

Special issue

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I. Reports from the XVIIth World Meeting ... Plge of the Union Internationale de Phlébologie

Boston, MA, USA, September 8-13, 2013

II. Second meeting of the Deep Venous Reconstructive Surgery (DVRS) Club

In the framework of the XVIIth World Congress of the Union Internationale de Phlébologie (UIP), 9-13 September 2013, Boston, MA, USA



AIMS AND SCOPE

Phlebolymphology is an international scientific journal entirely devoted to venous and lymphatic diseases.

The aim of *Phlebolymphology* is to provide doctors with updated information on phlebology and lymphology written by well-known international specialists.

Phlebolymphology is scientifically supported by a prestigious editorial board.

Phlebolymphology has been published four times per year since 1994, and, thanks to its high scientific level, is included in several databases.

Phlebolymphology comprises an editorial, articles on phlebology and lymphology, reviews, news, and a congress calendar.

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Phlebolymphology

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Reports from the XVIIth World Meeting of the Union Internationale de Phlébologie



Boston, MA, USA, September 8-13, 2013



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Medical Reporters' Academy (MRA)



The reports from the XVIWorld Meeting of the Union Internationale de Phlébologie, Boston, MA, USA were prepared by the following members of the MRA team:

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Editorial



Nick MORRISON

The XVIIth World Congress of the Union Internationale de Phlébologie (UIP) took place in Boston and was hosted by the American College of Phlebology (ACP), under the leadership of UIP Past-President Eberhard Rabe and current President Angelo Scuderi. During the meeting a new Executive Committee and President were elected. As UIP President Elect, I would like to thank all those who have entrusted me with the task of continuing, from 2015 to 2019, what my predecessors have started, and of enforcing the commitments of the UIP:

- To strengthen the links between societies and associations, existing or planned, that have a special interest in venous disorders,
- To promulgate recommendations on the teaching of phlebology as well as training and continuing medical education of phlebologists,
- To promote onsensus on all aspects of venous disorders,
- To encourage studies and research on disorders of venous origin,
- To promote joint meetings or international congresses,
- To encourage the activities of national societies or associations, and
- To encourage them to join the UIP.

Meetings like the XVIIth World Congress of the UIP in Boston represent one of the most important ways of transmitting information aknowledge. This is a unique occasion to exchange ideas with colleagues from all parts of the world. The initiative of Servier to report on important congresses in the field, thus keeping all venous specialists fully informed, meets the main concern of the UIP, which is to facilitate communication between all societies involved and, at the same time, offering training and continuing medical education.

This would not have been possible without the commitment of a group of young reporters from different countries who, together with the Chairman, perused the congress program and made an initial selection of the events and presentations likely to represent breakthroughs or new findings. Reports were written up hot from the auditorium, taking up a substantial amount of time for all concerned.

Many hanks to the Medical Reporters' Academy for their work in updating the skills of venous disease specialists.

Happy reading.

Nick Morrison UIP President Elect President of the UIP XVIIth World Congress in Boston, MA, USA

I. UIP Consensus, UIP Fellowships

Report from the President of the Union Internationale de Phlébologie

Angelo Scuderi, Brazil

The President of the Union Internationale de Phlébologie (UIP) summarized the 60-year history of the UIP, which evolved from national associations to supranational phlebological societies, to become an international learning society. It now represents 61 societies from 57 countries dive continents. In the last 5 years, more than 20 new societies have joined the UIP, and this year 10 new candidate countries wish to join the society.

Guidelines and consensus documents are a very important focus of a President's term and cover a variety of subjects, led by prestigious experts:

- Update on venous malformations (B.B. Lee)
- Phlebology training curriculum (K. Parsi)
- Invasive treatment b deep venous thrombosis (F. Lurie)
- Update on diagnosis and treatment of primary lymphedema (B.B. Lee)
- Venous edema (A. Scuderi, Thernard A.C.)
- Duplex ultrasound investigation of the veins in chronic venous disease, part I and II (A. Cavezzi)
- Duplex ultrasound investigation after treatment of varicose veins (M. Meissner)
- Superficial thrombophlebitis (E. Kalodiki)
- Compression therapy (H. Partsh)
- Venous symptoms in C0 and C1 patients (J.P. Benigni)
- Corona phlebectatica (P.L. Antignani)
- Endovenous thermal ablation for varicose vein disease (S. Schuller)
- Prevention and treatment of venous thromboembolism (A. Nicolaides)
- Venous hemodynamics (B.B. lee)
- Sclerotherapy (P. Coleridge-Smith)
- Venous ulcer (G. Mosti)
- Redefining venous disease (A. Caggiati)

The dissemination of UIP messages is funded by the excellent *internal Angiology* journal and electronically via www.uip-phlebology.org

UIP Consensus on corona phlebectatica

Pier Luigi Antignani, Italy

Corona phlebectatica is characterized by a fan-shaped pattern of numerous bluish, intradermal veins with a diameter less than 3 mm on the medial and/or lateral aspects of the ankle and foot in the inframalleolar area. The new recommendations recognize two grades of severity: grade 1 for insipient corona with more than five clusters of bluishnitradermal veins in the retromalleolar area; and grade 2 for definite corona with tortuous bluish intradermal veins with a diameter less than

3 mm in the submalleolar area, extending to over half the length of the foot or more.

Corona phlebectatica is a strong clinical predictor of chronic venous disease (CVD) and subsequent occurrence of skin changes, and has prognostic value for the progression of CVD. It is also a highly significant clinical sign for chronic venous insufficiency. The author stressedhat corona phlebectatica should be evaluated in every patient with CVD, and should be considered for inclusion in existing or future classifications/scoring systems of CVD.

UIP Consensus on venous symptoms in CO and C1 patients

Jean-François Uhl, France

The correlation between venous symptoms and the presence of telangiectases or reticular veins (C1) is very controversial. Even though the inflammatory reaction and subsequent interaction with venous nociceptors can explain the venous pain, other symptoms, such as a feeling of swelling and cramps, do not appear to be related to the nociception. A scoring system that could incorporate more specificity may help in distinguishing vein symptoms from other conditions. Furthermore, static foot disorders can be present in more than 30% of C0s and C1s patients. I fact, postural changes and impairment of the foot and calf pumps may lead to an increase in the pain. Current treatment of these specific patients may include compression, venoactive drugs, and reduction of risk factors. Meanwhile, future research should include epidemiological studies on venous pain in C0s and C1s patients, look at the possible relationship between female hormones and symptomatic telangiectases, and evaluate the potential relationship between venous pain, static foot disorders, and postural changes.

UIP Consensus on endovenous thermal ablation for varicose vein disease

Sanja Schuller-Petrovic, Austria

The recommendations on the use of endovenous thermal ablation for varicose vein disease (ETAV) were made based on the quality of evidence for efficacy, safety, tolerability, cosmetic outcome, patient satisfaction/preference and, where appropriate, on the experts' opinion. Most of the evidence accumulated so far relates to endovenous laser ablation and radiofrequency segmental ablation. As a result, 26 recommendations were presented concerning the qualification of ETAV providers, pretreatment and posttreatment evaluation and documentation, indications and contraindications, anesthesia to be delivered, vein cannulation and catheter introduction, infiltration of tumescent solution, treatment records, posttreatment advice, and complications.

UIP consensus on primary lymphedema: update

Byung-Boong Lee, USA

The management of primary lymphedema continues to be a challenge for patients and treating physicians worldwide. Progress in the past decades has been significant in both the diagnosis and treatment of this disabling condition. Yet, significant controversies relating to the nomenclature/definition of primary lymphedema and its contemporary management remained from the previous consensus, with many issues left open for future updating. For the 2013 consensus, 20 experts were gathered to give special consideration to the following topics:1) genetic issues; 2) molecular biology issues; 3) perspectives on edema; 4) lipedema as a differential diagnosis; 5) primary phlebolymphedema; 6) decongestive lymphatic therapy (DLT) based on compression therapy; 7) update on lymphatic microsurgery; 8) pharmacological treatment; and 9) elephantiasis management.

