of LMWH and warfarin. 7 patients were not treated with anticoagulation.

		Anticoagulation (6) [46.2%]	No anticoagulation (7) [53.8%]
Thrombosis at diagnosis	Complete	5 (83.3%)	4 (57.1%)
	Partial	1 (16.7%)	3 (42.9%)
Outcome	Complete resolution	1 (16.7%)	0 (0.00%)
	Partial resolution	0 (0.00%)	0 (0.00%)
	No resolution	5 (83.3%)	7 (100%)
	Bleeding	1 (16.7%)	0 (0.00%)
	Recurrence	0 (0.00%)	0 (0.00%)
	Death	4 (66.7%)	4 (57.1%)

Conclusion

With anticoagulation therapy, PVT resolution was higher along with higher bleeding risk. However, mean survival time was much longer in patients who received compared to those who did not receive anticoagulation (385 vs 55 days).

A 5-year retrospective study investigating the outcomes of clot resolution vs bleeding episodes in patients with portal vein thrombosis (PVT) in the setting of cirrhosis, with or without anticoagulation

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Aim
Retrospective (subgroup) study to investigate the outcomes of clot resolution versus bleeding episodes in patients with Portal Vein Thrombosis (PVT) and Cirrhosis of liver, with or without anticoagulation.

Methods
35 PVT cases were identified in 5 year (2011–2016) electronic records found in blue letter referrals to vascular medicine inpatient, after approval from ethics committee. Cases were classified into 3 groups: PVT with cirrhosis, PVT with malignancy, PVT with infections. Data (demographics, co-morbidities, treatment regimes, outcomes) were collected.

Results
6 patients (3 male, 3 female) were classified under PVT with Cirrhosis (mean age: 62.58, range: 38–83). 4 Chinese, 1 Malay, and 1 other race. 3 patients experienced strokes, 3 diabetic, 4 hypertensive. 3 patients have varices, 1 with previous variceal bleeding. All patients on anticoagulation were on combination low-molecular weight Heparin and Warfarin.

		Anticoagulation (3) [50%]	No anticoagulation (3) [50%]
Thrombosis at diagnosis	Complete	2 (66.7 %)	3 (100 %)
	Partial	1 (33.3 %)	0 (0.00 %)
Outcome	Complete resolution	1 (33.3 %)	0 (0.00 %)
	No resolution	2 (66.7 %)	3 (100 %)
	Bleeding	0 (0.00 %)	0 (0.00 %)
	Death	1 (33.3 %)	2 (66.6 %)

Conclusions
In this small group data, anticoagulation for patients with PVT and cirrhosis is effective. Bleeding risk in both groups is similar which confirms the success of treatment.

Ruptured acute type B dissection – specific issues and endovascular repair paradigms

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Objective
Ruptured acute type B dissection (r-ABAD) presenting with hemodynamic instability or shock condition have poor outcome. With a 30 day mortality of 50 % when managed with open aortic repair, rupture is the most catastrophic complication of ABAD. This study focused on the clinical features and outcomes of thoracic endovascular aortic repair (TEVAR) for r-ABAD.

Methods
A review of consecutive TEVAR for r-ABAD in our emergency center was performed. Of the 52 patients admitted with ABAD (2014–2017), 3 (5.8 %) underwent TEVAR for rupture. Two (67 %) were in shock (Systolic blood pressure < 80 mmHg) before surgery.

Results
Technical success was achieved in 100 %, and in all cases an improvement in hemodynamics was obtained. One patient had coverage of the left subclavian artery. Median length of aortic coverage was 190 mm, and median proximal oversizing was 11.0 % (range 6.3–14.3 %). Morbidity included permanent paraplegia (1) or esophageal necrosis (1) which was diagnosed with esophagography. There was one patient in hospital death, who died of mediastinitis due to esophageal necrosis on postoperative day 16. At last follow up CT scan, two patients (67 %) had complete remodeling of the aortic wall.

Conclusions
Esophageal necrosis is well known to bear high mortality and morbidity. The most causative factor is supposed to be mediastinal hematoma compressing esophagus. TEVAR in this emergency pathology may be feasible and is related to specific issues which must be understood to improve outcome.

Safety and efficacy of 4-french catheter antegrade approach/OUTBACK LT catheter in recanalization of chronic superficial femoral artery occlusion

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Rationale
The most common feature of failed angioplasty of chronic occlusion of the superficial femoral artery (SFA) is the inability to re-enter the true lumen. A percutaneous antegrade approach (PAA) using a 4-French catheter or, alternatively, the OUTBACK LT (OLT) catheter was proven successful in treating SFA chronic occlusion.

Methods
Between January 2016 and July 2016, 70 patients (aged 64.3 ± 9) received endovascular treatment for SFA chronic occlusion, 68 cases with percutaneous antegrade approach (PAA), using a 4-French catheter. In the remaining 2 cases subintimal recanalization was achieved using the OUTBACK LT catheter. Risk factors included hypertension (93.8 %), CRF (43.8 %), diabetes (62.5 %), hyperlipidemia (93.8 %), smoking (87.1 %). All patients had SFA occlusion with short proximal stump. Conventional approach had failed true lumen re-entry. Clinically, ankle-brachial index (ABI) averaged 0.63 ± 0.12. All patients were Fontaine stage IIb.

Results
The PAA/OLT could achieve recanalization and successful primary stenting in all patients. There were no procedure-related complications. Mean increase in ABI was 0.34 ± 0.18. Residual stenosis was less than 30% in all patients. At 10 ± 2 month follow-up, ABI went up to 0.97 ± 0.14, with significant improvement in pain-free walking distance.

Conclusions
Based on our experience SFA occlusion has a far better chance to be treated with PAA/OLT rather than with conventional technique. Thus, we recommend this approach to be considered in the event of challenging recanalization. Further studies with broader number of patients are required to evaluate long-term patency rate of PAA/OLT in patients with high risk profile.

Is factor V – leiden mutation a major risk factor for venous thrombosis among lebanese patients

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Background

Lebanon exhibits one of the highest prevalence of factor V-Leiden (FVL) in the world (14.4%). The aim of this study is to evaluate the incidence of FVL mutation among Lebanese patients with lower extremity venous thrombosis and the conditions associated with this mutation

Methods

From January 2000 to January 2017, 459 patients diagnosed with deep vein thrombosis were retrospectively reviewed. FVL was tested among patients with conditions highly suggestive of hypercoagulation state (110 patients).

Results

FVL mutation was detected among 51.8% of patients, 63.6% of patients younger than 50 years and .9% of patients older than 50 years. FVL was commonly reported among 29 young adults (50.8%), 23 patients with spontaneous thrombosis (47.3%), 18 with recurrent thrombosis (31.6%), 6 with family history (10.5%) and 5 with extended thrombosis (8.8%). FVL homozygote mutation was essentially observed with recurrent (5) and extended (3) venous thrombosis.

Conclusion

This high rate of FVL mutation observed with venous thrombosis is related to the high prevalence of this mutation in the Lebanese population. Thrombophilia screening should be tailored to accommodate a population's risk. In countries with high prevalence of FVL mutation screening must be done in young patients and in situations highly suggestive of hypercoagulation state.

Benefit of ultrasound carotid screening only in smokers and patients with manifested atherosclerosis

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Background

Duplex ultrasound of carotid arteries is common screening method mainly in cardio-vascular centres. However, the benefit of unselected screening is doubtful. According to a committee of the American Society of Neuroimaging, screening does not reduce stroke risk and is not cost-effective when the carotid stenosis prevalence is lower than 5%. The aim of this study was to specify subgroups of patients where ultrasound of asymptomatic carotid arteries is justified.

Methods

During the period of one month (January 2016) we performed duplex ultrasound in 242 consecutive patients (age 65 ± 10 years, M:F 167:75) with no history of stroke or TIA scheduled for coronary angiography. Duplex ultrasound (Vivid 7 Pro, 7.5 MHz linear transducer) was realised by 6 experienced operators. As positive result we considered $\geq 50\%$ stenosis of internal or common carotid artery.

Results

From overall group of patients carotid stenosis $\geq 50\%$ was found in 12 patients (5%). Higher frequency of positive carotid ultrasound was found only in smokers compare to non-smokers (13% vs 2%, $p = 0.003$),

Vasa (2017)

or in patients with at least one stenotic arterial territory (peripheral arteries, coronary arteries, renal, or mesenteric arteries), compare to patients without any arterial stenotic process (7.7% vs 1%, $p = 0.03$). On the contrary, in non-smokers without presence of PAD ($n = 161$), the positive carotid stenosis was only 1.9%, and even in the subgroup with combination of diabetes mellitus, hyperlipidemia, and hypertension it remained below 5% (4.3%). However, in patients older 65 years and combination of risk factors, the presence of carotid stenosis $\geq 50\%$ increased to 5.8%.

Conclusions

Duplex ultrasound screening is indicated in smokers and in patients with manifested atherosclerosis, irrespective of age. In patients older 65 years and multiple risk factors of atherosclerosis the carotid duplex could be reasonable. In other asymptomatic patients the usefulness of carotid duplex ultrasound screening seems to be not justified.

Aspiration thrombectomy of fulminant pulmonary embolisms in patients primarily unsuited for conventional intravenous anticoagulation treatment

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Objective

Review of interventional treatment of high-risk patients with acute pulmonary artery embolism by aspiration thrombectomy as an alternative to standard i.v. thrombolysis and surgical embolectomy.

Methods

Six high-risk patients with acute pulmonary artery embolism and contraindications for i.v. thrombolysis were treated with local aspiration thrombectomy using the Indigo Thrombectomy System (CAT8 aspiration catheter) by Penumbra Inc.

Results

All patients exhibited a decrease in pulmonary artery pressure, a reduction in catecholamine requirement, normalization of heart rate (< 100 bpm) and systolic blood pressure (> 100 mmHg), an increase in peripheral oxygen saturation ($paO_2 > 96\%$) as well as a reduction of the required inspiratory oxygen fraction (FiO_2) of the respirator unit. It has become apparent that clinical, therapeutic and local parameters are indicative for planning, exercising and evaluating the success of the interventional procedure, as opposed to mere imaging results.

Conclusion

Interventional treatment of high-risk patients with acute pulmonary artery embolism by aspiration thrombectomy presents a viable and low-risk alternative as well as a potent addition to standard i.v. treatment and surgical embolectomy. Indeed, in patients with contraindications to either of the standard treatments, particularly in neurosurgical patients and patients who have responded poorly to i.v. thrombolysis, it warrants special consideration. Surgical treatment, in turn, carries a high risk of mortality.

Current literature merely shows small cohort studies and case reports. Further studies are needed as present data does not permit a broader analysis.

Acute limb ischemia after intake of NBOMe

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Rationale/Objective

The phenylethylamine derivate 25I-NBOMe and its isomers emerged as new psychedelic agents. We report the case of a 30-year-old man admitted to the hospital because of acute ischemia of the left arm with clinical symptoms of pallor, pulselessness, paresthesia and a motoric deficit. The patient had a history of schizophrenia and drug abuse and disclosed during the hospital stay the sublingual intake of a substance bought as 25I-NBOMe the night before the ischemic event.

Methods

Initial color-coded duplex sonography of the upper left limb showed pathological flow profiles of the axillary, brachial, ulnar and radial artery with a reduced diameter of the brachial and radial arteries (0.9 mm each). In consequence, peripheral vasospasm, distal arterial thrombosis or arterial embolization was anticipated. As therapeutic measures, he immediately received intravenous systemic vasodilators (alprostadil) and therapeutic anticoagulation with low molecular weight heparin. The remainder of the drugs was analyzed using high performance liquid chromatography.

Results

Instant symptom improvement was observed within the first day after therapy initiation. In the subsequent computed tomography angiography of the heart and left arm no signs of thrombotic material or persisting vasospasm could be detected. The patient was released after five days. Treatment was continued with calcium-channel blockers, as the patient displayed arterial hypertension during the hospital stay. Chemical characterization of the drugs showed a composition of the isomers 25I-NBOMe, 25C-NBOMe, and 25H-NBOMe as well as traces of pentylone.

Conclusions

Ingestion of the drug NBOMe implicates the risk of peripheral vasospasms with severe, limb-threatening ischemia.

Chronic thromboembolic pulmonary hypertension – our experience

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Background

Chronic Thromboembolic Pulmonary Hypertension (CTEPH) is a rare complication of acute pulmonary embolism; about one third of patients have deep vein thrombosis. The treatment of choice is surgery with Pulmonary Endarterectomy.

Methods

In this study were enrolled 31 CTEPH patients (22 female; age: 70 ± 11 years). They underwent laboratory tests, echocardiographic assessment, respiratory tests, 6-MWD, ventilation-perfusion lung scintigraphy and computed tomography scan. Diagnosis was confirmed by right heart catheterization. Our objectives were to (1) clarify the association of

DTV type with CTEPH and (2) test the hypothesis that there are echocardiographic variables associated with an increased risk for the presence of Pulmonary Hypertension 1 year later.

Results

Among 31 patients, 29 were classified as having “unprovoked VTE”, without transient or permanent risk factors. A history of acute pulmonary embolism was reported in 12 patients. Deep vein thrombosis, with or without acute pulmonary embolism, was found in 15 patients (distal: 3, proximal: 12). In patients with a right Ventricular-Atrial Gradient ≥ 45 mmHg at the time of diagnosis, the risk for persistent Pulmonary Hypertension increases 3-fold.