The author underlined that primary lymphedema can be managed adequately as a form of chronic lymphedema by a sequenced and targeted treatment and management program based around a combination of DLT with compression therapy. Treatment in the maintenance phase should include compression and selfcare (self-massage, thorough personal hygiene and skin care, lymph transportpromoting exercises, and pneumatic compression therapy applied at home). When conservative treatment is not effective, the management of primary lymphedema can be improved with suitable surgery, either reconstructive or ablative. Both surgical techniques are very effective for initiallyntcolling the progression of lymphedema, but ultimately initial success cannot be maintained without additional postoperative DLT. Compliance with a long-term commitment to postoperative DLT is actually the most critical factor determining the success of any new treatment strategy, whatever the surgical procedure. The future management of primary lymphedema may be significantly enhanced with the prospectnew gene-, and perhaps, stem cell-oriented.

UIP consensus on primary lymphedema: lipedema issue

Gyozo Szolnoky, Hungary

Lipedema is a bilateral, symmetrical, 'bike pant' or column-shaped fatty swelling of the lower limbs; upper limbs are less commonly involved. It is a female disorder; males usually only develop lipedema as a result of a hormonal disturbance. The general incidence of lipedemanong women is estimated to be around 11%.

The diagnosis is mostly clinical (no involvement of the foot, absent Stemmer's sign, bilateral fat pads, filling of the retromalleolar sulci, non- or minimally-pitting edema, pinch test), but can be complemented by several noninvasive (waist-to-height ratio, vacuum suction method for capillary fragility, assessment of aortic stiffness, ultrasound, computed tomography, magnetic resonance imaging [MRI]) and minimally invasive tests (lymphoscintigraphy, MRI lymphoscintigraphy, fluorescent microlymphoscintigraphy). The condition has a high familial incidence with X-linked or more likely, autosomal dominant, inheritance with sex limitation. There are three progressive stages. Treatment is based on dietary restrictions for

weight control, and decongestive lymphatic therapy followed by compression in the maintenance phase. A surgical approach (liposuction) may be considered, but must always be followed by compression.

UIP Consensus on primary lymphedema: genetic issue

Sandro Michelini, Italy

Primary lymphedema is an inherited condition caused by mutations in three genes *VEGFR3*, *FXOC2* and *GJC2*. Diseases causing mutations in single probands affected by lymphedema have also been identified in another two genes from eight different families: HGF and MET.

To understand more clearly the role of mutations in *genesrR3* and *FOXC2* in the manifestation of lymphedema the author designed a study with two objectives:

Define the detailed pedigree for each lymphedema family and establish the genotype for the familial mutation identified in the proband for each individual family member.

Perform lymphoscintigraphy in family members who, although characterized by the presence of the familial mutation, do not show clinically manifest signs of the disease.

Among seven families (twt/EGFR3-related, one FOXC2-related) at least one subject carried the familial pathogenic allele despite clinically silent disease. In some families (VEGFR3 and FOXC2-related), lymphoscintigraphic data from individuals with clinically silent disease showed a monolateral delay in lymphatic drainage through the inguinal nodes.

In four subjects, mutant alleles of lymphangiogenic genes (*VEGMRBOXC2*) were identified without clinical signs of lymphedema; lymphoscintigraphic data from one family revealed an insufficiency of the lymphatic system in one clinically silent subject.

These data suggest that additional genes may be involved in cases of incomplete penetrance of lymphedema, which may *WEGFR3*-related or due to variable expressivity of *VEGFR3*, or *FOXC2*-related. These "additional genes" could be identified by the use of next generation technologies for the analysis of subjects belonging to large families.

Nonsense or missence mutations are detectable in cases of both familial and sporadic lymphedema. Among probands with lymphedema and wild VFGGFR3, *FOXC2, GJC2, HGF*and*MET* genes, it is plausible that others genes are responsible (Mendelian Disease), and the molecular analysis of large pedigrees is recommended. A conspicuous number of subjects (in particular in "sporadic cases") are affected by a complex genetic disorder (non-Mendelian disease), where a major causative

gene is not identifiable, but a complex pattern of inheritance (in which the person is at increased risk for developing the condition) could be involved.

<u>Further</u> <u>reading:</u>

Northup KA, Witte MH, Witte CL Syndromic classification of hereditary lymphedema. *Lymphology*. 2003;36:162-189.

Ferrell RE, Kimak MA, Lawrence EC, Finegold DN. Candidate gene analysis in primary lymphedema.*Lymphat Res Biol.* 2008;6:69-76.

Adams RH, Alitalo K. Molecular regulation of angiogenesis and lymphangiogenesis. *Nature Rev.* 2007;8:464-478.

UIP consensus on venous malformations

Byung-Boong Lee, USA

The diagnosis of venous malformations for therapeutic decisions can be made with non- to minimally-invasive investigation alone. The full integration of open surgical and endovascular therapies by a multidisciplinary team will be the main strategy for the contemporary management of venous malformations. A team approach using new treatment strategies can improve long-term treatment outcomes and reduce the morbidity and recurrence/persistence rate compared with more conventional approaches.

UIP consensus on venous hemodynamics

Byung Boong Lee, USA

Venous hemodynamic issues, concepts, and measurements in the study of lower limb venous disease have remained unchanged for a long time because of their complexity. However, the improvements in diagnostic technologies (ultrasound) that have taken place in thastldecades have increased our knowledge in this area.

The aim of this document is to provide guidelines on venous hemodynamic measurements in the investigation of lower limb venous disease according to the best currently available scientific evidence. This will provide clinicians and researchers involved in the diagnosis and management of lower limb venous disease with a clear and concise account of the hemodynamic evidence for various concepts in the management of venous disorders. The information will either back up previous recommendations or show that they are unfounded.

Where scientific evidence was lacking or weak, a consensus of opinion among the expert members of the panel was reached to support the recommendations.

The chairmen of the document (B.B. Lee, A. Nicolaides, and M. Meissner), with the editorial secretary (E. Kalodiki), led a group of more than 50 prestigious authors to summarize this knowledge in 13 review chapters.

UIP Consensus on sclerotherapy

Philip Coleridge-Smith, UK

Foam sclerotherapy is a safe and effective treatment for venous disorders when carried out by trained physicians following the recommendations of this consensus.

The consensus provides a tool for decision making in foam sclerotherapy that could help in all aspects of treatment, and provides general recommendations to physicians practicing this technique:

- Suitability of patients for treatment
- Clinical findings with an indication for foam sclerotherapy
- Duplex ultrasound investigation
- Relative and absolute contraindications
- Equipment and methodology
- Follow-up standardization

UIP award presentations

The in vitro effects of detergent sclerosants on endothelial cells (Kreussler award) David Connor, Australia

> This study is designed to improve knowledge of sclerosant agents at sites distant from the endothelium of the target vein, as sclerosants can produce microparticles when interacting with cellular membranes, which promote angiogenesis and procoagulant activity.

The study will determine the in vitro effect of sclerosants on endothelial cells at sites 5, 15, 30, and 45 cm distant from the target in both superficial and deep veins. While this has been previously studied in other cells (eg, platelets), this is the first time such a study has been performed in endothelial cells.

Venous outflow increases significantly with below knee graduated elastic compression (GEC) stocking in healthy subjects (Bauerfeind award)

Christopher Lattimer, UK

The effects of graduated elastic compression (GEC) in veins of the calf are to reduce venous volume and reflux, and to assist venous return. The aim of this study is to assess the effects of GEC in healthy subjects. The study will be prospective, performed in 20 consecutive right legs, with three groups of subjects: those with no compression, those with class 1 compression, and those with class 2 stockings. Venous outflow parameters (venous volume, incremental pressure

causing the maximum increase in volume [IPMIV], outflow at 1 sec, and time taken to empty 90% of venous volume [VET90) will be assessed using air plethysmography (APG). Preliminary results show a dose-response improvement in parameters of venous outflow, suggesting that stocking performance is quantifiable and that APG could be an adequate tool to customize stockings f patients.

Chronic venous disorders (CVD) of the lower limbs in a sub-Saharan population from Cameroon (Servier award) Markus Fokou, Cameroon

There is a lack of evidence on the incidence and prevalence of chronic venous disorders (CVDs) in tropical regions around the world, where more than 700 million people live. There is only one study in a black population, but this was performed in the USA (Sanie@o) and does not provide any valid data on sub-Saharan countries.

The current study will examine 400 patients over a 24 month period to determine, using clinical examination (CEAP), quality of life, and Doppler ultrasound, the epidemiological characteristics of CVDs in sub-Saharan populations.

The role of innate immunity in venous ulcer healing (Servier award)

Gyozo Szolnoky, Hungary

Several other factors in addition to venous congestion play a role in ulcer formation. The aim of the study was to clarify the role of the immune response in venous ulcers. The authors used measures of several humoral and cellular parameters to determine the characteristics of ulcers from patients with normal control, and to differentiate between ulcers with a capacity for healing and those without this capacity. Cellular immune activity was determined by measuring xIL-A, IL-6, CXCL8 (IL-8), IL-10, TNF, Tyro3, and Avl.

The study was performed in 69 patients with venous leg ulcers and 42 age- and sex-matched controls. The authors found that patients with leg ulcers have lower *Candida* killing activity and a "silencing" counteraction againtse to the innate immune response.

Venous education around the world

This session was particularly interesting for physicians specializing in patients with chronic venous disease (CVD). Physicians intending to start a practice in phlebology require a high-quality basic education in this field, and those who are already working must keep their knowledge and skills up to date.

One of the goals of E. Rabe's (Germany) presentation was to demonstrate the need for a well-organized education system in the world, in view of the fact that about 30% of the population has pronounced forms of CVD. He also stated that despite the huge incidence of CVD, phlebology is not recognized as a specialty in all parts of the world. The way to change the situation accept phlebology as a multidisciplinary specialty. It is also mandatory to maintain a worldwide cooperation between vascular societies when establishing phlebology training, educational programs and certification.

The experience of the Australasian College of Phlebology was presented by K. Parsi from Australia. This College has created a training program with three tiers. Physicians wanting & confine their treatment to sclerotherapy attend a 1-year course. Those wanting to perform more advanced procedures such as laser or radiofrequency ablation, require a 2-year training program. For physicians interested in managing all types of venous pathology, a 4-year training is mandatory. The system uses online training models to cover the whole curriculum. After every level, physicians perform riveten and clinical exams – the higher the tier, the more in-depth and difficult the tests become.

S. Zimmet (USA) described venous education in the USA. He underlined that in an ideal world, a venous specialist would be able to manage all patients with all the acceptable tools. However, currently no single specialty provides a comprehensive curriculum covering all aspects of venous diseases. The American Board of Venous and Lymphatic Disorders has composed an exam test with 200 items across six categories. This exam is not yet mandatory, but can help an examinee improve his/her knowledge base.

B. Eklöf described the situation in Europe where two countries, France and Germany, have a well-developed system of postgraduate training in phlebology as a sub-specialty. However, these are the only countmieEurope with such a program and certification process. This was confirmed by M. Kurtoglu (Turkey) who has analysed the issues surrounding venous education in other European countries. The main problem, in his opinion, is the absence of standardized training models in phlebology.

Current efforts to create a standardized education in Europe were presented by M. Neumann (The Netherlands), one of thunklers of the European College of Phlebology. The aim of this organization is to cooperate with scientific societies and authorities to create a Europe-wide system of venous education and certification.

*Take-home message:*Phlebology is a multidisciplinary specialty. A unified system of phlebology training is required worldwide.

II. Anatomy

The terminal and pre-terminal valves of the anterior accessory saphenous vein Alessandro Pieri, Italy

An anterior accessory saphenous vein (AASV) is found in only 44%-52% of individuals, but it is incompetent in approximately 50% of cases, and is a very important source of reflux when the terminal or pre-terminal valves are not competent.

The other differential characteristic of the AASV is **that** the only saphenous junction tributary that joins the saphenofemoral junction against gravity. Its length ranges from 3 to 30 cm (mean 10 cm), and it is located over the muscular fascia in alignment with the femoral artery.

The lymph nodes of the groin drain into the AASV, and these lymphoganglionar relationships have special importance in inguinal varicose recurrence.

To avoid recurrences whenhe AASV is insufficient, endovascular treatment of the greater saphenous vein should be performed with associated crossectomy.

Ask the experts

Venous anatomy

Jean-François Uhl, France

The author's research group produces realistic 3D vectorial models of human embryo lower limbs. The technique used is computer-assisted anatomical dissection with immune markers and manual segmentation. The results appeaconfirm Gillot's theory regarding "angioguiding" nerves. In fact, it is possible to observe a close relationship between the main venous axis and the nerves.

Focusing on the anatomy of the small saphenous vein (SSV), the author underlined the complexity of the popliteal fossa, which can be better understood by a thorough knowledge of embryology. According to the author, the clinician needs to be aware of potentially hazardous areas in the treatment of the SSV, either by sclerotherapy, surgery, or endovenous procedures. Due to the possible existence of a "short saphenous artery," it is advisable to perform sclerotherapy under echoguidance because of the highly variable location of this artery.

The superficial veins are in close proximity to associated nerves at the ankle level, apex of the calf, and in the popliteal fossa, and clinicians should be aware of these anatomical pitfalls in order to avoid nerve injury.

The foot pump is not located at the level of the "sole of Lejars," but appears instead to be situated in the lateral plantar veins. These veins make a deep plexus positioned between the muscles of the sole. Their blood content is about 25 ml and is injected with each step into the posterior tibial veins. This explains the relevance of static foot disorders in chronicemous disease (CVD), as impairment of the foot pump will worsen venous return. Indeed, the frequency of static foot disorders is roughly 18% in the normal population, compared with 37% in CVD patiAnta result, the author recommends a thorough examination of the foot in these patients and a correction of the foot disorders when they are observed.

The discussant, Alberto Caggiati (Italy), stated that the introduction of techniques for vein imaging in living subjects has transformed classic anatomic knowledge based on cadaver studies. In fact, it is now possible to define the "dynamic anatomy" of the inferior limb veins.

The author described the presence of three different pumps located in the calf: the distal leg pump, which empties during dorsiflexion of the ankle (in contradiction to what is currently considered); the anterior leg pump, which mostly empties the anterior tibial veins during dorsiflexion of the ankle; and the proximal posterior pump, which empties the posterior tibial, peroneal, and sural veins during the plantar pump. The author also described the popliteal pump, whose associated vein is completely compressed during knee extension the anterior thigh or femoral pump; the femoral vein is compressed by muscles in Hunter's canal, where it is squeezed by the Sartorius during flexion of the hip. Finally, he described the posterior thigh pump, which works during flexion of the knee, and the inferior vena cava pump, which drives the blood when intra-abdominal pressure increases.

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Frontiers in phlebology research

The anatomy of microvenous disease

Andre van Rij, New Zealand

Until relatively recently, it was assumed and published that veins <2 mm in diameter do not have valves. However, contemporary studies have provided robust evidence for the existence of valvesveins <2 mm diameter in the skin. Accordingly, the author presented his work on the role of the microvenous valves

of the superficial venous system in the development and progression of chronic venous disease.

The author's group examined several amputated limbs (some without any clinical venous disease, and others with varicose veins and ulcers) with retrograde venography corrosion casting. They were able to demonstrate that valvular incompetence can occur independently in smallporficial veins in the absence of reflux within the great saphenous vein (GSV). Microvalves were identified down to the sixth generation of tributaries from the GSV. They were also able to show that once the third generation microvalves are incompetent, reflux can extend into the entire microvenous networks in the skin, despite the presence of subsequent competent valves, bypassed in the network. In limbs with varicose veins and venous ulcers, reflux into the microvenous networks and capillary loops was more extensive with more dense networks and greater tortuosity.