Conclusions

CTEPH is a relatively common, serious complication of pulmonary embolism. Diagnostic and therapeutic strategies for the early identification and prevention are needed. The factors that increase the risk of CTEPH after acute Pulmonary Embolism are an idiopathic pulmonary embolism at presentation and the history of Proximal DVT. The study shows that an early echocardiographic assessment can identify patients with persistent Pulmonary Hypertension and may be of value in planning the follow-up and care of these patients.

Post-procedural pseudoaneurysms and predictors of their surgical treatment

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Rationale/Objective

Postcatheterization pseudoaneurysms are the most common iatrogenic vascular complications. They can be treated by compression, ultrasound-guided thrombin injection, endovascular or surgical repair. The purpose of our study was to determine the risk factors predicting the conservative (non-surgical) treatment failure.

Methods

Our study was undertaken using retrospective data analysis of all patients with post-procedural pseudoaneurysm between January and December 2015. We evaluated characteristics of patient, procedure and pseudoaneurysm, and their effect on the treatment success.

Results

We diagnosed pseudoaneurysms in 92 patients (45 men) with mean age 68 years. 52 of them occurred after coronary angiography or angioplasty (incidence 1.10%) and 42 after peripheral vascular intervention (incidence 2.26%). There was 14.9% of smokers, 29.8% of diabetics and 63.8% with arterial hypertension, mean BMI was 27.4 kg/m². Mean size of pseudoaneurysm was 3.9 x 2.2 x 1.9 cm with mean neck diameter 1.2 x 0.4 cm. We used compression in 28.7%, ultrasound-guided compression in 20.2% (primary success rate 47.4%), ultrasound-guided thrombin injection in 28.7% (primary success rate 85.2% after first application, no complications) and surgical repair in 32.9%. There were differences between surgical and conservative subgroup in using of compression (29% vs 84%) and ultrasound-guided thrombin injection (15% vs 38%). On multivariate analysis, the risk of surgical repair necessity was associated only with the pseudoaneurysm diameter larger than 3 cm (p = 0.004, OR 4.7).

Conclusion

The result of our study is that the size of pseudoaneurysm more than 3 cm increases the risk of surgical repair 4.7-times. The other factors were not found to be significant.

Laser doppler assessment of the limb before and after below-the-knee angioplasty in critical limb ischemia

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Background

Critical limb ischemia (CLI) refers to a condition characterized by ischemic rest pain or ulcer/gangrene of the leg. Laser Doppler (LD) and transcutaneous oximetry (tcpO2) measurements assess microcirculation providing data regarding flow reserve capacity and viability.

Methods

The aim of the study was to investigate microcirculation (LD and tcpO2) in CLI patients before and after below-the-knee (BTK) angioplasty and to follow up outcome regarding wound healing, amputation and death. We enrolled 39 CLI patients. We used the PeriFlux 5000 (Perimed, Stockholm). LD perfusion and tcpO2 were measured at rest and during stress (heat and 100 % O2 challenge) conditions, and the percentage change was analysed. Measurements were performed prior, after angioplasty and at 3 and 12 months follow up.

Results

11 patients suffered from rest pain and 28 patients had ulcer/gangrene. By the 12 months follow up 10 patients had a major event (amputation and/or death), wound healing was complete in 11 patients. Patients with rest pain became all symptomless. Patients suffering a major event compared to patients with ulcer had significantly lower LD% change prior and after intervention and baseline tcpO2 prior to intervention. Regarding patients with proper wound healing LD% change was significantly higher after intervention than prior to intervention compared to patients with no melioration. When compared the cases with convalescence to the rest part of the cohort LD% change was significantly higher.

Conclusion

LD and tcpO2 measurements are important methods to investigate microcirculation in patients with CLI and could be useful tools to predict the prognosis.

Prognostic value of heart-type fatty acid binding protein in patients with acute coronary syndrome (ACS)

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Background

Heart-type fatty acid binding protein is released into the circulation following myocardial ischemia and necrosis and therefore may be add a prognostic value when caring for patients admitted to hospital with a clinical diagnosis of ACS.

Objective

To establish the prognostic value of rapid Heart-type Fatty Acid Binding protein (H-FABP) test in patients with Acute Coronary Syndrome (ACS).

Patients and methods

Ninety patients admitted to critical care department with acute coronary syndrome (ACS) within 24 h duration) irrespective of ECG changes, were subjected to detailed and full history taking and thorough clinical examination, 12 lead ECG and echocardiography, full laboratory investigations including cardiac enzymes, troponin and H-FABP, coronary angiography to assess the severity of coronary artery disease using modified Ginssini score and follow-up for the incidence of cardiac events either during hospitalization or during six months follow-up.

Results

Mean patient age was 56 years (SD12), 88 % was male, H-FABP test was performed within 24 hr after symptom onset and was elevated in 80 % of the patients. The value of H-FABP correlated with the severity of coronary artery lesion as determined by modified Ginssini score ($r = 0.749$) ($p < 0.001$) and with long hospital stay ($p, 0.001$). Increasing h-FABP concentration remained statistically significant as independent predictors of long-term risk (namely; heart failure with 75 % and 92 % sensitivity and specificity respectively (at H-FABP 44.50 mg/ml) during six months follow-up.

Conclusion

Increasing H-FABP value has a prognostic role in prediction of incidence of heart failure and ischemic heart diseases during six-months follow-up irrespective of troponin level.

The role of exercise tests and non-invasive methods in the evaluation of vascular patients for lower limb ischaemia

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Background

The examination with hand-held Doppler ultrasound (DUS) at rest has insufficient sensitivity to explore the peripheral artery disease (PAD). Moreover, severe lower limb ischaemia (SLI) often remains hidden without exercise tests.

Methods

Doppler US, transcutaneous tissue oxygen pressure (tcpO2) and toe pressure measurements were obtained in 120 patients with known peripheral artery disease or at high risk of PAD at rest and after a walk test. The differential power of the instrumental examinations for the presence or absence of SLI were determined by multi-category statistical analysis (PRIMA). The cut-off values of SLI were considered as ankle/brachial index (ABI) ≤ 0.4 , toe/brachial index (TBI) ≤ 0.25 and tcpO2 ≤ 30 mmHg. Examining the diagnostic value of the methods, receiver-operating curves (ROCs) were determined based on the post-exercise DUS as the non-invasive standard.

Results

At rest abnormal ABI was detected in 64 % of patients including severely abnormal ABI in 16 % of patients; following the walk test these values increased to 75 % and 43 %, respectively. After the walk test, ≥ 20 % decrease in ABI was observed in 48 % of patients. Abnormal TBI was detected in 88 % of the patients including severely abnormal TBI obtained in 24 % of patients at rest, following the walk test these results altered to 93 % and 38 %, respectively. Impaired tcpO2 was found in 38 % of patients at rest including severely impaired tcpO2 in 19 %; following the walk test these values increased to 63 % and 41 %, respectively. According to PRIMA, tcpO2, TBI, ABI and ≥ 20 % decrease in ABI measured after the walk test can differentiate the SVI more adequately than these values measured at rest ($p < 0.001$). According to ROC analysis, the highest area under the curve (AUC) was found for ≥ 20 % decrease in ABI (AUC: 0.935), post-exercise TBI (AUC: 0.860), and post-exercise tcpO2 (AUC: 0.720), respectively ($p < 0.001$).

Conclusion

The hand-held Doppler examination at rest could not reveal the real functional stage of PAD. The walk test completed with ankle and toe pressure and tcpO2 is able to reveal the severe limb ischaemia.

Effect of cutting balloon angioplasty on primary patency of hemodialysis access stenosis

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Objective

Aim of this study was to compare the primary patency achieved by cutting balloon angioplasty and conventional high pressure balloon angioplasty to treat hemodialysis access stenosis.

Methods

Overall 89 patients were analyzed retrospectively. 21 patients were excluded because of predefined criteria such as central stenosis or re-stenosis, leaving 68 subjects for statistical analyses (70% male, median age 67 years). Thirty-seven patients were treated primarily with cutting balloon angioplasty (CB-PTA) and compared with 31 individuals in whom plain high pressure balloon angioplasty (POBA) was performed. Kaplan-Meier-Analyses were used to compare primary patency rates at pre-defined time points and time intervals of primary patency until need for re-intervention. Primary endpoint was defined as first restenosis requiring repeat revascularization.

Results

Primary patency [%] after interventional treatment of stenosis (all types of stenosis included)

	Cutting-balloon	Plain high pressure balloon
3 months	86.0 %	71.0 %
6 months	71.2 %	61.3 %
12 months	58.6 %	51.6 %
18 months	55.1 %	36.2 %
Time to re-intervention (months, median)	24	13

P = 0.32

Conclusions

Initial treatment in hemodialysis access stenosis of the forearm and upper arm performing cutting balloon angioplasty substantially increased primary patency rate compared to plain high pressure angioplasty at defined time points. In addition, time interval until the need for re-intervention increases from 13 after POBA to 24 month after cutting balloon angioplasty. Thus, cutting balloon angioplasty should be considered the first treatment option in these patients.

Non-invasive tools and exercise tests in patients with atypical limb pain

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Background

Patients presenting with atypical limb pain can pose a diagnostic challenge in the angiological practice. Arterial and non-arterial origin of the complaints may not be distinguished by the physical and hand-held Doppler examinations, and the ankle-brachial index (ABI). The overuse of an imaging with radiation and contrast agents should be avoided. The non-invasive methods at rest and after exercise could be beneficial.

Methods

Hand-held Doppler, transcutaneous partial tissue oxygen tension (tcpO2) and toe pressure measurements were done at rest and following a walk test in 19 patients (63 ± 8 yrs) with atypical lower limb pain. Their results were compared to those of 44 patients (68 ± 9 yrs) with known peripheral artery disease (PAD) and ABI > 0.9.

Results

Lower limb pain at rest was reported by 10 of the 19 patients and 12 of them suffered from pain at walking. Ankle-brachial index was not statistically different in patients with non-arterial and arterial disease (1.19 ± 0.14 vs 1.12 ± 0.16). Non-arterial patients had significantly higher toe pressure compared to the PAD patients (102 ± 25 vs 79 ± 29 mmHg, p < 0.001). An increasing tendency of toe pressure could be observed in the non-arterial patients, while it tended to lower values in the PAD patients (107 ± 25 vs 74 ± 34 mmHg, the difference remained significant between the groups, p < 0.05). TcpO2 values were similar in the two groups at rest (47 ± 5 vs 44 ± 15 mmHg) remaining at the same level in the non-arterial patients after the walk test, while a decreasing tendency could be detected in the PAD patients (47 ± 7 vs 35 ± 19 mmHg). In our patients with atypical lower limb pain, chronic venous insufficiency, vertebral or joint disease, or peripheral neurogenic origin could be revealed as a background.

Conclusion

The non-invasive functional (tcpO2, toe pressure) evaluation of patients with lower limb pain at rest and after a walk test is a harmless and appropriate approach to reveal the arterial, non-arterial or mixed background.

Percutaneous endovascular stentgraft implantation in patients with abdominal aortic aneurysm – single institution trends in 6-year period

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Background

Percutaneous endovascular aneurysm repair (PEVAR) has become the standard treatment modality in patients (pts) with abdominal aortic aneurysm (AAA). In recent years more liberal criteria for PEVAR indication were adopted. Accordingly, the aim of our retrospective analysis was assessment of safety, technical success, and 1 year results of elective PEVAR implantations, in relation to the trends in indications in time period of 2009–2010 compare to 2013–2014.

Methods

Sixty-two consecutive pts in period 2009–2010 (age 70 ± 9 years, maximal AAA diameter 61 ± 14mm) (Group A), and 83 pts in period 2013–2014 (age 74 ± 8 years, maximal AAA diameter 61 ± 14mm) (Group B) underwent elective PEVAR in local anesthesia by completely percutaneous approach. The indication criteria for stentgraft (SG) implantation according to established instructions for use (IFU), the immediate technical success of SG implantation, the presence of 30-days and 1-year complication rate, and need for re-intervention were analyzed.

Results

There was strong shift of PEVAR indications towards the more complex aortic anatomy, and significant increase of pts treated outside the established IFU (11/62 pts in group A /18% /vs 8/83 pts in group B /46%/, $p < 0.001$). In spite of this, there was no need for immediate conversion to open surgery in both groups, and no significant change in mortality in 30-day (3.2% vs 2.4%, $p = 1.0$), as well as in 1-year follow-up (9.7% vs 7.2%, $p = 0.76$). Overall event-free survival without serious complications (mortality, myocardial infarction, stroke, re-intervention, severe ischemic complication) at 1-year follow-up was 76% (47/62) vs 73% (61/83), ($p = 0.85$). However, there was a trend towards lower incidence of pseudoaneurysm of the puncture place (13% vs 8%, $p = 0.17$), and towards decrease in severe anaemia with need of blood transfusion (13% vs 6%, $p = 0.24$).

Conclusion

Percutaneous endovascular aneurysm repair is linked with low mortality and acceptable complication rate in mostly polymorbid pts scheduled for SG implantation. Despite the use of PEVAR as the first line treatment modality, and even in pts with more complex aortic anatomy, there is no increase in early complication rate and in mid-term results of PEVAR procedures.

Keywords: abdominal aortic aneurysm, endovascular treatment, stent-graft, percutaneous approach

Effects of persistent or transitory thrombocytopenia during anticoagulant therapy a retrospective analysis of a real-world single thrombosis center

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Rationale/Objective

Management of oral anticoagulation in patients with thrombocytopenia is challenging and even guidelines are discordant. As thrombocytopenic patients' hemorrhagic risk has known to be high, risk-benefit assessment of starting or discontinuing oral anticoagulation is mandatory.