The presence of microvalves in the very small veins in the skin and their dysfunction may be decisive for the development of skin changes in venous insufficiency. This may also explain why some patients with longstanding varicose veins do not develop venous ulcers. Additionally, degenerative changes in the microvenous network in the skin may be related to the appearance of reticular veins, corona phlebectatica, and venous flare's.

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III. Pathophysiology

a. Primary chronic venous disease

Heritability of chronic venous disease

Andreas Fiebig, Germany

This presentation described the results of a study performed in Germany in a group of 2701 patients with chronic venous disease (CVD), examined clinically and by duplex ultravenography. The patients' genetic contribution was assessed by estimating the heritability of CVD using a pedigree-bakedillood approach as implemented in the SOLAR software package.

The results of the study confirm that heritability in CVD is high. Heritability was found to vary only little with disease severity by CEAP classification (18.5% C2 and 16.7% C4). There was a statistically significant association between heritability and a higher CEAP class after adjusting for age and sex.

Revisiting heredity of chronic venous disorders: an epidemiological study in 21 319 patients

Vincent Crebassa, France

The heredity of chronic venous disease (CVD) has been examined in a French prospective, observational, multicentric study, performed by 1040 GPs, which enrolled 21 319 adult patients, over two consecutive days. The conclusions from the study were that CVD is most probably either autosomal recessive or autosomal dominant with incomplete penetration and variable expression. The female hormonal influence can explain increased female prevalence. In patients with parenteral antecedents, CVD treatment should probably commence earlier. The final conclusion: the end of the maternal heredity dogma!

Modulation of matrix metalloproteinases and cytokines by glycosaminoglycan sulodexide in macrophage-like cells: possible ple and treatment in chronic venous disease

Ferdinando Mannello, Italy

This "in vitro" study examined the action of sulodexide (SDX) in macrophagelike cells. SDX showed a dose-dependent inhibitory effect on inflammatoryinduced isoforms of matrix metalloproteinase 9 (MMP-9) in macrophage cells (both leukocytes and active proteases are known to play key roles in chronic venous disease [CVD] and chronicenous ulcers). SDX is able to down-regulate the secretion of several inflammatory interleukins from macrophages (also found in tissues and fluids collected from patients affected by CVD and chronic venous ulcers). SDX specifically reduces MMP-9 activity in endothelial cells of varicose veins. These new findings related to SDX underline the pleiotropic properties of this GAG mixture, not only as antitabrombotic profibrinolytic agent, but also as an inhibitor of specific macrophage pathways involved in the biomolecular mechanism of CVD. The conclusion drawn from this study is that SDX may be a potential treatment for patients with CVD and venous ulcers.

Size doesn't matter - patient symptoms do not correlate with vein diameter

Tristan Lane, UK

Patients with larger vein diameters presented with worse clinical disease severity (CEAP and VCSS), but not with a worse quality of life.

Hemodynamics in venous disease

Hemodynamic effect of abolition of reflux in superficial veins

Alun Davies, UK

For decades, the primary aim of interventions has been the correction of aberrant flow into the saphenous vein to reduce venous hypertension and improve the clinical signs and symptoms of chronic venous insufficiency. High ligation and stripping of the saphenous vein and later endovenous lasendoofnequency of the saphenous vein were the standard methods employed for the surgical management of superficial venous disease. Some reports suggest that surgical saphenectomy may reverse deep reflux in the majority of patients with both superficial and deep vein reflux. The ablation of truncal reflux improves the hemodynamics, but the correlation between hemodynamic measurements and anatomical reflux (number of refluxing veins or Venous Segmental Disease Score [VSDS]) is poor. Abolition of saphenous reflux while sparing the saphenous vein is the basis of ASVAL and CHIVA treatment strategies.

The pattern of hemodynamic abnormality may influence the clinical severity of chronic venous insufficiency. Accurate preoperative assessment of reflux is thus key to determining the most appropriate treatment strategy for the patient. There is a weak correlation of anatomical reflux or hemodynamic function and quality of life at baseline, but no significant correlation is found post-intervention.

Further studies are required to determine which disease pattern is best suited to one or a combination of therapeutic options, permitting individualization and optimization of treatment.

Proximal deep vein obstruction and hemodynamic impact

Nicos Labropoulos, USA

Venous obstruction can be intraluminal, extraluminal, or both. The consequences of venous outflow obstruction are seen during thrombotic events or in cases of iliac vein compression syndrome. Symptoms are more pronounced and more often present during standing or walking. When should we evaluate for iliac obstruction? If signs and symptoms of venous claudication schanges, diffuse limb pain, or swelling are present, or when a history of iliofemoral deep venous thrombosis is found, exploration of the superficial and deep venous system is advised.

Hemodynamic effect of compression in chronic venous disease

Hugo Partsch, Austria

The target of compression is gravity! So, how much compression should we apply in venous incompetence? To summarize, the comfortable resting pressure is around 40 mm Hg. Pressure is increased by stand**B0g40** mm Hg) in order to work against the increased pressure in the veins. The pressure peaks during walking at 70-90 mm Hg. Good compression is a balance between application of the most efficient pressure to reduce reflux and a comfortable compression pressure to achieve compliance with treatment.

Hemodynamic effect in the microcirculation

Joseph Raffetto, USA

The microcirculation is composedf derminal arterioles, capillaries and venules, which drain capillary blood and have several functions such as regulating blood flow, perfusion to tissues, fluid homeostasis, oxygen, and carbon dioxide transport. The endothelium is a key regulator of vascular tone, hemostasis, and coagulation. In chronic venous disease, there is a persistent elevated ambulatory venous pressure leading to altered shear stress on the endothelial cells, which causes them to release vasoactive agents, express E selectin, intercellular adhesion molecule (ICAM-1, CD54), and transient receptor potential vanilloid channels (TRPVs). ICAM-1 is overexpressed in chronic venous disease (CVD) and is important in initiating inflammation in the venous wall. In addition, endothelial glycocalyx, composed of glycosaminoglycans, is an important structure that prevents leukocyte adhesion, inflammation, and thrombosis. Altered shear stress and stretch could lead to injury and loss of the glycocalyx. A key component of inflammation is the expression of matrix metalloproteinases, which have effects on the endothelium, venous smooth muscle, and adventitia. Due to venous hypertension, inflammation and remodeling, a fibrin and collagen deposition i formed in the postcapillary venule, resulting in a major abnormality in the dermal microcirculation and the formation of a postcapillary cuff. Recently, venous microvalves have been found in a network of the venous microvasculature with up to six generations of microvalves in the microvenous network of the skin. A microvalve reflux could exist in the absence of greater saphenous vein reflux, and once it has compromised the third generation set of microvalves, there is a greater risk for the development of dermal venous ulceration. In patients with CVD, reflux in the microvalve and microvenous network is more extensive. Further research will make it possible to have specific pharmaceutical targets to restore the integrity of the microcirculation.

Understanding venous pain, a Servier symposium

The aim of the symposium entitled '**Understanding venous pain**, ared by Jean-Jérôme Guex (France) and Bo Eklöf (Sweden), was to release the latest evidence on the epidemiology, pathophysiology, and clinical research on venous disease, with a focus on venous pain.

Why focus on venous pain? It is acknowledged thatailegisp the commonest complaint in venous disease, and its chronic nature means that it impacts significantly on patients' quality of life.

Little is known about the prevalence of venous pain around the world for the simple reason that venous symptoms are usually not sought in epidemiological surveys, wherever the survey is performed, Europe or USA.

Eberhard Rabe, Germany raised the question as to whether **should consider venous pain as part of chronic venous diseative** recent Vein Consult Program (VCP), which updated information on the prevalence of primary chronic venous disease (PCVD) in 22 different geographic areas, showed that there are many similarities between continents in venous pain perception and in the prevalence of both venous symptoms and signs. The program revealed that three symptoms are common to all surveyed countries and that risk factors for these symptoms are also common with those of PCVD. In addition, a systematic search for venous symptoms helped detect PCVD in 6 out of 10 subjects in the VCP population. For all these reasons, one should consider venous symptoms, even at an early stage, as part of PCVD.

*Nicos Labropoulos, USA*explained the current understanding of the pathophysiology of pain during venous disease, anvalhat triggers symptoms For this, it is necessary to take into account the properties of the venous and perivenous nociceptors described by Vital's teamas well as the inflammatory mechanisms that characterize venous disease from its earliest stages. The likely trigger for these mechanisms is disturbed blood flow in large veins and capillaries that cause changes in the forces exerted on the venous endothelium. These mechanical changes activate endothelial cells resulting in the synthesis and local release of mediators that modulate pain and are pro-inflammatory. Evidence of such an inflammatory reaction has accumulated dramatically in recent years and the biochemical changes identified suggest that endothelial cells and neutrophils are the source of his local inflammation?.

Interest in the mechanisms underlying PCVD has received new impetus with the increasing recognition of the importance of the venous microvalves in the occurrence of skin changes, and possibly venous symptoms. Extension of microvalvular reflux into the microvenous network and the resulting activation of the perivenous nociceptors in the microcirculation could lead to painful sensations. This new hypothesis needs to be validated.

In his presentation entitlets venous pain reduction a meaningful treatment outcome?, Peter Neglén, Cyprus, emphasized the importance of targeting pain in

the treatment of PCVD, knowing that CEAP and VCSS classifications as well as hemodynamic parameters are not sufficient to judge the success of a treatment. Symptoms can be present at all stages of PCVD and should not be neglected as they have an important impact on patient quality of life. The availability of specific and validated scales such as CIVIQ-14 now permita@curate assessment of the impact of PCVD on patients' quality of life and how it can be improved with treatments such as Micronized Purified Flavonoid Fraction (MPFF)*.

In a**review of the efficacy of MPFF on venous symptoms***ando Mansilha, Portugal,* summarized the positive results of MPFF on symptoms and edema that have ensured its recognition as a grade 1 venoactive drug in the latest consensus documents.⁴

It is hoped that enhanced awareness among physicians of the impact of venous symptoms will result in more patients receiving effective treatment in the early stages. This will improve quality of life and delay or prevent the progression of the disease and the development of severe complications.

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*Also registered as Ardium Alvenon, Arvenum 500, Capiver, Daflon 500 mg Detralex, Elatec[®], Flebotropin, Varitor, and Venito

b. Secondary venous disease

The basic science of thrombosis

The use of animal models in venous thrombosis research and the role of selectins Daniel Myers, USA

Even though Virchow's triad is still relevant, the author introduced a variation and believes that thrombus may arise from a combination of activated endothelium, altered blood flow, and thrombophilianflammation therefore has an important role in triggering thrombosis. In this context, the author's group looked at the potential relevance of P-selectin in the thrombotic process. The expression of this glycoprotein is first increased in activated platelets and endothelial cells. The interaction of P-selectin with its receptor P-selectin glycoprotein ligand-1 (PSGL-1) facilitates the initial rolling of neutrophils and thrombus amplification. Accordingly, they have demonstrated thaolsble P-selectin is elevated in acute thrombosis and consequently may be considered as a biomarker for the diagnosis of venous thromboembolisn Amoreover, they have demonstrated the effectiveness of oral P-selectin inhibition for modifying venous thrombogenesis, increasing vein lumen opening, and decreasing inflammation in a primate model.

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The role of leukocytes in venous thrombogenesis

Peter Henke, USA

Leukocytes play an important role in thrombosis leading the author's group to examine how different leukocytes act during the thrombotic process. They found that polymorphonuclear leukocytes (PMN) may contribute to very early venous thrombogenesis by neutrophil extracellular traps and elastase-mediated functions. PMN may also impair venous thrombosis resolution via matrix metalloproteinase 9 (MMP-9) and urokinase-type plasminogen activator (uPA). On the other hand, monocytes appear to be more involved in mid to late thrombosis. They also appear to participate in the recanalization of the thromb**Tike** role of stem cells remains unclear.

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The role of tissue factor in venous thrombosis

Nigel Mackman, USA

Tissue factor (TF) is essential for hemostasis, but can also contribute to thrombosis in many pathological conditions. TF can be present in the active form (the most prevalent form; located in theessel walls) and in an encrypted form (with little or no thrombogenic activity; at very low levels in blood where it is transported in small membrane vesicles released from activated or apoptotic cells, the so-called microparticules [MP]). Cancer patients have an increased risk of thrombosis. Importantly, tumor cells express high levels of TF and release TF+MPs. Consequently, the author's group hypothesized that TF+MPs may trigger venous thrombosis. In fact, they were able to demonstrate that TF+MPs can enhance venous thrombosis in an animal model. Furthermore, they have found that elevated levels of TF+MPs were associated with an increase of venous thrombosis and a worse prognosis in pancreatobiliary cancer patients.

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Galectin, a new factor in venous thrombogenesis

José Diaz, USA

Galectins are a family of carbohydrate-binding proteins that have a high affinity for galactosides on cell surfaces and extracellular glycoproteins. They are involved in a variety of biological functions, including modulation of cell apoptosis, cell activation, and inflammation. Using microparticle proteomics analysis, the author's group has shown that galectin-3 binding protein (Gal-3BP) is upregulated in patients with deep venous thrombosis (DVT) compared with negative controls. These proteins also appear to be able to promote an upstream regulation of both P-selectin and phosphotidylserine. As the inhibition of these two molecules prevents thrombus amplification, *s*pecific galectin inhibitor could be a potential new pharmacological approach to venous thromboembolism management.

Invited lecture

The natural history of deep venous thrombosis Mark Meissner, USA

The pathophysiology of deep venous thrombosis (DVT) is related to abnormalities of blood, blood flow, and the vessel wall, but blood stasis and venous injury are also involved. DVT is a chronic disease configuration, where hypercoagulability plays a primary role. If DVT is a multicausal disease, risk factors are synergistic and not additive.

The early natural history is a dynamic balance between recanalization and recurrent thrombotic events. Neutrophils and then monocytes are involved in the early stage of recanalization as well as tissue plasminogen activator (t-PA), urokinase plasminogen activator (u-PA), and plasmin. The greatest changes in thrombus load occur over the first 3 to 6 months, and 55% of DVT cases have complete recanalization at 6 months. Thrombolysis, organization, peripheral fragmentation of the thrombus, and cellular migration can all be observed. Determinants for recanalization are sex (better if female vs male), and thrombus localisation (calf vein > proximal vein), but there is no relation regarding age. Activated coagulation and fibrinolytic inhibition are, of course, highly correlated with recanalization. The restoration of the venous lumen is not always associated with a reflux.

The late natural history of DVT is dominated by recurrent venous thromboembolism (VTE). Early anticoagulation therapy prevents recurrence because recurrent VTE is a systemic disease with underlying thrombotic risk factors. An incomplete recanalization of the thrombus is a powerful factor for recurrent VTE.

The long-term outcome of DVT is related to the natural history: a rapid recanalization protects valve function and a recurrent DVT predicts reflux and postthrombotic syndrome.

IV. Investigations

The need for a consensus on venous ultrasound-guided sclerotherapy

Fernando Vega Rasgado, Mexico

Although the UIP has published two venous consensus guidelin**asltrasoundguided sclerotherapy**(UGS), the authors of this paper suggest that a standardized report of venous ultrasound is required for uniformity in applying the method. This standardization should take into account details the equipment used for UGS, pictures or drawings of varicose veins, ulcers or other findings, a systematic description of the venous system emphasizing permeability, reflux after Valsalva's maneuver, as well as further details such as diameter, wall thickness, intensity of reflux, etc. Thus, a consensus report on venous UGS should provide a standard for the correct interpretation of the examinationd aresults by all specialists.