Methods

A retrospective analysis was performed upon data from 48 (2.43%) thrombocytopenic patients out of 1970 patients administered with VKAs at our thrombosis Centre (the FCSA's 223rd Centre) between January 2010 and December 2015.

Eligibility criteria was the transient or persistent platelet count less than or equal to $100 \times 10^9/L$. Primary end point was the number of moderate-severe and mild bleedings according to WHO criteria. All patients underwent clinical assessment, recording also last 6 months TTR, HAS-BLED score, hepatic or oncologic comorbidities and Creatinine Clearance.

Results

Most of thrombocytopenic patient were warfarinized due to NVAf (81.25% of cases). Median age was 77 years and the 39.59% were older than 80 years. M/F ratio was 1.4. 29 bleeding events were registered in 23 patients (47.91%), which were moderate-severe in the 44.82% of cases. Hemorrhagic risk appeared not to be significantly influenced by platelet count, thrombocytopenia duration, HAS-BLED score or comorbidities. On the contrary, TTR was significantly lower in patients with severe bleedings.

Conclusion

Thrombocytopenia does not always contraindicate oral anticoagulation, but patients' bleeding risk assessment is necessary to prevent serious hemorrhagic events. Most common foci of bleeding have to be screened as well as comorbidities which modify AVKs' pharmacodynamics. As a high TTR does not protect from bleedings, NOACs could find a role in thrombocytopenic population.

Thromboangiitis obliterans (Buerger's disease) – long-term surgical treatment results in patients with critical limb ischemia

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Introduction

Buerger's disease, or thromboangiitis obliterans (TAO) is an segmental occlusive inflammatory disease of the small and medium-sized arteries primarily in young smokers. The aim: estimation of long-term combined surgical treatment results in patients with TAO and critical limb ischemia (CLI).

Methods

A retrospective review of 229 patients (aged from 22 to 58, median 46.0 ± 1.6) with Buerger's disease and CLI between 1997–2014. Young men and smokers 94.6%. All patients had rest pain, 86% ischemic ulcers. Lumbar sympathectomy (LS) was used in 188 (82%), LS with minor amputation-44 (19.2%), LS with thrombendarterectomy-10 (4.4%), surgical bypass-10 (4.4%), isolated minor amputation-22 (9.7%), secondary major amputation-9 (3.9%) cases. In 129 (56.3%) persons perioperative medical therapy was combined with prolonged epidural analgesia, in 65 (28.4%) – with ozonated autohemotherapy. Instrumental methods: angiography, multispiral computed tomography angiography, duplex angioscanning, transcutaneous oximetry.

Results

Bypass procedures was performed in 10 limbs, with primary patency rates of 30 to 20% at 2 to 10 years. The limb salvage rate in sympathectomy group (188 patients) at 2 to 10 years was 86% to 71%. Isolated minor amputation was undertaken in 22 limbs: the incidence of secondary major amputation at long-term period was consisted 27.2%.

Conclusion

LS completed with smoking cessation provides decrease of pain intensity and promotes to reliable regression of CLI, ulcer healing in TAO patients, improves the long-term treatment results. The use of vascular reconstructions in TAO patients is extremely limited due to unsatisfactory condition of distal arteries. Performing of minor amputations without previously sympathectomy or arterial reconstruction does not provide a successful outcome of long-term treatment results.

Prevention of venous thromboembolism through the Implementation of a risk assessment tool – a comparative study in medical and surgical patients

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Rationale/Objective

Hospitalised patients are at high risk of venous thromboembolism (VTE). Underutilisation of thromboprophylaxis despite existing clinical guidelines is common. To evaluate the implementation of a state wide standardised adult VTE risk assessment tool (RAT) to assist in the screening of inpatients and prescribing of appropriate thromboprophylaxis.

Methods

234 patients were audited using clinical notes and spot assessments for VTE risk at Western Sydney Local Health District over a two year period. Patients were stratified into pre- (n = 133) and post-implementation (n = 101) of the RAT. Intervention involved continuing education of staff and passive dissemination of guidelines. Prescription of pharmacological and mechanical prophylaxis and the development of thromboembolic events were evaluated.

Results

39.0% of medical and 63.0% of surgical patients were risk assessed during pre-implementation versus 39.2% and 92.2% during post-implementation ($P < 0.0001$). Usage of pharmacological prophylaxis increased from 72% to 79% and mechanical prophylaxis from 41% to 48%. VTE rates in moderate to high risk medical patients decreased from 15.2% pre-implementation to 6.5% post-implementation. Rates of non-fatal and fatal pulmonary embolism (PE) were 2.3% and 0.8% respectively prior compared to 1.0% and 0.0% post-implementation.

Conclusion

Standardised VTE RAT increased thromboprophylaxis usage and decreased PE rates with a greater improvement reflected in surgical patients, highlighting the importance of a multifaceted approach to VTE prevention using regular audits with feedback, electronic reminders systems, prescribing tools and continuing education.

Case series – venous thromboembolism in hyperhomocysteinaemia

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Objective

Hyperhomocysteinaemia predisposes to arterial thrombosis and rarely venous thromboembolism (VTE).

Methods

To report two cases of VTE in patients with hyperhomocysteinemia and to review literature on hyperhomocysteinaemia associated VTE.

Results

Case 1: 47-year-old lady with underlying diabetes mellitus, hypertension, and hyperlipidemia, history of VTE secondary to hyperhomocysteinaemia in May 2010 completed 4-month warfarinization then preferred to discontinue, later in September 2011 she developed right leg swelling. She was not taking contraceptive pills, no recent surgery or taking long-haul flight. Ultrasound Doppler scan showed VTE in right femoral and iliac veins. Her thrombophilia screening was normal except homocystein level was 36mcmol/L. She was started on enoxaparin bridging to warfarin and infinite folic acid, thereafter was discharged well.

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Case 2: 64-year-old gentleman with underlying diabetes mellitus, hypertension, and hyperlipidemia. He presented to Emergency Department with sudden breathlessness. There was no recent surgery or taking long-haul flight. Ultrasound Doppler scan showed VTE in right popliteal vein, left mid superficial femoral to popliteal vein. Echocardiography showed right ventricular overload with pulmonary hypertension. His thrombophilia screening was normal except homocystein level was more than 50mcmol/L. He was started on enoxaparin bridging to warfarin and infinite folic acid, thereafter was discharged well.

Conclusion

In women between 30 to 50 years old, risk of VTE increases seven times with hyperhomocysteinemia compared to normal levels and twice higher than men with hyperhomocysteinaemia in some studies.

Inherited thrombophilia and the clinical course of venous thromboembolism in young patients from the north-west of Russia

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The association between patient's genotype and the nature of clinical manifestations of venous thrombosis (VTE) remains debatable.

Aim

To study the features of the polymorphism of nine genes associated with VTE in different clinical groups of acute thrombotic episode.

Patients and methods

250 patients up to the age of 45 with VTE (117 men and 133 women, mean age – 37.4 years) were genotyped by PCR-RFLP method for polymorphisms in nine genes (F1 Thr312Ala, F1 -455 G/A, FII 20210 G/A, FV 1691 G/A, FXII 46 C/T, FXIII Val34Leu, PAI-1 -675 4G/5G, TPA 311 bp I/D, EPSR Ser219Gly). We had compared the distributions of hereditary risk factors in two clinical groups: DVT only (n = 146; 58.4%) and "DVT+PE" (n = 104; 41.6%). Intergroup differences were assessed by Fisher's exact method with odds ratios (OR), 95% confidence intervals (CI) and p-values (SPSS, vol. 17.0, Chicago, IL, USA).

Results

We found different distribution for several gene polymorphisms between the clinical groups. The presence of FV 1691A (OR = 2.3; 95% CI: 0.9–6.0; $p = 0.07$), EPCR 219Gly (OR = 1.5, 95% CI: 0.4–4.8, $p = 0.47$) and/or FXIII 34Val/Leu (OR = 0.5, 95% CI: 0.2–0.9; $p = 0.024$) variants was typical for DVT only with a low risk of thromboembolic complications.

Vasa (2017)

On the contrary, detection of the mutation FII 20210 G/A (OR = 1.5; 95% CI: 0.6–4.3; $p = 0.4$) and/or FXIII 34Leu/Leu genotype (OR = 1.8, 95% CI: 0.6–5.3; $p = 0.25$) was associated with severe disease duration, including increased risk of pulmonary embolism.

Conclusions

Several genetic risk factors may affect the clinical course of VTE in young patients. Further research is needed to confirm our data.

Endovascular interventional management of transplant renal artery stenosis

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Renal transplantation is the therapy of choice in patients with end stage renal disease. Vascular complications after renal transplantation are frequent non-immunological cause of resistant hypertension, allograft dysfunction, increase cardiovascular complications that lead to deterioration of long term prognosis of these patients. Transplant renal artery stenosis (TRAS) is the most common vascular complication that occurs in 1–23 % transplant recipients. Percutaneous angioplasty (PTA) or combination of percutaneous angioplasty with the stent placement are the treatment of choice in case of TRAS. The aim of this study was to evaluate retrospectively the clinical presentation and effect of endovascular interventions in patients with TRAS.

Methods

We performed a retrospective single-institutional review of all kidney transplant procedures performed at our institution from 2009 to June 2016. We diagnosed 13 patients with TRAS out of 404 kidney transplantations.

Results

Mean time from transplantation to TRAS diagnosis was 70 days. Stenoses were located at the anastomosis (9), branch of the renal artery (3) and hemodynamic significant kinking was located at the proximal portion of the renal artery (1). PTA was performed in 3 (23.1 %) cases, primary balloon expanding stenting was performed in 8 (61.5 %) of cases. 1 patient with kinking of the renal artery was treated surgically. Conservative treatment without endovascular or surgical intervention was indicated in 1 patient with side branch renal artery stenosis. Early technical success of endovascular repair was 91.7 %. Local complication rate was 0 %. Serum creatinin level dropped significantly after intervention and also during follow up period. No deaths occurred.

Conclusion

Endovascular treatment of TRAS has high technical success with minimal complications. It also provides satisfactory clinical success with improvement in overall transplant renal function and renovascular hypertension.

Treatment of chronic periaortitis with a combination of steroids and cyclophosphamide – a single centre retrospective analysis

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Background

Chronic periaortitis is a rare disease, characterised by fibro-inflammatory tissue surrounding abdominal aorta and iliac arteries, with the risk of renal failure and aneurysms. Early therapy with corticosteroids and new immunosuppressive drugs seems to be effective. In our retrospective study, we evaluated safety and efficacy of combination therapy with prednisone and cyclophosphamide in idiopathic retroperitoneal fibrosis (RF).

Patients and methods

Between 1996 and 2016 we treated 17 patients with RF. Patients with established disease activity were given corticosteroids in combination with cyclophosphamide for 12 months. After systemic symptoms and inflammatory markers were decreased, prednisone was gradually reduced. Where indicated, surgical procedures were applied. A CT scan was performed after six months of treatment. Follow-up abdominal ultrasound was planned every six months. Clinical, biochemical and immunological parameters were periodically monitored.

Results

16 patients were treated for 12 months according to described protocol. Patients with ureteral obstruction and renal failure were treated with stent implantation or with nephrostomy. Endovascular aortic repair was performed in 2 patients. 2 patients achieved complete regression of disease. We obtained reduction of the fibrotic mass in 14 patients and stabilization in one. Relapse was observed in one patient after one year. All patients achieved and maintained a normal renal function. The five patients with ureteral stenting removed stent during the first year. 2 patients died for malignancy during the follow-up period.

Conclusions

Combination treatment with cyclophosphamide and prednisone was safe and effective in patients with chronic periaortitis.

Absence of the left common carotid artery in a 39-year-old female with Raynaud's phenomenon

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Introduction

The absence of the common carotid artery with a separate origin of the external and internal carotid artery is an extremely rare variation. Here we describe a case of a young woman evaluated for Raynaud's phenomenon in whom this variation was detected incidentally by ultrasonography.

Case

A 39-year-old female patient was referred to our department for evaluation of a suspected Raynaud's phenomenon. Duplex sonography of the extracranial carotid and arm arteries was performed to rule out macrovascular causes of decreased arm perfusion. Whereas a normal anatomy of the carotid artery was found on the right side, the carotid artery bifurcation could not be visualized on the left side. Two vessels with typical flow velocity and waveforms for the external and internal carotid artery were present in the caudal cervical region on the left side. All other supra-aortal arteries appeared normal. A subsequently performed computed tomography revealed the absence of the left common carotid artery with the internal and external carotid arteries arising directly from the aortic arch.

Discussion

Ultrasonography is a fast, inexpensive and non-invasive imaging modality. Among other advantages, individual arteries can be identified by their typical waveform and flow velocity. The identification of vascular anomalies, as the one described in our case, is especially important prior to elective surgical procedures. For definite diagnosis, other imaging modalities like compute tomography or magnetic resonance tomography are often necessary. Our case demonstrates the usefulness of duplex-sonography as the first diagnostic approach of anatomical variations of the vascular system.

Endovascular treatment of anomalous coronary arteries

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Objective

Coronary artery anomalies contribute for about 1 % of all the angiographic population. Most of them are benign and have no clinical manifestation. But some of them can not only be symptomatic, but even can lead to sudden cardiac death. There is an opinion that some of them are more proun to atherosclerosis and in-stent restenosis than normal arteries, but researches didn't support it.