Sourcing-based diagnosis of severe venous leg ulcers

Alfred Obermayer, Austria

The authors introduce a simple and helpful method of Duplex investigation for atypical and severe venous leg ulcers, which they refer to as "Duplex Sourcing," and which they describe both theoretically and by the use of images. The technique may be used to differentiate venous ulcers from mixed ulcers or from leg ulcerations with different etiologies (eg, Erithema nodosum), by detecting the origin of the local venous hypertension. A "swinging blood column" is described by Obermayer as a blood column that swings back to refill empty veins when manual compression of the ulcerated area is released. The author considers that exposing this sign using duplex is evidence for "venous ulcer" diagnosis even in the 19.7% of patients who have no visible varicose veins. Obermayer underlines that a crossover pattern or a small diameter may lead to wrong diagnosis, inaccurate treatment, and early recurrence. "Duplex Sourcing" can help detect the responsible superficial reflux routes, eg, postthrombotic syndrome and peripheral arterial disease in mixed ulcers.

The different sources of reflux of the incompetent great saphenous vein on duplex scan examination Frederic Vin, France

In this study of 750 patients with an incompetent great saphenous vein (GSV), the authors performed a duplex scan examination of the groin to locate the different sources of reflux. The results of the study demonstrate that incompetence of the GSV is not always due to incompetence of the terminal valve (only 46.3% of cases inhis study). The incompetence of the saphenofemoral junction was the source of the reflux in 62.4% of cases, and in 37.6% of cases the source o reflux was the pudendal veins, perforating veins, intersaphenous connections, or other sources of reflux. The lymph node network was involved in 1.2% of cases,

but is more frequently involved in recurrent varicose veins after surgery. The authors concluded that duplex scan examination of the source of GSV reflux is necessary before any treatment in order to avoid early recurrence. The competence or incompetence of the saphenofemoral junction should be checked and other sources of reflux identified.

Correlation between great saphenous vein diameters and venous clinical severity score

Erika Mendoza, Germany

Recent data by Mendoza confirm that the diameter of the great saphenous vein (GSV) is a relevant criterion correlated with clinical class and venous clinical severity scores (VCSS). This is found in all groups (good discrimination between presence or absence of reflux between healthy and diseased legs). The measurement of GSV diameter at the proximal thigh level is more sensitive and more specific than measurement at the saphenofemoral junction. The diameter of the GSV at proximal thigh level also has a better correlation with reflux. The study also demonstrated a moderate correlation in the group with refluxing GSVs, and an even stronger correlation between VCSS and the diameter of the GSV at the proximal thigh as ompared with the groin.

Distibution and extent of reflux and obstruction in patients with active venous ulceration

Nicos Labropoulos, USA

The authors performed a PubMed search for the period 1991 to 2012 for papers discussing the impact of venous pathology in patients with leg ulcers. Twelve studies were selected for systematic review. Isolated deep venous reflux caused by either primary insufficiency or postthrombotic syndrome was infrequently reported (range 2.1%-19%). This does not, however, contradict the significant role played by deep reflux in ulcer development, as it is commonly found in conjunction with reflux in other systems. Combined insufficiency is associated with a greater risk of ulcer recurrence after surgical intervention. Concerning mixed disease, simultaneous involvement of the superficial and deep venous system was frequently reported, and triple system disease was cited as the most common cause of ulceration in most papers that examined all three systems. A previously documented episode of deep vein thrombosis was reported in a median of 33% of ulcerated limbs. The study has some limitations. Obstruction was rarely investigated in the studies analyzed in this paper and in the instances when obstruction was reported, the severity was not clarified. The patient population in the papers examined varied greatly and there was insufficient information provided about their status at the time of the study. As the papers examined spanned at least two decades, there may have been variability in the quality of information obtained from venous duplex in earlier studies due to the inevitable evolution of equipment!

Hemodynamic patterns of calf perforating veins

Stefano Ermini, Italy

The role of perforating veins in venous disease is a topical issue. Doppler ultrasound scan is a useful tool for understanding the role of perforators, but such a technique requires dynamic exploration and training. The exploration must be performed with the patient in an active standing position, with maneuvers than can reproduce the perforator flow activity with muscle systole and diastole (contraction and relaxation outward flow).

V. Treatments

a. Compression therapy and primary chronic venous disease

Ask the experts

New concepts in compression treatment

Giovanni Mosti, Italy

During this session, several accepted dogmas regarding compression therapy were questioned, and new concepts supported by scientific data were presented.

- 1 The pressure exerted by the bandage depends on the person applying it rather than the bandage. It haseb shown that even experienced nurses may be unable to apply a bandage correctly so that the intended pressure range can be achieved.
- 2 The stiffness of the material is crucial for its behavior. The static stiffness index (SSI) allows one to distinguish between elastic and inelastic material and is calculated by subtracting the supine pressure from the standing pressure.²
- 3 In contrast with whats been accepted in the past, stiff material is not associated with a low pressure at rest. In fact, inelastic materials allow both high pressure at rest and high increase in pressure during walking, whereas elastic materials only allow moderate resting pressure with no significant increase in working pressure.
- 4 By permitting a much higher pressure during walking than at rest, stiff or inelastic bandages **p**pear to be able to restore a kind of pump and valve mechanism during exertion⁴.
- 5 Stiff material maintains its effectiveness overtime.
- 6 Graduated compression is not mandatory. It appears that high compression over the calf may be more effective than graduated compression.
- 7 Compression in patients with a mixed ulcer is possible if the perfusion pressure is higher than 70 mm Hg. In such cir**ancest**, compression with inelastic bandages exerting a pressure lower than 40 mm Hg does not lead to a measurable reduction in perfusion, but seems rather to increase the arterial flow by improving the venous pumping function, reducing the venous pressure, and thus increasing the arteriovenous pressure gradient.

Dr Mosti concluded that, whatever the material, pressure and stiffness, compression therapy is always beneficial. Compression with stiff material makes it possible to achieve strong and effective pressure during standing and walking, starting from a lower, more comfortable, supine pressure. Compression stockings, on the other hand, exert a minimal hemodynamic effect and are indicated at the end of the therapy phase, to maintain the results and prevent recurrences.

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b. Treatment of chronic venous leg ulcer

Chronic lower limb ulceration - much progress to be made?

Marc McCafferty, Ireland

Dr McCafferty presented the results of a prospective survey which enrolled 51 consecutive new patients referred to the Vein Unit at St. James Hospital, Ireland, by primary care physicians. The aim of the study was to evaluate the assessment and management of chronic lowermb ulceration in the community. The results showed that mean time from ulcer management in the community to referral was 8 months (2 weeks-60 months), and two-thirds of these patients did not have a working diagnosis referral. Clinically, 70% of patients were considered to have venous ulcer and treated with full compression, 74% of these cases did not have compression prior to referral, or they handh pression that was discontinued or inadequate. Four months follow-up was completed in 85% of cases, 72% were fully healed, and 2% of cases did not improve. The authors conclude that management of lower extremity ulceration in the community remains suboptimal. Additional education is required to ensure accurate diagnosis and management. When community ankle-brachial index testing is not available, criteria for the safe use of compression therapy should be instituted. Earlier referral of nonhealing ulcers should also be encouraged.

An International Perspective on the Management of Venous Ulceration

Chronic venous ulceration benefits from one-shot surgery: abolition of sourcing-positive reflux routes and ulcer surgery Alfred Obermayer, Austria

After a brief presentation of the duplex "sourcing" technique as a way of detecting the responsible superficial reflux routes (eg, post-thrombotic syndrome and peripheral arterial disease), Obermayer discussed surgery in patients with venous ulcers. He considered that "Single-shot surgery" is a good standard for treating recalcitrant venous ulcers, although it is not internationally accepted. The technique enables and accelerates ulcer healing, with evidence for this approach provided by the ESCHAR randomized controlled trial.

Reducing the incidence of venous ulceration: initiatives of the 6th Pacific Vascular Symposium Fedor Lurie,USA

This paper presented the results of the 6th Pacific Vascular Symposium (PVS), which took place between 12th and 15th November 2009. The aim of the PVS was to initiate collaborative effort, aimed at a practical and achievable goal: to decrease the prevalence of venous ulcers by 50% in 10 years. The results were multiple: critical issues, practical solutions, landmarks of success and calls for action. PVS established many priorities: awareness of venous ulcers and chronic venous disease, both professionally and for the public; and standardization of CVD diagnosis (practical and reproducible ultrasound scans to identify axial/segmental reflux and obstruction, noninvasive and invasive diagnosis of iliac obstructive isease, and collaboration with Wound Care Centers to diagnose and treat venous ulcers by these standards). Another priority of the PVS was to change the therapeutic behavior of C4-C6 patients: compression for control of venous/lymphatic swelling, correction of superficial axial reflux, perforator reflux and treatable deep vein obstruction, and last but not least, surveillance for progressive axial reflx, and compliance with compression and pharmacologic management of anticoagulation for various stages of CVD. Another topic debated was the prevention of postthrombotic syndrome. This requires provision of appropriate compression, ambulation, and anticoagulation for acute deep venous thrombosis (DVT), prevention of recurrent DVT, early thrombus removal in patients with iliofemoral DVT, and elimination of postthrombotic iliocaval obstruction. The PVS also paid special attention to research, and in particular an initiative to determine the prevalence of venous ulcers over the next 10 years, defining the natural history of primary disease progression from C2 to C6, and the effect of early intervention to prevent this progression. A PVS action plan for the coming 5 years (2010-2015) was also conceived.

The American Venous Forum guidelines for the prevention and treatment of venous ulceration Thomas O'Donnell, USA

Clinical Practice Guidelines are "systematically developed statements to assist practitioner and patient decisions about appropriate heath care for specific clinical circumstances." "The need for an Intersociety Consensus Guideline for venous ulcer" was published in the Journal of Vascular Surgery in 2011 by Thomas O'Donnell and Ethan Balk. It presented the compulsory stages in guideline development and discussed several aspects of the prevention and treatment of venous ulceration, as well as levels of recommendation: strong recommendation (high degree of agreement), weak recommendation (low level of agreement), and areas of "controversy." The author concluded that it is imperative for specialty societies to collaborate and develop a consensus document on venous ulcers.

South American Consensus Guidelines for the prevention and treatment of venous ulceration

Oscar Bottini, Argentina

In South America, the prevention and treatment of venous ulceration was disadvantaged because of disparities in diagnosis and treatment criteria, a lack of objective and local data, a lack of statistics and epidemiology, and in particular, no strong consensus recommendations based on scientific evidence. Starting out with this reality and using models such as the Spanish National Consensus Conference on Lower Extremity Ulcers (CONUEI, 2006), the Pacific Vascular Symposium Consensus (2010), and the American Venous Forum Consensus (2011), consensus guidelines for the prevention and treatment of venous ulceration have now been developed for South America. The project was started in 2010 and published in 2013. The implementation of this Consensus should lead to the prevention, fast diagnosis, and correct treatment of venous ulceration in South America.

c. Sclerotherapy and primary chronic venous disease

Cosmetic sclerotherapy of leg veins

Selecting the proper sclerosant, sclerosant concentration and volume

Mitchel Goldman, USA

The author reviewed the main sclerosant substances currently in use. He briefly reminded the audience of their mechanism of action, therapeutic indications, secondary reactions, and their efficacy as demonstrated by clinical trials. He also established some sclerotherapy rules, the most important of which seems to be first the elimination of igh-pressure reflux, and second the treatment of small varicose and reticular veins with associated telangiectasias on the same day.

To the question "How do we select the type of sclerosant, the sclerosant concentration and volume?" his answer was the following: "by consolidating, of course, the data in the specialty literature and broad personal experience.

Sclerosant is what you are comfortable with, concentration depends on the size and type of vein and the volume depends on the size and diameter of the vein."

Reticular veins: evidence is strong

Robert Weiss, USA

The focus of this presentation was that reticular veins must be treated for successful management of associated telangiectasias. Treatment of the form**iso a**educes side effects such as pigmentation by reducing venous pressure. New telangiectasias appear when compression of reticular veins has not occurred.

Compression after cosmetic sclerotherapy: critical evaluation of the evidence

Albert Adrien Ramelet, Switzerland

Although a study by Nootheti from 20000nfirms that wearing medical compression stockings (MCS) for longer after sclerotherapy of telangiectasias improves results, phlebologists worldwide still have different opinions, and some patients continue to be denied the use of MCS. Several hypotheses have been proposed for the mechanism of action of MCS. Based on the results of several clinical studies published in the specialized literature, Ramelet asserts that MCS should be proposed for all patients after sclerotherapy of telangiectasiasusb the wearing of MCS (for an additional 3 weeks after sclerotherapy treatment) improves clinical vessel disappearance, avoids treatment failures, and reduces the incidence of pigmentation.

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Alternatives to sclerotherapy

Neil Sadick, USA

Laser therapies were presented by the author as viable alternatives to sclerotherapy. Pulsed dye lasers are considered by Sadick as a **gaud**ard for the treatment of facial telangiectasias, hemangioma, and port wine stains. External laser therapy is recommended for non-cannulisable leg veins, and can be used in combination with liquid sclerosing techniques. Endovascular Laser Therapy (EVLT) is recommended for axial vein incompetence. The combination of EVLT with foam sclerosing techniques or ambulatory phlebectomy is also possible. For best results, sclerosants should be combined with long-pulsed Nd:Yag lasers. EVLT is the optimal treatment for axial varicose veins (ie, long or short saphenous veins).

Safety of foam sclerotherapy

Pathophysiology of neurosensory symptoms following foam sclerotherapy

Jean-Luc Gillet, France

Although foam sclerotherapy (FS) is a safe and effective treatment for varicose veins, specific complications and neurological symptoms related to its use such as visual disturbances and cerebrovascular events have been reported. Visual disturbances after FS correspond to migraine aura and have been related to a spreading depression of cortical activity caused by release of endothelin and microemboli. The disturbances are not secondary to a transient ischemic attack. These auras are fully reversible visual, sensory, or dysphasic speech disturbances.

Cerebrovascular events following FS can be secondary to specific complications of FS treatment, but can also appear with other endovascular ablative events (RFA, EVLA), as well as liquid sclerotherapy. The time of onset after the procedure differs for paradoxical clot embolism (delayed onset of symptoms) and paradoxical gas embolism (immediate onset). Such events can be prevented by the use of more viscous foam, limiting volume, and avoiding Valsalva maneuvers after treatment.

While millions of FS sessions have been performed, no deaths from stroke have been described, and only a few cases of stroke related to air embolism, with complete or near complete recovery have been described.

Small volume injection to reduce foam migration

Takashi Yamaki, Japan

A patent foramen ovale (PFO) is present in half of the populations arelated to the risk of foam sclerotherapy (FS) complications. The aim of our study was to minimize foam migration, compare multiple injections of low dosages (< 0.5 ml of 15 POL foam) versus a few large volume injections (>0.5 ml), and monitor the presence of foam in superficial veins (great and lesser saphenous) and the deep system (common femoral, femoral, popliteal, anterior and posteribiaet vein, and perforating veins) with ultrasound.

The study findings indicate that multiple small-dose injections can reduce the amount of sclerosant foam entering the deep veins. Higher volumes have superior efficacy, but promote venous spasm that can cause migration of foam via perforating veins to the deep venous system

Is pretreatment for foam sclerotherapy warranted?

Alessandro Frullini, Italy

Deep venous thrombosis risk can be 1 in 455 after foam sclerotherapy according to Myers, although this figure varies slightly in other studies. The indications for

foam sclerotherapy are changing, and there is a trend to treat increasingly larger veins in office procedures (a procedure that may increase risk in case of adverse events). For this reason, prophylaxis can be an option.

Adverse events may be related to allergic reactions and microbubble embolization and endothelin release. They can also be related to the presence of right-to-left shunt (patient foramen ovale [PFO]), incomplete spasm of the treated vein, patient variability responses to endothelin release, and interaction with other coagulation substances with anti-endothelin activity (vasodilators and cardiovascular drugs). PFO can elevate risk, as we know now, because the lung bed is a scavenger for emboli and for endothelin release. When instituting prophylaxis, coagulation disorders and endothelin release should be considered. Since the author has started using prophylaxis, the rate of neurological and visual disturbances has decreased from 1.11% to 0.16%.