Methods

34 patients (aged from 33 to 82, median 54.1 ± 2.8) with ischemic heart disease. In basic group (17 patients) stenting was performed on anomalous coronary arteries, in control (17 patients)-on anatomically normal coronary arteries. Arterial hypertension was noted in 32.4 %, diabetes mellitus-44.1%. ECG and echocardiography were used to all, treadmill stress test to some of the patients before angioplasty. After 6 and 12 months after stenting all patients were evaluated with non-invasive testing.

Results

In 29.4% patients were documented a CTO which was successfully crossed. At most cases drug eluting stents were implanted (68 % and 76 % respectively). There were no death and perioperative myocardial infarction. Recurrence of angina after 1 year: in 12 % of basic and in 10 % of control group ($p > 0.05$). Significant in-stent restenosis: in 2 (11.8 %) of basic and 3(17.6 %) of control group.

Conclusion

There was no statistical significant difference in clinical results of normal and abnormal coronary artery stenting: the incidence of perioperative myocardial infarction, recurrence of angina and in-stent restenosis in two groups were identity.

Short stretch compression therapy in venous ulcer treatment

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Objective

There is a need to objectify wound healing and to try as much as possible to describe the outcome in those patients where ulcers didn't heal

Material and methods

We treated 20 legs with active venous ulcer (CEAP 6). The treatment consisted of cleaning ulcers, application of appropriate dressing and application of short stretch bandages till knee. All patients wore these bandages 24 hour per day. Patients were evaluated by Venous Clinical Severity Score (VCSS) at the beginning and at the end of the treatment. According to the results all patient were divided into 4 groups concerning clinical status.

Results

There is statistically significant difference ($p < 0.05$) between VCSS before and after the treatment, which proves the effectiveness of treatment. 45 % of patients didn't have pain at the entrance of study, and 80 % of them didn't have it at the end of study, mild cellulitis had 50 % patients at the beginning and 30 % of them had it at the end, 15 % patients had severe cellulitis or significant venous eczema at the beginning, and at the end none of them had it. 45% patients had only one ulcer at the beginning and 25 % of them had it at the end. The percentage of healed ulcers in all groups is 40 % (patients with one, two or more ulcers). In 40 % ulcers were completely healed.

Conclusions

Short elastic bandage compression therapy combined with cleaning and dressing application to the wound remains the base of venous ulcer treatment.

Prevention of venous thromboembolism in sports

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Background

Sport is an activity recommended by angiologist in the prevention of venous thromboembolism (VTE). Van Stralen et al. demonstrated in the large population-based case-control study (MEGA study) that regular sport activities decrease the risk of VTE.

Aim

We collected our clinical experiences of VTE patient care and formulated VTE prevention principles.

Method

219 patients with VTE were followed during the last 6 years by the Out-patient Department of Angiology. Phlebothrombosis was diagnosed by colour duplex ultrasound and pulmonary embolization by CT pulmonary angiography or ventilation/perfusion lung scan.

Results

7 of our patients suffered from VTE in context of sport activity.

Case No.1: 25-year-old university student of the Faculty of Physical Education and Sports suffered as World Cup skier a knee injury during the race. Fracture was complicated by development of VTE.

Case No. 2: 53-year-old patient, who was intensely devoted to many kinds of sport throughout his life suffered repeatedly of VTE due to travelling. It was difficult to find a safe way of continuing the sport activities at the top level in anticoagulant therapy.

Conclusion

We have formulated principles of VTE prevention in sportsmen: 1. Be knowledgeable about VTE sign, 2. Adequate liquid supply, 3. Don not use diuretics in order to „draw“ muscles, 4. Do not use anabolic steroids, 5. Do not take doping, 6. Be alert in using hormonal contraceptives, 7. Consider screening of inherited thrombophilia (genetic tests) in sportsmen, 8. Consistent prevention of travellers' thrombosis, 9. Be alert in case of trauma, 10. Do not smoke.

Measurement of ankle-brachial index – a new modality in the hands of general practitioners

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² Slovak Society of General Practice, Bratislava, Slovakia

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Background

Peripheral arterial disease (PAD) is one of the possible manifestations of systemic atherosclerosis. A measurement of ankle-brachial index (ABI) is simple, highly sensitive and specific, thus fulfilling the WHO criteria for screening.

Method

Slovak Angiological Society of Slovak Medical Society and Slovak Society of General Practice have for years devoted to intensive education of general practitioners in ABI measurements. In 2009 they were published the results of a pilot study: 24 general practitioners under supervision of 7 angiologists carried out ABI examinations in 2,207 consecutive patients older than 60 years. 67.4 % of patients had normal ABI (0.9–1.2), 9.4 % of patients had a decreased ABI (< 0.9) and 23.2 % of patients had increased ABI (> 1.2).

This study, numerous workshops and other educational activities resulted in the inclusion of ABI measurements by automatic devices to preventive examination in patients with risk factors for over 50 years and in all over 60 years and it is covered by health insurance from 01.04.2016.

Conclusion

The general practitioners are primary care physicians who determine the dominant way and rate of health care. They must rationally dispose of ABI measurement results, to take responsibility in caring for patients with peripheral artery disease, how it holds, especially in the management of risk factors for atherosclerosis. After measurement of ABI they consider consulting a specialist – angiologist. The aim is to prevent the development of critical limb ischemia, amputation on the one hand, and of fatal cardio-vascular events on the other.

Impact of compulsory and extra-curricular physical activity on cardio-vascular risk factors

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Introduction

Physical activity is an essential part of the development of young people. Project Respect for Health was focused on cardio-vascular risk factors in students. Project was organized by Public Health Authority Bratislava in the school of Petržalka district during the years 2011–2013. Students of the Faculty of Public Health Slovak Medical University in Bratislava actively participated in anthropometric measurements in the project.

Method

The target group consisted of 760 students (295 boys and 465 girls). Subgroup of 211 students (119 boys and 92 girls from 55 secondary schools in the Bratislava region aged 15–18 years) was analyzed in participation in compulsory physical education and extra-curricular sports. Data were collected by student questionnaire and the parents' questionnaire. We measured anthropometric parameters and blood pressure. Physical fitness was assessed by Ruffier test.

Results

73 % of students participated regularly in physical education, but 1/7 of students are consciously avoiding compulsory school physical education. Students regularly participated in physical education are more physically fit compared to those who avoid it ($p = 0.012$). Students who spend more hours daily at computers are less physically fit ($p = 0.02$). Obese students spend more time watching TV (2.8 h). Students smokers avoid physical education twice more than their classmates nonsmokers. This is an example of risk factors multiplication. 21 % of girls compared to 5.7 % boys avoid compulsory school physical education. Students attending compulsory physical education are physically stronger than those who avoid compulsory school physical education for various reasons ($p = 0.059$). Obese pupils spent time watching television significantly more (2.8 hours / day) than at computer. BMI ($p = 0.03$) rises with an increasing hours spent watching television. Number of students smokers who avoid compulsory physical education is twice higher compared to non-smokers in the group.

Conclusion

Participation in compulsory physical education in schools has a positive impact on the physical health and mental development of children and youth, it helps to create a positive habits to sport and physical activity. Keywords: physical education, anthropometric parameters, physical fitness, cardio vascular risk factors

Serial heparin binding protein (HBP) compared to SOFA, APACHE II, MODS & Charlson scores as predictors of mortality in critically ill septic patients

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Abbreviations: heparin binding protein (HBP); Sepsis-related Organ Failure Assessment score (SOFA); Multiple organ dysfunction score (MODS); Acute physiology and chronic health assessment (APACHE II) Context: early detection & management of severe sepsis is crucial for successful outcome. We hypothesized that the progression of sepsis to severe sepsis is preceded by vascular leakage, which is caused by neutrophil-derived mediators, as HBP.

Aim

To identify the role of serial Heparin-binding protein (HBP) measurement as a predictor of morbidity and mortality in critically ill septic patients in comparison TO SOFA, APACHE II SCORE, MODS scores & Charlson scores.

Settings and design

An observational prospective controlled study.

Methods and material

Patients were classified into two groups GROUP I which included (40) patients with evident sepsis. Control group: GROUP II includes 10 critically ill non septic patients.

Results

Significant difference was detected between Survivors and Non-survivors in max SOFA score, APACHE II, MODS, WBCs and serial HBP. (ROC) curve using Admission HBP for prediction of severe sepsis shows sensitivity 94.7% specificity 100% at cut-off level > 1.9 ng/ml, and for prediction of mortality sensitivity 91.6%, Specificity 100% at levels > 1.9 ng/ml.

Conclusions

Serial plasma HBP levels can predict severe sepsis and mortality in ICU septic patients without significant difference compared to SOFA, APACHE & MODS scores.

Keywords: APACHE II; Heparin binding protein, MODS, severe sepsis mortality; SOFA.

Keymessage: Plasma HBP levels can predict severe sepsis & mortality in ICU septic patients with high sensitivity and specificity & could have beneficial additive value to other ICU scores.

White blood cell count to mean platelet volume – a novel marker for critical limb ischemia in peripheral arterial occlusive disease patients

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Objective

Mean platelet volume (MPV) was published recently as a possible marker in coronary artery disease for patients with a high risk for major adverse cardiac events. As platelets play a key role in atherosclerosis we investigated MPV and its association with critical limb ischemia (CLI) in peripheral arterial occlusive disease (PAOD) patients.

Methods

In our cross sectional study we included 2124 PAOD patients treated at our institution. To analyze potential predictors for CLI univariate logistic regression was performed. Significant variables in univariate analyses were selected for multivariate logistic regression. Variables in the final model were selected with a backward stepwise procedure. ROC analyses were performed to identify the best cut off value for MPV to predict CLI. Therefore the Youden's index was calculated.

Results

Multivariate regression analysis revealed diabetes ($p < 0.001$, OR 2.4, 95% CI 2.0–3.0), CRP ($p < 0.001$, OR 1.012, 95% CI 1.008–1.014), age ($p < 0.001$, OR 1.05, 95% CI 1.04–1.06), presence of thrombocytosis ($p = 0.025$, OR 1.84, 95% CI 1.08–3.14), and MPV ($p = 0.003$, OR 0.84, 95% CI 0.75–0.94) as significant predictors for CLI. ROC analysis (AUC: 0.55, 95% CI 0.52–0.58, $p < 0.001$) showed < 10.2 as the best cut off value for MPV to predict CLI.

Conclusions

Low MPV is significantly associated with a high risk for CLI in PAOD patients. MPV is an easily determinable, broadly available and cheap marker, which could be used to highlight patients at high risk for CLI.

Impact of compulsory and extra-curricular physical activity on cardio-vascular risk factors

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21% of girls compared to 5.7% boys avoid compulsory school physical education. Students attending compulsory physical education are physically stronger than those who avoid compulsory school physical education for various reasons ($p = 0.059$). Obese pupils spent time watching television significantly more (2.8 hours/day) than at computer. BMI ($p = 0.03$) rises with an increasing hours spent watching television. Number of students smokers who avoid compulsory physical education is twice higher compared to non-smokers in the group.

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Keywords: physical education, anthropometric parameters, physical fitness, cardio vascular risk factors

Prevention of venous thromboembolism in sports

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Objectives

To assess the bleeding risk profile using the HAS-BLED score in patients with symptomatic peripheral artery disease (PAD).

Background

There is growing interest in intensifying antithrombotic therapy in PAD patients to prevent major adverse cardiovascular and limb events. A better understanding of the bleeding risk profiles in these patients may help in the risk:benefit assessment of antithrombotic therapy.

Methods

A post-hoc analysis was performed using the data of a series of consecutive patients with symptomatic PAD undergoing endovascular revascularization. The endpoint of the study was to assess bleeding risk using the HAS-BLED score, which was previously validated in cohorts of patients with and without atrial fibrillation.

Results

A total of 115 patients were included in this study. The mean HAS-BLED score was 2.76 ± 1.16 . 56 % of all study patients had a HAS-BLED score ≥ 3.0 . Patients with Rutherford classes 5 and 6 had an even higher mean HAS-BLED score (3.20 ± 1.12). Logistic regression analysis revealed aortoiliac or femoropopliteal segment involvement, as well as Rutherford categories 5 and 6 to be independent risk factors associated with a HAS-BLED score ≥ 3.00 .

Conclusion

Patients with PAD, especially those presenting with Rutherford classes 5 and 6, have high HAS-BLED scores, suggesting increased risk for major bleeding. Prospective clinical validation of the HAS-BLED score in patients with PAD may help with the risk:benefit assessment when prescribing antithrombotic therapy.

Technical results of vacuum assisted thrombectomy for arterial clot removal in patients with acute limb ischemia

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Purpose

To assess the efficacy and safety of a vacuum assisted thrombectomy catheter system for treating patients with acute limb ischemia (ALI).

Materials and methods

A retrospective study evaluated VAT systems (Penumbra, Alameda, California) in a consecutive series of 30 ALI patients. ALI was defined as clinical symptoms within 2 weeks of presentation. The primary endpoint was improvement in blood flow across a lesion by improvement in thrombolysis in myocardial infarction (TIMI) score that was adapted to peripheral arteries. Concomitant balloon angioplasty and/or stent placement in addition to VAT was considered a complimentary treatment. Additional thrombectomy treatments such as thrombolysis and mechanical thrombectomy were considered technical failures. Target lesions were grouped anatomically into above (ATK) or below the knee (BTK) lesions.

Results

A total of 33 lesions (ATK: n = 13, BTK: n = 20) in 30 patients were treated. No complications were attributed to the VAT systems. The primary endpoint was obtained in 24/33 (72.7 %) lesions (BTK: 17/20 [85.0 %], ATK: 7/13 [53.9 %], p = 0.050 by χ^2 -test). TIMI scores were similar at baseline, but differed after VAT between the ATK and BTK lesion groups (p < 0.025 by t-test). In addition, ATK lesions required more concomitant angioplasty and/or stent placement (p < 0.015 by χ^2 -test).

Conclusion

VAT is a safe and technically successful short-term therapeutic option for thrombus removal in patients with ALI.

Hybrid technique for the treatment of chronically occluded ilioacaval stent

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Rationale/objective

Iliacal stenting is deployed in the treatment of ilioacaval stenosis and occlusion. Restenosis has been described to occur in up to 10% of patients undergoing stenting for post thrombotic disease. Reports describing the management of totally occluded ilioacaval stents are lacking. This case report details the use of a hybrid, combined open and endovascular approach in the treatment of a totally occluded ilioacaval stent.

Methods

Case report.

Results

The patient had undergone recanalization and stenting of a partially occluded IVC filter and occluded iliac veins three years prior. He had a remote history of iliac DVT, IVC filter and subsequent left to right femoral femoral vein bypass which thrombosed. He represented to the clinic with complaints of recurrent left thigh pain and left leg nonhealing venous ulcer of three months' duration. CT venography demonstrated occlusion of the left iliac vein stent, with thrombus extending into the caval stent.

Initial attempts were made at percutaneous crossing of the left iliac stent which were unsuccessful. The decision was made to proceed with hybrid repair, and successfully underwent open exposure of the left common femoral vein, open recanalization of the occluded iliac veins stents, and relining of the occluded stents with Wallstents. Following surgery, his wound has healed and he has had resolution in his left thigh pain. Three month follow up DUS shows patency in the iliac stents.

Conclusions

A hybrid technique is a suitable option in treating patients with occluded venous stents which are not amenable to a percutaneous approach.

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Direct oral anti-coagulants

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Direct oral anti-coagulants (DOACs) are challenging the six decade long monopoly of oral vitamin-K antagonists (OVKAs). The OVKAs enjoyed a virtual monopoly in the management for 4 clinical settings – (1) minimize or prevent stroke and systemic embolization in adult non-valvular atrial fibrillation (AF), (2) prevent venous thrombo-embolism (VTE) following hip and knee replacement surgery and (3) treat acute deep vein thrombosis (aDVT) and pulmonary embolism (PE) and (4) prevent recurrent aDVT and pulmonary embolism (PE). However there are disadvantages of using OVKAs.

Most of the drawbacks of OVKAs were overcome with use of Low Molecular Weight Heparins (LMWHs), specially, in preventing and treating aDVT. Despite the therapeutic advantage of LMWHs they never became popular due to the cost, inconvenience of administration and requirement of platelet monitoring. Early in the last decade, two classes of DOACs passed became available as prescription drugs. These DOACs have convenient dosing and do not require routine monitoring but have no easily available antidote. We have no information on use during pregnancy, lactation and on long-term use.

There is a theoretical advantage of using DOACs. Vitamin K, can be used with DOACs and this could potentially enhance their activity as well as enhance the systemic beneficial effects of vitamin K. Role of vitamin K as a supplement requires a rethink in lines with that of Vitamin D, in preventing morbidity and mortality related to calcifications and thrombosis.

Saphenous obstruction syndrome (SOS) is a poorly recognised complication following endovenous laser ablation of the great saphenous vein

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Objective

The incompetent great saphenous vein is a bi-directional conduit. It carries harmful reflux downwards and beneficial upward flow to drain the ankle and foot. The objective was to identify the cause of disabling antero-medial calf claudication in a 36 year old active man. This occurred immediately after left endovenous laser ablation (EVLA), from groin to upper calf, that persisted for over 6 months.

Methods

Investigations consisted of a duplex ultrasound examination, air-plethysmography (APG), saphenous nerve conduction velocities, saphenography with direct puncture into the lower patent part of the GSV and dynamic saphenous pressure studies using an intravenous pressure transducer.

Results

Ultrasound revealed GSV occlusion to the upper calf with mild distal GSV reflux. The gravitational venous filling index and drainage index of APG were normal indicating the absence of reflux or obstruction at 0.8 and 17.2 ml/s, respectively. Saphenous nerve conduction velocities were excellent at both ankles excluding significant axonal nerve damage: right 49 m/s, left 59 m/s. Saphenography demonstrated the GSV was obstructed with 2 large blind ending collaterals attempting to drain the antegrade flow. The pressure in the GSV increased from stationary standing to tip-toe exercises, from a median of 49 to 70.5 mm Hg.

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Conclusions

Saphenous obstruction syndrome (SOS) is a rare but distinct clinical entity in patients who present with calf claudication after saphenous ablation. It occurs when there are no perforating veins to drain inwards the obstructed GSV. Saphenous claudication in conjunction with elevated saphenous pressure measurements after exercise confirm the diagnosis.

High, not low levels of endostatin serum levels predict event-free survival in patients with peripheral arterial disease

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Objective

Endostatin is an antiangiogenic protein that is cleaved from Collagen XVIII by matrix-metalloproteases in atherosclerotic lesions. Lack of Endostatin increases both plaque size and density in animal models, but its role in human cardiovascular disease remains uncertain.

Methods

Serum Endostatin was measured in 366 patients with peripheral arterial disease using a commercially available ELISA kit. The study cohort was followed-up for 5 years for the incidence of major cardiovascular events (MACE) defined as any death, non-fatal myocardial infarction, and non-fatal stroke. Correlation analysis, Kaplan-Meier survival tables and multivariable Cox regression were applied.

Results

The KM Analysis for MACE (n = 60) revealed that patients of the first quartile had significant more events after 5 years than those of the fourth quartile (log-rank p=0.013). Each decrease of 1 SD logEndostatin resulted in an unadjusted HR of 1.35 (95% CI: 1.04–1.77). Adjustment for age, gender, LDL-C, HbA1c, systolic blood pressure, smoking and CRP slightly strengthened this association to an adjusted HR of 1.41 (1.08–1.87). Since serum creatinine correlated with Endostatin also in our cohort, creatinine was added to the model, resulting in an HR of 1.46 (1.12–1.91) for MACE per 1SD decrease of Endostatin.

Conclusion

Our data provide first evidence for a possible protective effect against cardiovascular events by higher serum Endostatin levels. Our findings are contrary to a previous study in the general population. We conclude that serum Endostatin in patients with generalized atherosclerosis is more specific to intraplaque remodelling.

TSP-2 levels are higher in patients with type 2 diabetes mellitus, but do not increase with severity of PAD

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Objective

Mechanisms on accelerated atherosclerosis in diabetic patients cannot solely explained by typical risk factors. Experimental animal data linked increased Thrombospondin-2 (TSP2) levels to suppressed angiogenesis in diabetic conditions. The aim of this study is to evaluate the significance of TSP2 in peripheral arterial disease (PAD) patients with or without type 2 diabetes mellitus (T2DM).

Methods

TSP2 was measured in 353 patients in PAD with a commercial ELISA kit. T2DM was defined by the 2009 ADA criteria. T2DM and prediabetes were consolidated to disturbed glucose tolerance (DGT, $n = 306$; normal glucose tolerance NGT $n = 47$). Statistical analysis included Mann-Whitney-U test and binary logistic regression analysis.

Results

The NGT cohort had significant lower median TSP2 values than those of the DGT cohort (296.29 (IQR: 217.46–409.27) vs 372.85 (265.33–507.48); $p = 0.018$). In contrast, TSP2 values were not different between patients with PAD stage I vs stage II (351.06 (253.53–473.10) vs 379.13 (264.19–503.25); $p = 0.261$). The binary logistic regression analysis between NGT and DGT revealed a crude odds ratio (OR) of 1.47 (1.11–1.96) for every increase of 1 standard deviation of TSP2. After adjustment for HDL-C, triglycerides, BMI, systolic blood pressure, smoking habits, CRP and serum creatinine OR remained stable with 1.45 (1.07–1.95).

Conclusion

This study uncovers for the first time an association between TSP2 and diabetic conditions in humans. TSP2 could be a novel marker for augmented vascular complications in this major subgroup of cardiovascular patients, since TSP2 did not increase with severity of PAD, but with coexistence of DGT in a PAD cohort.

Endogenous thrombospondin-4 levels increase with severity of peripheral arterial disease and are associated with type 2 diabetes in a secondary prevention cohort study

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Objective

Thrombospondin-4 (TSP4) is a proangiogenic protein and deficiency reduces plaque size significantly in mouse models. Conventional risk factor can only explain 50% of the increased risk for cardiovascular (CV) events in patients with peripheral arterial disease (PAD) and type 2 diabetes mellitus (T2DM). This study investigates the influence of TSP4 in patients with PAD and T2DM.

Methods

Plasma TSP4 (ng/ml) was measured in 351 patients with PAD, using a commercial ELISA kit. Main exclusion criteria were critical limb ischemia and type 1 diabetes mellitus. Glucose tolerance status was assessed by an OGTT. TSP4 values were logarithmically transformed and subjected to Student's t-test and binary logistic regression.

Results

Plasma levels of TSP4 significantly differed between asymptomatic patients ($n = 180$; median: 108.8 (IQR: 80.9–142.2)) and patients with intermittent claudication (IC) ($n = 171$; 117.9 (88.4–157.1); $p = 0.049$). The comparison between NGT ($n = 100$; normal glucose tolerance) and disturbed glucose tolerance ($n = 251$; DGT = impaired glucose tolerance and/or T2DM) revealed a significant difference (102.4 (77.7–139.2) vs 117.9 (88.4–151.1); $p = 0.032$). Logistic regression was performed and showed a crude OR of 1.28 (95% CI: 1.01–1.62) for DGT by each increase of one standard deviation of logTSP4. Adjustment for age, gender, HDL-C, triglycerides, waist circumference, systolic blood pressure, smoking habits, serum creatinine, CRP and IC slightly increased the OR to 1.30 (1.01–1.68).

Conclusions

Our data provides first evidence for an association of TSP4 and the severity of PAD as well as DGT. Since TSP4 is elevated in PAD patients with DGT compared to NGT, TSP4 might be involved in diabetes-associated accelerated atherosclerosis.

Osteocalcin levels predict survival in a PAD cohort with T2DM in a 5-year follow-up period

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Objective

Osteocalcin is a well known marker for bone metabolism. Animal data suggest a link to diabetes progression and human data shows lower osteocalcin levels in type 2 diabetes mellitus (T2DM) and atherosclerosis. Significance on cardiovascular survival for this observation is unknown.

Methods

Osteocalcin (ng/ml) was measured in 104 patients with peripheral arterial disease (PAD). 52 with a major adverse cardiac event (MACE) with T2DM or prediabetes were matched with age, gender and diabetic controls. MACE data was evaluated after 5 years.

Results

The MACE cohort had significant higher osteocalcin values (median (25; 75 percentile); 23.8 (12.0; 31.4) vs 15.8 (6.9; 24.8); $p = 0.035$). Osteocalcin correlated with fasting glucose (-0.203 , $p = 0.031$), HbA1C (-0.204 , $p = 0.030$) and eGFR (-0.356 , $p < 0.001$). A cut-off value for osteocalcin by 23.77 ng/ml showed the highest combination for sensitivity and specificity by using ROC curves (AUC = 0.605). KM-analysis showed significant more events in the cohort above the cut-off value (log-rank $p = 0.006$). Crude Cox-regression analysis revealed a hazard ratio (HR) of 2.06 (95% CI 1.14–3.76). Adjustment for age, gender, fasting glucose and eGFR resulted in an increased HR of 2.5 (1.29–4.86).

Conclusion

This data shows for the first time the predictive value of osteocalcin in patients with PAD and T2DM regarding outcome. Osteocalcin could be a marker for increased atherosclerosis in patients with enhanced bone metabolism.

Microparticles carrying the angiogenic mediator sonic hedgehog – association with peripheral artery disease and antiplatelet therapy

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Rationale

Shh is a prototypical angiogenic agent with a crucial role in the regulation of angiogenesis. Shh may be found on the surface of circulating MPs and MPs bearing Shh contribute to reparative neovascularization after ische-

mic injury. We compared the number of circulating MPs harboring Shh (MPs^{Shh+}) in a large cohort of patients with peripheral artery disease (PAD) and in healthy controls. We also assessed the number of MPs of endothelial origin that bear Shh on their surface (endothelial-derived MPs^{Shh+}). The concentration of plasmatic Shh protein was also estimated.

Methods

60 patients with PAD and 60 healthy subjects were enrolled. The number of MPs^{Shh+} and endothelial-derived MPs^{Shh+} was estimated by cytometric analysis. The concentration of plasmatic Shh was calculated by a dedicated ELISA test.

Results

We did not find any difference regarding the concentration of plasmatic Shh between the two groups. A significant upregulation of both MPs^{Shh+} ($p < 0.0001$) and endothelial-derived MPs^{Shh+} ($p < 0.01$) was found in PAD patients compared with controls. We did not find an upregulation of non-endothelial derived MPs bearing Shh between patients and controls. The number of MPs^{Shh+} and endothelial-derived MPs^{Shh+} was increased in subjects that were taking anti-platelet drugs compared with those who were not on anti-platelet treatment.

Conclusions

Shh bound to MPs is increased in subjects with PA, while plasmatic Shh is not. The use of anti-platelets therapy is associated with higher number of circulating endothelial-derived MPs^{Shh+}. Our findings provide unexpected insights on novel mechanisms through which anti-platelet drugs exert endothelial protection and promote recovery from ischemia.

Comparative Studies on the anticoagulant actions of recombinant thrombomodulin and heparin and their neutralization by FEIBA as measured by thromboelastography

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Objective

The aim is to compare the anticoagulant effects related to bleeding risk of recombinant thrombomodulin (rTM) and unfractionated heparin (UFH) at various levels, and their neutralization by factor eight inhibitor bypass activity (FEIBA).

Materials and methods

Citrated whole blood samples were supplemented with rTM or UFH in a concentration range of 0–10 µg/ml ($n = 10$). A thromboelastography (TEG) analysis was performed on a Haemoscope 5000 instrument. The relative neutralization profiles of rTM by FEIBA at 1&0.1U/ml were also studied.

Results

rTM exhibited much weaker anticoagulant effects compared to UFH. At 1 µg/ml rTM did not produce any anticoagulant effects. At levels > 2.5 µg/ml and up to 10 µg/ml, rTM produced a concentration dependent and relatively weak anticoagulant effect. UFH was a much stronger anticoagulant and completely inhibited clot formation for the duration of TEG analysis at concentrations > 2.5 µg/ml. FEIBA at 1U/ml completely neutralized the anticoagulant effect of rTM at 10 µg/ml and UFH at 0.5 µg/ml. FEIBA at 0.1 U/ml neutralized the anticoagulant effects of rTM at 10 µg/ml completely, but only partially neutralized the anticoagulant effects of heparin at 0.5 µg/ml.

Conclusion

rTM is a relatively weaker anticoagulant versus UFH. The expected concentration of rTM in its given indications is between 0.5–1.5 µg/ml. At these concentrations, rTM is not expected to produce any anticoagulant

effects. In contrast UFH, at therapeutic concentrations of 1–2 µg/ml produces strong anticoagulant effect. These TEG studies indicate that rTM is an antithrombotic agent mediating its effects via multiple mechanisms whereas heparins primarily produce anticoagulant effects. Supratherapeutic levels of thrombomodulin and heparin are neutralizable by FEIBA.

Idarucizumab, a specific antidote for dabigatran, cross-reacts with melagatran and may also interact with other benzamidine-containing compounds

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Objective

Dabigatran etexilate is used to prevent embolic stroke in patients with atrial fibrillation. Idarucizumab is an anti-dabigatran Fab fragment that binds to its benzamidine group and inhibits its anti-thrombin activity. The aim is to determine the relative specificity of benzamidine as a sole antidote for dabigatran.

Materials and methods

Several anti-thrombin (argatroban, melagatran, hirudin, bivalirudin, human antithrombin, thrombomodulin, heparin cofactor II, heparin-AT complex and anti-factor Xa (rivaroxaban, apixaban and DX-9065a) agents were supplemented to citrated plasma at concentrations ranging from 0.1–100 µg/ml. Idarucizumab was added to each mixture at a concentration of 1 mg/ml. The anticoagulant activity was assessed using prothrombin time (PT), thrombin time (TT), activated partial thromboplastin time (aPTT), chromogenic anti-IIa/Xa and flurometric thrombin generation assays.

Results

Idarucizumab itself did not produce any effect on whole blood or plasma clotting profile at concentrations of < 1.0 mg/ml. The antibody showed strong specificity for the inhibition of dabigatran and did not affect the anticoagulant and other effects of the other synthetic and natural thrombin and FXa inhibitors with the exception of melagatran. The prolongation of the PT, aPTT and TT by melagatran was completely inhibited by idarucizumab. Idarucizumab more effectively inhibited the prolongation of TT by dabigatran than the prolongation induced by melagatran.

Conclusions

The cross-reactivity of idarucizumab with melagatran may result from the presence of a common benzamidine. Benzamidine is present in serine protease inhibitors and drugs as pentamidine, propamidine and dibromopropamidine. Therefore, simultaneous administration of idarucizumab may compromise the pharmacodynamics of benzamidine derived drugs such as anti-malarials, anti-psychotic, anti-fungal etc.

Dabigatran neutralizing antibody, idarucizumab, exhibits procoagulant and platelet activation responses in whole blood

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Objectives

Idarucizumab is a humanized monoclonal antibody fragment, clinically available to neutralize Dabigatran. The aim is to determine idarucizumab's effect on blood coagulation and platelet activation.

Materials

Idarucizumab was purchased commercially as a 50 mg/ml solution. Synthetic dabigatran was obtained from Sellec Chemical (Houston, TX). Whole blood from healthy volunteers was collected for thromboelastography (TEG) and activated clotting time (ACT) analysis. Citrated whole blood was used for the preparation of platelet rich plasma (PRP), used in platelet aggregation studies. Arachidonic acid, adenosine diphosphate (ADP), epinephrine, thrombin and collagen were used as agonists.

Methods

Whole blood was supplemented with idarucizumab at 0–10 mg/ml and studied with TEG. The ACT studies were carried out in celite tubes in a concentration range of 0–5 mg/ml. The agonist-induced platelet aggregation and heparin induced thrombocytopenia (HIT) antibody mediated platelet aggregation profiles were studied after pre-incubating PRP with idarucizumab at a concentration of 1.0 mg/ml.

Results

Idarucizumab produced a dose-dependent hypercoagulable effect in the TEG profile, reducing R time by 35 % and max amplitude by 45%. At high concentrations, idarucizumab significantly affected clot retraction. Idarucizumab at 5 mg/ml reduced the ACT by 6 %. Idarucizumab variably augmented the different agonist mediated platelet aggregation profiles. Idarucizumab at 1.0 mg/ml increased HIT antibody mediated platelet aggregation by almost 20 %.

Conclusions

Idarucizumab produces mild procoagulant effects as studied by TEG and ACT. It also augments the platelet aggregation profile by various agonists including Anti-heparin platelet factor IV antibodies. These procoagulant effects of idarucizumab may contribute to potential hypercoagulable/prothrombotic events associated with its use.

Biochemical and pharmacological differentiation of recombinant thrombomodulin and activated protein-C with reference to the effect on the hemostatic and fibrinolytic processes

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Objectives

The aim is to demonstrate biochemical and pharmacological differences between a clinically developed recombinant thrombomodulin (rTM) (ART-123) and a plasma derived recombinant activated protein-C (rAPC).

Materials and methods

The anticoagulant profile of both agents was profiled in native whole blood using the activated clotting time (ACT), thromboelastography (TEG), thrombin time (TT), prothrombin time (PT) and activated partial thromboplastin time (aPTT) assays at a concentration range of 0–10 µg/ml. The TT, PT, aPTT and antiprotease (Xa and IIa) inhibitory studies were performed in citrated plasma.

Results

In the ACT assays rAPC produced a markedly stronger anticoagulant effect in a concentration range of 0–10 µg/ml with a doubling time at 3 µg/ml. Whereas rTM produced marginal effects, even at 10 µg/ml. The TEG profile of APC exhibited much stronger anticoagulant effects versus rTM. APC also facilitated activated mediated fibrinolysis in contrast to rTM. In the whole blood and plasma based assays rTM produced a concentration dependant anticoagulation effect whereas the APC had marginal effects. In the PTT, rAPC produced a much stronger anticoagulant effect versus rTM. Both agents did not produce any modification of agonist induced platelet aggregation. Regarding anticoagulant potency the rAPC exhibited 70+6 USP U/mg whereas the rTM was much weaker <10 USP U/mg. rAPC exhibited amidolytic activities with specific substrates for thrombin while, rTM did not.

Conclusions

The rAPC is a much stronger anticoagulant than rTM. Both agents produced different modulation of fibrinolysis and hemostasis. At therapeutic levels rAPC and rTM may have differential impact on hemostatic balance.

Comparative anticoagulant effects of recombinant thrombomodulin, unfractionated heparin, and antithrombin; hematological implications

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Objectives

Recombinant thrombomodulin (rTM), unfractionated heparin (UFH) and, antithrombin (AT) are all anticoagulant/antithrombotic agents. Currently, a human rTM, ART-123 (Recomodulin ©) is undergoing clinical trials to treat sepsis-associated coagulopathy. The aim is to compare the anticoagulant and platelet modulatory effects of rTM, UFH and AT.

Materials

rTM, UFH and AT were obtained commercially. Their effects were measured at 0–5 µg/ml on glass with activated clotting time (ACT) and thromboelastography (TEG). Prothrombin time (PT), thrombin time (TT) and activated partial thromboplastin time (aPTT) were measured in citrated whole blood and retrieved plasma. The effect of these drugs on agonist induced platelet aggregation (arachidonic acid, adenosine diphosphate (ADP), collagen, thrombin, and epinephrine) was measured in platelet rich plasma from healthy donors.

Results

In contrast to UFH and AT, rTM showed no anticoagulant effects in ACT and TEG at 1.25 µg/ml. At higher concentrations of up to 5.0 µg/ml, rTM was a much weaker anticoagulant. In the clotting assays, all agents produced anticoagulant effects as follows: UFH > AT > rTM. UFH mildly increased aggregation with some agonists. AT and rTM did not produce any effects at concentrations of up to 5U/ml and 10 µg/ml, respectively, for all of the agonists except thrombin.

Conclusion

rTM is much weaker versus UFH and AT, and at therapeutic concentrations, does not produce measurable anticoagulation. The circulating levels of rTM for the management of sepsis-associated coagulopathy range from 0.5–1.5 µg/ml. At supratherapeutic concentrations of > 2.5 µg/ml, which may occur in patients with renal dysfunction, rTM exhibits weak anticoagulant effects i.e. it is unlikely to cause bleeding.

Type B acute aortic dissection: on associated complications and complex approach – case study

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Type B aortic dissection is a life-threatening condition which demands a complex approach of relevant specialists. Contemporary, sophisticated endovascular methods ensure an effective solution even in difficult conditions. The endovascular treatment is crucial, but presents only one step in the care that should contrive in providing a life for the patient that is worthwhile. We present a case of a female patient with a type B acute aortic dissection presented with symptoms of severe visceral and lower extremity ischemia.

Case report

40 year old female patient with a history of hypertension complaining of severe chest pain which spread to the lower extremities with an overall weakness was examined in the neighbouring hospital. The CT angiography showed a type B acute aortic dissection with a total collapse of the true lumen. The dissecting channel was located from the left subclavian area and involved the superior mesenteric artery, the right renal artery and left superficial femoral artery.

Due to uncontrollable hypertension and a worsening condition the patient needed to be analgesated and connected to mechanical ventilation. The condition was resolved by implanting a stent graft into the descending aorta. The affected right renal artery and the superior mesenteric artery were treated by stent implantation. Extensive stenting of the affected left lower limb arteries was needed. The procedure which consisted of implantation of stents reaching from the left external iliac artery towards to the proximal third of the superficial femoral artery was performed. Complications which resulted from the aortic dissection included a severe ischemic-reperfusion syndrome with multi-organ dysfunction syndrome and a transitional left side hemiplegia.

Due to the development of severe bilateral lower limb edema it was necessary to perform a fasciotomy. The consequence of the fasciotomy was a paresis of the peroneal nerve on the left lower extremity. Diarr-

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hoea with enterorrhagia, as a result of temporary intestinal ischemia followed by *C. difficile* infection was treated conservatively, without a need for surgery given the clinical finding and a renewed visceral perfusion. Chronic kidney disease in the pre-existing hypertensive nephrosclerosis enhanced by the use of a contrast agent and myoglobinemia resulted in renal failure requiring hemodialysis. Gradual renal function reparation to nearly physiological values followed.

The initial neurological signs with brain edema responded well to antiedema therapy. Brain MRI did not fully explain the plegic symptoms. Complex rehabilitation had a positive effect. The only residual symptom was a fibular nerve plegia. The patient was dismissed in a good clinical condition and health.

Preclinical atherosclerosis of carotid arteries and cardiovascular events

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Abstract

Investigation of large superficial arteries, especially the carotid, using high-resolution B-mode ultrasonography has emerged as one of the methods of choice for determining the anatomic extent of atherosclerosis and for assessing cardiovascular risk. It includes measurement of intima-media thickness (IMT) and identification of carotid atherosclerotic plaques. Atherosclerotic plaques represent advanced atherosclerosis and their presence in carotid arteries indicates the risk for coronary, cerebral and peripheral events. Population studies have shown a strong correlation between carotid IMT and several cardiovascular risk factors, and it has also been found IMT to be associated with the extent of atherosclerosis and end-organ damage of high-risk patients. Therefore, increased carotid IMT is a measure of atherosclerotic burden and a predictor of subsequent events.

Measurement of carotid IMT could influence a clinician to intervene with medication and to use more aggressive treatment of risk factors in primary prevention, and in patients with atherosclerotic disease in whom there is evidence of progression and extension of atherosclerotic disease. For more extensive use of this method in clinical practice a consensus concerning the standardization of methods of measurement and precise definition of threshold between normal and pathologic IMT value is urgently needed.

Comparison of efficacy of rivaroxaban and warfarin in prevention of post-thrombotic syndrome

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Background / Objective

Post-thrombotic syndrome (PTS) is a chronic complication of deep vein thrombosis (DVT) that affects 20% to 50% of DVT patients. Anticoagulation is the basis of DVT treatment. No data are available comparing the effect of rivaroxaban and warfarin on the development of PTS, therefore we investigated possible associations.

Methods. One hundred consecutive patients that had been treated for DVT with a vitamin K antagonist (warfarin) or rivaroxaban for 6 months were included. We assessed symptoms and signs of PTS, and calculated Villalta scale 23 months (median) after acute DVT diagnosis. Demographic and clinical differences between PTS-positive and PTS-negative patients were compared, as well as differences between patients treated with rivaroxaban and warfarin.

Results

61 patients were treated with rivaroxaban and 39 patients with warfarin. Patients with PTS were older ($p = 0.007$) and more frequently had recurrent DVT ($p = 0.030$). Patients in the rivaroxaban group had a lower incidence of PTS than those treated with warfarin (25% vs 49%, $p = 0.013$). Logistic regression showed odds ratio of 2.9 (1.2–6.8, $p = 0.014$) for PTS development in warfarin group compared to rivaroxaban group. When adjusted for other variables, the odds ratio was 3.5 (1.1–11.0, $p = 0.035$).

Conclusions

Treatment of DVT with rivaroxaban might be associated with a lower risk for PTS development.

Role of ABI in screening and follow up of PAD

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A detailed history and clinical examination of patients with suspicion of peripheral arterial disease (PAD) enable confirmation of the diagnosis. However, for estimation of the extent and stage of PAD different invasive and non-invasive procedures are used. The most frequently used non-invasive screening test includes measurement of ankle brachial pressure index (ABI). Measuring of ABI is easy, inexpensive, and non-invasive and should be a part of clinical examination of patients with suspicion of PAD. A normal ABI is 1.0 or slightly above to 1.4. Its value below 0.9 is generally accepted as indicative for the presence of obstructive arterial disease of lower limbs. In the diabetic patients because of the hardening of the arterial wall, making their arteries incompressible, higher values of ABI are observed. In such cases alternative diagnostic procedures need to be performed. These include direct pulse volume recordings and wave-form analysis in arterial segments and toe-pressure measurements.

The ABI can also assist in estimating the cardiovascular morbidity and mortality because of accompanied other atherosclerotic disease of PAD patients. Low and elevated ABI ($ABI > 1.4$) predicts a worsened prognosis.

The determination of ABI should be performed in subjects with suspected PAD and in patients with other atherosclerotic disease.

Comparison of structure of atherosclerotic plaques using PET/CT with histologic findings

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Abstract

The identification of inflamed and vulnerable plaques is of the utmost importance, as this may allow the implementation of more effective preventive and therapeutic interventions. Fluorodeoxyglucose positron emission tomography (FDG-PET) has been shown to be useful for tracing inflammation within plaques. We aimed to determine whether plaque inflammation could be measured by PET in combination with computer tomography (CT) using FDG and what is the relationship between FDG uptake and immunohistochemical findings in the removed atherosclerotic lesions of the femoral and carotid arteries. The study included 31 patients, 21 patients with high-grade stenosis of the internal carotid artery (ICA) and 10 patients with occlusion of the common femoral artery (CFA), all of whom underwent endarterectomy.

Before endarterectomy in all patients, FDG-PET/CT imaging was performed. FDG uptake was measured as the maximum blood-normalized standardized uptake value, known as the target to background ratio (TBR

max). The density of T lymphocytes and macrophages was significantly higher in subjects with stenosis of the ICA than in subjects with occlusion of the femoral arteries: lymphocytes, 1.26 ± 0.21 vs 0.77 ± 0.29 ; $p = 0.02$ and macrophages, 1.01 ± 0.18 vs 0.69 ± 0.23 ; $p = 0.003$. In the whole group of patients, the density of inflammatory cells significantly correlated with FDG uptake represented by PET-TBR max: T lymphocytes, $r = 0.60$; $p < 0.01$ and macrophages, $r = 0.65$; $p < 0.01$. The results of our study show that FDG uptake is related to the accumulation of inflammatory cells in atherosclerotic lesions.

Development of wall stiffness parameters in diabetes mellitus type II – evaluation of therapeutic effect of sulodexide vs naftidrofuryl: an open controlled 2-year study

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The vascular complications of type II diabetes are partially linked to vascular wall changes, modified permeability and increasing stiffness. Being the glycosaminoglycans the common components of the vascular wall, we evaluated whether oral GAGs (sulodexide) affected the progression of vascular wall stiffness.

We performed study on type II diabetic patients treated with either sulodexide 500 LSU/day or naftidrofuryl 200 mg/day. A group of diabetic controls and a group of healthy controls were also monitored. There were evaluated ABI parameters as a standard for the peripheral limb perfusion and CAVI (cardio-ankle vascular index) as an improved modality of the PWV measurement.

There was no evidence of impairment on ABI in any group. The changes in CAVI differed significantly among naftidrofuryl-treated ($P = 0.004/P = 0.009$) and sulodexide-treated ($P = 0.014/P < 0.001$) patients in comparison with diabetic controls. At 2 years, the diabetic controls differed significantly also from healthy controls ($P = 0.024$). The proportion of patients with abnormal (≥ 9.0) CAVI on the least affected side remained constant in healthy controls and naftidrofuryl-treated patients; increased significantly in diabetic controls ($P=0.006$) and decreased significantly in the sulodexide group ($P = 0.021$).

CAVI resulted to be more sensitive than ABI in detection of early vessel wall damage. Sulodexide appeared as effective in preventing the progression of vascular wall stiffness.

Effectiveness of paclitaxel-coated Luminor® balloon catheter vs uncoated balloon

Dr. Marcus Thieme

Regiomed Vascular Center Sonneberg/Dept. Angiology/Cardiology/Diabetology and Jena University Hospital, Clinic for Internal Medicine I

EffPac Trial

Effectiveness of Paclitaxel-Coated Luminor® Balloon catheter versus uncoated balloon catheter in the superficial femoral and popliteal arteries to prevent vessel restenosis or reocclusion: study protocol for a randomized controlled trial.

Study Objective

The aim of this investigator-initiated trial is to evaluate the safety and efficacy of the novel. Luminor® paclitaxel-coated drug-eluting balloon (DEB) (iVascular, S.L.U., Barcelona, Spain) in inhibiting restenosis and in ensuring long-term patency.

Methods / Trial Design

This multicenter randomized-controlled trial included patients from 11 German centers with stenotic or occlusive lesions (length: ≤ 15 cm) in the superficial femoral artery (SFA) and popliteal artery (PA) up to the P1 segment. 172 Patients were treated with either DEB or POBA in a 1:1 randomization. Primary endpoint is late lumen loss (LLL) at 6 months. Secondary endpoints are patency rate, target lesion/vessel revascularization, quality of life (assessed with Walking Impairment Questionnaire (WIQ) and EQ5D), change of Rutherford stage and ankle-brachial index, major and minor amputation rate at index limb, number of bailouts and all-cause mortality.

Results

Baseline demographics and preliminary data of the primary endpoint (LLL) and 6 months follow-up results will be presented.

Discussion

EffPac represents a randomized controlled trial that will provide evidence on the effectiveness of Luminor® paclitaxel-coated DEB catheter for the reduction of restenosis compared to POBA of SFA and PA. The results of EffPac will allow direct comparison to other already-completed RCTs applying paclitaxel-coated DEB from different manufactures in the same target vessel.

Trial registration

Trial registration: Clinicaltrials.gov NCT02540018. Registered 17 August 2015.

Sonic hedgehog signaling pathway – a novel player in brain arteriovenous malformations

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Rationale/Objective

The Sonic hedgehog (SHH) pathway is a crucial regulator of angiogenesis both in embryonic and post-natal life. In this study, we tested the hypothesis that the SHH signaling is a player in the pathophysiology of human brain arteriovenous malformations (AVMs).

Methods

We analyzed the expression levels of various components of the SHH pathway in human brain AVMs and human normal brain. The possibility to induce the growth of an arteriovenous angiogenic process by activating the SHH pathway was tested in ephrinB2-lacZ mice, which carry the lacZ reporter gene under the control of the arterial-specific ephrinB2 gene. Two experimental models were used: the corneal model of angiogenesis and the intracranial injection of a plasmid containing the human Shh gene (phShh).

Results

SHH is expressed in the endothelial layer of human brain AVMs, while it is not detectable in the endothelium of normal human brain vessels. Gli-1, the major transcription factor of the SHH pathway, is present in the endothelium of human brain AVMs. The SHH inhibitory protein HHIP is significantly down-regulated in human brain AVMs. In mice, both the implantation into the cornea of pellets containing SHH and the injection into the brain of phShh induce an angiogenic process characterized by the presence of arteries and veins, which are connected to each other by complex sets of arteriovenous shunts, without an interposed capillary bed.

Conclusions

SHH is aberrantly expressed in human brain AVMs and SHH-induced angiogenesis has characteristics similar to those seen in AVMs in humans.

Endovascular treatment of a very large splenic-artery-aneurysm

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Aims

To present a successful treatment of a large splenic artery-aneurysm with a Viabahn®-stentgraft.

Methods

The patient presented with abdominal pain. In duplex-scan we found a large aneurysm of the splenic artery, which was confirmed in CT-Scan with a diameter of 35 mm. Because of the risk of perforation, we planned an interventional isolation of the aneurysm.

Result

Via an access in the left groin we localized the aneurysms in the splenic artery. The vessels were convoluted in several double-eighth, the aneurysm was difficult to canalize and a good support hard to reach. After multiple attempts, we could place a stiff wire in the splenic artery and change for an 8F guiding-sheath. Then we introduced a diagnostic-catheter and an 0.18" control-wire to canalize the way through the aneurysm. Finally, we placed a 6/100 mm Viabahn®-stentgraft in the splenic artery to cover the Aneurysm completely.

Conclusion

The treatment of large visceral artery-aneurysms with covered stents is a feasible, safe and successful method if the vessel-diameter is large enough, even in heavily torqued vessels

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Endovascular treatement for long steno-occlusive disease of femoro-popliteal arteries – a retrospective study

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Purpose

The aim of this study was to evaluate efficacy, safety, and midterm patency of long femoro-popliteal steno-occlusive disease (≥ 15 cm) treated by endovascular treatment in patients with intermittent claudication or chronic critical limb ischemia.

Methods and Materials

From January 2012 to March 2014, twenty patients (22 legs) were treated for TASC C (57 %) and D (43 %) femoro-popliteal lesions by angioplasty with provisional stenting (bare-metal self-expandable stent). The patients were followed for up to 12 months by Doppler ultrasound examinations, ankle-brachial index and assessments of Leriche and Fontaine class.

Results

Technical success was achieved in 100 % of procedures. The one-year primary patency rate was 54 %. Ten out of 22 legs underwent successful drug eluting balloon angioplasty because of endofibrotic in-stent restenosis. At twelve months, the primary assisted patency rate was 100 %.

Conclusion

Percutaneous endovascular treatment of TASC C and D atherosclerotic disease of the femoro-popliteal arteries is a safe and clinically effective procedure. It offers a durable patency provided that patients obtain a close angiologic follow-up.

Impact of ozonated autohemotherapy on lipid peroxidation and antioxidant protection

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Objective

It is known, that oxidative stress significantly affects the course and prognosis of disease in patients with thromboangiitis obliterans (TAO) and critical limb ischemia (CLI). The aim: The aim: estimated the influence of ozonated autohemotherapy (OAH) on lipid peroxidation (LPO) and antioxidant protection (AP) in patients with TAO and CLI.

Methods

LPO and AP were investigated in 125 patients with TAO and CLI, divided into 2 groups: in control group (n = 60) perioperative basic therapy included rheological drugs, anticoagulants, vasoactive drugs, hormones, aggregation inhibitors, in basic group (n = 65) along with basic therapy OAH was employed. Comparison groups were comparable in terms of nosological form, sex, age, nature of comorbidity. LPO and AP parameters were studied during three-week treatment course. For LPO evaluation diene conjugates (DC) and malondialdehyde (MDA), for AP evaluation antioxidant enzymes-catalase and superoxide dismutase (SOD) were determined.

Results

After a three-week, in basic group the most significantly tendency to decrease of LPO products was observed: MDA decreased by 1.7 ± 0.16 nmol/ml ($p = 0.002$), in control group- 0.79 ± 0.17 nmol/ml ($p = 0.103$), DK decreased by 1.21 ± 0.12 D233/ml ($p = 0.043$), in the control group- 0.34 ± 0.1 D233/ml ($p = 0.456$). Basic group showed a significant increase of antioxidant enzyme activity: catalase activity increased by 18 % (from 456 ± 9.0 U/g Hb/min to 574 ± 10.1 U/g Hb/min ($p = 0.048$), SOD activity increased by 23 % (from 536 ± 3.3 U/g Hb/min to 660 ± 3.2 U/g Hb/min ($p = 0.036$).

Conclusion

We consider that employing of OAH improves the lipid peroxidation system and antioxidant status in patients with TAO and CLI, which promotes to optimization of complex surgical treatment results.

Circulating cocoa flavanols enhance angiogenesis and stimulate endothelial cell migration, increasing HIF-1 α and VEGF expression in vitro

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Objective

We hypothesized that flavanols may enhance angiogenesis.

Background

Epidemiological studies suggest that the intake of flavanol-rich foods is associated with longterm cardiovascular benefits. While clinical intervention studies show that the intake of flavanol-rich foods and isolated flavanols acutely and chronically enhance eNOS dependent endothelial function, the mechanisms are not well established.

Methods and results

We first performed cell migration and proliferation experiments with (-)-epicatechin in endothelial cells (HUVEC) and circulating angiogenic cells (CACs). As flavanols are readily absorbed and metabolized, we isolated fasting plasma samples from young healthy subjects before (CP = control plasma) and at 2h after ingestion of intervention drinks containing 900 mg of total flavanols (FP = flavanol plasma). We investigated the effect of CP and FP on viability, proliferation, migration, wound closure, and tubeformation in HUVECs. Finally, we measure the protein and mRNA expression HIF-1 α and of the downstream target gene VEGF after incubation with CP and FP.

Results

Our results showed that (-)-epicatechin dose-dependently increases chemokinesis and chemotaxis with a maximum at 100 ng/ml but not cell proliferation in HUVECs and CACs via an eNOS-dependent mechanism. In endothelial cells, coincubation with FP, but not CP led to a significant enhancement in NOS-dependent wound closure and of tubeformation which was paralleled by increased HIF-1 α protein and increased mRNA and protein expression of VEGF.

Conclusion

Our data suggest that circulating cocoa flavanols can enhance angiogenesis in vitro involving HIF-1 α activation.

The use of dedicated venous stents for recurrent thrombosis upon ilio caval implantation of non-dedicated venous stents

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Background

Manifest postthrombotic syndrome as well as major residual thrombosis after catheter-directed thrombolysis (CDT) are potential indications for iliac venous stenting. Dedicated venous stents provide satisfying patency rates and freedom of recurrent thrombosis. The present case emphasizes the value of dedicated venous stents in comparison with arterial stents for venous lesions.

Case

In October 2016, a 40-year-old female patient presented with swelling and feeling of heaviness of the left leg at the outpatients' clinic of the Division of Angiology, Department of Medicine II (Vienna General Hospital). Previously the patient had undergone CDT and implantation of two arterial stents in her left common iliac vein and in the vena cava inferior at another hospital upon acute deep venous thrombosis. Despite ongoing anticoagulation the patient now presented with a recurrent iliac venous obstruction. Duplex ultrasound and magnetic resonance venography at our clinic revealed a >70% recurrent thrombosis of the previously stented segment. The venous obstruction was confirmed by catheter-guided venography and intravascular ultrasound (IVUS). During this procedure the left common and external iliac veins were predilated and the venous ilioacaval axis was reconstructed by implanting three dedicated venous stents. Immediately after the intervention, therapeutic anticoagulation was re-initiated. Up to now, the patient is free of symptoms and the stented ilioacaval segment is patent.

Conclusion

Venous stenting by using non-dedicated venous stents results in high recurrence rates. Recurrent thrombosis upon previous implantation of non-dedicated venous stents can effectively be treated by high-pressure balloon venoplasty and implantation of dedicated venous stents.

Associations of nailfold capillaries and autoantibodies with all-cause mortality in Raynaud's phenomenon according to the future diagnosis of a connective tissue disease

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Background

Abnormal nailfold capillaries and autoantibodies are related to all-cause mortality in patients with Raynaud's phenomenon without previously known connective tissue disease (CTD). This association might be attributed to the future emergence of a CTD, such as systemic sclerosis (SSc) or systemic lupus erythematosus (SLE). Whether the associations of nailfold capillaries and autoantibodies with all-cause mortality differ between patients with and without future diagnosis of a CTD is not known.

Methods

In total, 2954 patients with Raynaud's phenomenon without previously known CTD were included. Initially, all patients underwent nailfold capillaroscopy and laboratory tests for antinuclear antibodies (ANA) and ANA subsets. Patients' mortality was prospectively recorded over a median follow up period of 9.3 years. The future diagnosis of a CTD was evaluated by distribution of standardized questionnaires and by screening patients' medical records.

Results

Over the observational period, SSc was diagnosed in 8.8 % and SLE was diagnosed in 3.8 % of included patients. During follow up 44 % of patients with a future diagnosis of SSc and 14 % with a future diagnosis of SLE died. Neither in patients with a future diagnosis of SSc, nor in patients with a future diagnosis of SLE abnormal nailfold capillaries or autoantibodies were associated with all-cause mortality. The presence of abnormal nailfold capillaries and autoantibodies was closely related to all-cause mortality in patients without future diagnosis of SSc or SLE.

Conclusion

Associations of abnormal nailfold capillaries and autoantibodies with all-cause mortality do not depend on the future diagnosis of a CTD, such as SSc or SLE.

Leukotrienes E4 – new prognostic biomarker of restenosis after endovascular treatment in patients with lower limb ischemia?

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Background and Objectives

One method of treating advanced peripheral artery disease (PAD), an inflammatory vascular disease of increasing incidence in developed countries, is percutaneous transluminal angioplasty (PTA), which is less successful in patients with recurrent restenosis. Even though the role of leukotrienes, as pro inflammatory mediators is well-known, their influence on restenosis has not been studied yet. We, therefore, wanted to establish prognostic features of urinary leukotrienes E4 (uLTE4) in occurrence of restenosis.

Methods

In this prospective study 179 patients with PAD admitted for planned lower extremities PTA were recruited. Urine samples were collected before, 2 hours after as well as day after intervention. Also during control visits (1, 3, 6 and 12 months) uLTE4 level was measured and success of the PTA was evaluated by complex assessment of restenosis. Patients have been divided into 2 groups: A-without restenosis; B-with restenosis.

Results

Significant peak of uLTE4 after PTA was observed in both groups of patients. The difference in average uLTE4 on every follow-up between groups A and B was statistically significant (3 months: 85.57 vs 157.64, $p < 0.0001$; 6 months: 83.17 vs 158.28, $p < 0.0001$; 12 months: 76.81 vs 150.25, $p < 0.0001$). The dependence between increased uLTE4 level in 1-month follow-up and occurrence of restenosis in 3 months as well as increased in 3 months and restenosis within 6 months has also been observed (1 month $p = 0.002$, 3 months $p = 0.016$).

Conclusions

Increased level of uLTE4 correlates with restenosis occurrence in PAD patients after PTA. Leukotrienes rise also can be a predictor of the restenosis in next months. These results let us believe, that the uLTE4 level may become the significant patients prognosis biomarker after endovascular treatment.

Influence of myocardial injury after endovascular treatment on major adverse cardiovascular events in patients with critical lower limbs ischemia

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Background and Objectives

One of common complications after noncardiac surgery is myocardial injury that has been defined as prognostically relevant injury that happens due to ischemia that happens during of up to 30 days after surgery. Myocardial injury that happens due to endovascular treatment (EVT) in patients with critical lower limbs ischemia (CLI) has not been well studied yet. Our aim was to evaluate myocardial injury after endovascular treatment (MIEVT) and its impact on postoperative major adverse cardiovascular events (MACE).

Methods

In this prospective study we enrolled patients admitted for EVT due to CLI. Blood samples for High Sensitive Serum Troponin (hsTnT) measurement, were collected before procedure, 6–12 hours and 1 day after it. MIEVT criteria has been defined as elevation of hsTnT over 14 ng/l after EVT with at least 30% increase from the baseline hsTnT. Patients have been covered with 1-year follow-up observation.

Results

We enrolled 239 patients, 62.1% had preoperative hsTnT above the threshold level of 14 ng/L, however it didn't significantly influence MACE ($p = 0.89$), nor 1-year mortality ($p = 0.98$). During 1-year observation, cumulative MACE occurred in 48 patients (20.5%) and 34 died (14.2%). Significant dependence of MIEVT (61 patients; 25.5%) on death [OR = 2.73 (1.3–5.8); $p = 0.01$] and MACE [OR = 2.94 (1.50–5.73); $p = 0.003$] has been observed.

Conclusions

Troponins, commonly elevated in patients with CLI undergoing EVT, indicate high rate of cardiac diseases. At least one quarter patients may experience MIEVT. In which at least 25% will die during 1 year indicating on the periprocedural ischemia as a trigger for future outcomes. Significant majority of the patients that experienced MIEVT did not present clinical signs of myocardial ischemia, and may be unnoticed without troponin screening.

Financial incentives for smoking cessation medication in european countries from the perspective of the angiology outpatient clinics

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Rationale

Smokers represent significant number of patients in the vascular practices. Smoking represents independent risk factor for peripheral artery disease and thrombosis. Less is known about incentives and financial coverage of the medication that can be prescribed by angiologists and other specialists in European countries.

Vasa (2017)

Methods

We gathered the information regarding the financial support to cover the medication used in European countries, mainly from the publicly available informations, ministries of health and medical societies.

Results

The obtained data show large scale from no financial support (such as some Balkanic countries and post-sovietic republics), to partial ex-post support from some health insurances (Czech Republic), to full coverage of the medication every 6 months (United Kingdom). There is large differentiation even between different insurance companies, as the smoking cessation medication in some cases is covered only after the completion of certain conditions such as visit in Nicotine Dependency Center, collaborating pharmacy (but not vascular practices) or after becoming a member of a Premium club of insurance companies.

Conclusions

There is large disproportion in the access to the smoking cessation medication across European countries, with lower financial support in the eastern and central Europe. Majority of the European population suffers of limited access to the medication used for smoking cessation due to limited or no financial coverage by their health insurance companies. This gap is even bigger by restricted support for the prescriptions by vascular and other specialists.

Knockout of lipocalin-2 is associated with an impaired outcome in the hind limb ischemia and carotid artery injury model

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Rationale

We hypothesized that the acute phase protein lipocalin-2 (Lcn-2) influences endothelial cell (EC) function and improves experimental limb ischemia.

Methods/results

To test our hypothesis the mouse hind limb ischemia (HLI) model was performed. Compared to background mice (C57BL/6 = wild type = WT) the Lcn2^{-/-} mice showed significantly more tissue defects and the ischemia-associated lesions were more severe as determined by a necrosis score ($P < 0.01$). As possible mechanism we detected an impaired activation of the mitogen activated protein kinase (MAPK) in ischemic muscles of Lcn-2^{-/-} animals. Transplantation of WT bone marrow to irradiated Lcn2^{-/-} mice did not rescue this phenotype suggesting that the observed effects depend on endothelium function and not on an inflammatory response. Interestingly, treatment of WT animals with a Lcn-2 expressing plasmid significantly improved the outcome of the animals in the HLI model. In the carotid artery injury model an impaired re-endothelialization was observed in Lcn-2^{-/-} mice when compared with WT animals ($P < 0.001$).

In the mouse aortic ring assay Lcn-2 induced outgrowth of EC. In-vitro Lcn-2 mediated proliferation ($P < 0.001$) and capillary tube formation ($P < 0.01$) of venous and arterial EC. All observed effects were comparable to the prominent angiogenic factor VEGF. Additional experiments revealed activation of the MAPK and eNOS signaling pathway by Lcn-2. Finally, real-time PCR analyses in EC showed a hypoxia dependent up-regulation of Lcn-2 and its receptor (rel. mRNA normoxia vs hypoxia: Lcn-2, 1.6 fold, $P < 0.05$; Lcn-2-receptor 2.6 fold, $P < 0.001$).

Conclusions

Our data suggest a possible therapeutic application of Lcn-2 in limb ischemia.

Endovascular treatment of visceral arteries aneurysms: our experience

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Aneurysms of the visceral arteries represent a rare but important vascular disease with high mortality. The incidence in post-mortem reports varies from 0.098 to 10.4 %, about 0.01–2 % in vivo. The arteries affected are : splenic artery 60 %, hepatic artery 20 % and superior mesenteric artery 5 %, other arteries of coeliac artery in smallest percentage. Splenic artery aneurysms are four time more common in women, particularly during pregnancy, while hepatic artery aneurysms are more common in men. Etiology is multifactorial. Most of the time visceral arteries's aneurysms are asymptomatic and diagnosis occurs occasionally through TC or angiography undertaken for some other reason. In the 20 % of cases this disease is manifested with a severe and deadly complication: ropture. The approach to this disease is multimodal: surgical, and endovascular. This study was conducted between January 2009 and December 2016. The aim of this article is to demonstrate the superiority of endovascular treatment compared to traditional surgery concerning safety and decreased mortality.

Peripheral aneurysms – endovascular treatment

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Aneurysms of peripheral arterial lesions are quite rare, can remain asymptomatic or present a variety of complications that put at risk the integrity of the involved limb. Popliteal district is the the most affected (70–80 %), followed by the femoral: common femoral artery (26 %), superficial femoral artery (3.5 %), deep femoral artery (0.5 %). From a clinical point of view the first manifestation of symptoms is represented by thrombosis and more rarely by breaking.

Therefore is important an early diagnosis in order to proceed to an appropriate preventive treatment. The traditional surgical technique is aneurismectomy with or without the interposition of a prosthesis. In the case of popliteal district we proceed to packaging of a femoropopliteal bypass after the exclusion of the aneurysm sac with proximal and distal ligation. More frequent is the use of endovascular technique with endoprotheses.

Our series includes 27 peripheral aneurysms treated with endovascular technique from January 2009 to December 2017: 21 men and 6 women range 46–74 years old. The localization of aneurysmal lesions was: 13 in popliteal level, 16 in iliac level, 7 in femoral level. 31 patients (85 %) were treated by placement of stents graft, 5 (11 %) with simple stents. There has not been any periprocedural complication. The mortality rate was affected in one case at 7 months after treatment cause of earlier comorbidities and for reasons not related to the angiographic procedure. The reconstruction of endovascular aneurysm of peripheral arteries demonstrates minimal invasivity, a low mortality rate and eliminates the need for blood transfusion. Therefore it's an effective and safe method, with a high success rate in short and medium term.