In extensive sclerotherapy one can use nadroparin (once daily), aminaphtone 75 mg/12 hours starting 3 days before sclerotherapy and continuing until the sclerotherapy cycle ends, and cetirizine 10 mg 1 hour before sclerotherapy. For minor sclerotherapy he use of low molecular weight heparins is not necessary.

What is the evidence that total foam volume is related to safety?

Stephen Guggenbichler, Germany

In several studies, complications related to foam sclerotherapy appear to be dosage dependent. In 2008, Myers concluded that the incidence of venous occlusion rises with higher volumes of foam, veins greater than 5 mm, and sclerosant concentration. **1** 2006, Wright had to change the Varisolve study protocol (up to 60 ml) because of a higher rate of thrombotic events. The relationship between neurological effects and dosage still remains unclear.

There is only a small amount of evidence that foam volume is related to safety, but 15 years of experience in Europe in which the amount of foam has been limited to under 10 ml per session has shown that it is safe. Volume should therefore be limited for safety reasons. It is better to increase the number of sessions and not the volume in one session.

The term "sclerosophy" aims to control varicose vein disease with multiple injection sessions of small volumes. The safety of the method is the most important factor.

Is routine duplex control indicated for detection of DVT following FS?

Andrew Bradbury, UK

In the Varisolve study there was a high rate of deep venous thrombosis (DVT) (2.5%), but usually the risk of thrombosis with foam sclerotherapy is lower (Birmingham experience, 1027 patients, 3 proximal DVT and 1 pulmonary embolism; Cheltenham, 776 patients, 17 DVT (1.5%) and 1 pulmonary embolism).
However, the majority of thrombotic events are asymptomatic, limited, and can be considered as echography findings.

For this reason, ultrasound control of the whole deep system is not cost-effective, because clinically significant DVT is very rare with homemade foam. The numberneeded-to-scan to detect one DVT is >150 and the cost for a detected DVT is higher than \$0000. In addition, the timing of DVT is variable, with a single scan the protocol would be inadequate. The benefit of performing duplex screening is therefore uncertain.

Is there a difference in the safety profile of manufactured foam versus homemade foam? Katy Darvall, UK

In general, there are few complications in studies that have compared physiciangenerated air-based foam with manufactured foamheTlow frequency of side effects prevents statistical analysis.

There are insufficient data to determine the best methodology for performing foam sclerotherapy including the differential preparation of foam with sclerosant and gas mixtures, as well as injection techniques.

Does the type of syringe and needle used for foam sclerotherapy alter safety aspects?

Attilio Cavezzi, Italy

At present we do not have enough evidence to make any claims in terms of safety. We can produce foam with more efficacy, and this improved efficacy could promote better safety, but we need more data to reach any conclusions.

In terms of efficacy, smaller bubbles have a higher active surface of foam in the vein wall and a longer half-life, which increases the amount of contact with the venous wall.

In terms of safety, smallerubbles could have a lesser impact in the pulmonary or cerebral circulation, and faster reabsorption.

The material used can alter the stability of the bubbles. The best results are achieved with silicon free syringes, and the best combination using the Tessari technique is BD Discardit 5 ml + Terumo 2.5 ml. When using air, smaller syringes produce smaller bubbles. Using air or soluble gases, smaller syringes produce longer-lasting foam. The use of 21 to 25 G needles will not denature foam, but 27G will. The use of 4F catheters does not denature bubble size or foam duration in a significant manner.

What is the efficacy of maneuvers intended to restrict foam migration from the injection site? Douglas Hill, Canada

To decrease foam migration and its effects (neurological events such as stroke, seizure, transient ischemic attack, migraine and thrombotic events) we should take several precautions: identify patients at risk, limit foam volume, post-injection immobilization, avoid Valsalva, block the foam in the target area and the junctions with the deep system with the probe, attempt to remove the foam, use physiologic gas, and leg elevation (decreases the volume of the target vein and limits the volume required to refill the vein). In addition, one should remember that elderly patients seem to be more vulnerable to the effects of foam migration.

Is pretreatment testing for right-to-left shunt warranted?

Pauline Raymond-Martimbeau, Canada

Can we improve the outcomes of patients by defining the utility of pretreatment testing for right-to-left shunt? Is there any supporting, scientific opinion-based evidence to warrant pretreatment testing? What is the strength of the evidence?

In a systematic search of the literature the author identified 1038 articles, but only 45 studies were of interest. The overall number of patients was 11,236. There were 142 cases of visual disturbance and migraine (1.26%), 6 cases of transient ischemic attack and reversible ischemic neurologic deficit (0.05%), and 13 cases of stroke (0.001%). Most of these events were related to female gender (70%), mean age 45 yrs (33-72), and 72% associated with large veins (great saphenous vein, small saphenous vein, and perforating veins). The majority of patients had no residual deficit and most cases of embolism were confirmed to have right-to-left shunt (PFO).

There are no randomized studies to answer the question and thus, it is impossible to assign a high or even a moderate quality of evidence to any of the questions dealing with this issue, because evaluation is mostly based on exposed or the is no grading of PFO and there is a lack of consistency in reporting the details of the gas and technique used.

Air emboli occur in other therapeutic procedures in whom pretesting for PFO is not warranted (neurosurgery, laparoscopy, hip artroplasty, central line catheter placements, cesarean and gastric endoscopy).

The wide use of sclerotherapy with very low neurological complications, with n evidence of death or major stroke, indicates that sclerotherapy is safe and effective. Pretreatment testing for right-to-left shunts is therefore not warranted for people without symptoms. It can pose a risk, may not be conclusive, and can add expense.

Pre-screening for PFO is only warranted in patients at risk of PFO (history of cryptogenic stroke, severe migraine with aura, sleep apnea, platypnea orthodeoxia,

stroke with chronic obstructive pulmonary disease, and pulmonary hypertension and severe comorbidities).

The controversy of the day

Foam sclerotherapy is the treatment of choice for most patients with superficial venous reflux.

Pro – Philip Coleridge Smith, UK

Con - Andre van Rij, New Zealand

PRO: Coleridge Smith began by talking about patients who are more informed, desire minimal postoperative visits, and a rapid return to normal activities.

He described a retrospective questionnaire that was given to patients undergoing surgery, radiofrequency (RF), ablation, laser and foam sclerotherapy to provide insight on how patients felt.

In response to the question about how many days after varicose treatment patients took pain killers, the answer of the foam group **whys** b day, the RF group, 1-12 days, and the laser group, 10-14 days. When asked how soon they returned to work after varicose vein treatment, the response of the sclerotherapy group was the same day, the surgery group after 5 days, and the RF and laser group, after 14 days.

In defense of foam sclerotherapy, Coleridge Smith argued that it is the least technical treatment, with the lowest costs, and is acceptable to patients under most circumstances.

Further reading:

Rasmussen LH, Lawaetz M, Bjoern L, Vennits B, Blemings A, Eklöf B. Randomized clinical trial comparing endovenous laser ablation, radiofrequency ablation, foam sclerotherapy and surgical stripping for great saphenous varicose veBmsJ Surg. 2011;98:1079-1087.

Gohel MS, Epstein DM, Davies AH. Cost-effectiveness of traditional and endovenous treatments for varicose vein *Br J Surg.* 2010;97:1815-1823.

Shadid N Ceulen R, Nelemans P, et al. Randomized clinical trial of ultrasoundguided foam sclerotherapy versus surgery for the incompetent great saphenous vein. *Br J Surg.* 2012;99:1062-1070.

Bradbury AW, Bate G, Pang K, Darvall KA, Adam DJ. Ultrasound-guided foam sclerotherapy is a safe and clinically effective treatment for superficial venous reflux. *J Vasc Surg.* 2010;52:939-945.

CON: Prof Van Rij began his presentation by discussing the 2004 Cochrane systematic review by Rigby KA et al. The paper highlighted that there are huge variations in practice, demonstrating high levels of recurrence after foam treatment, the need for multiple treatments, deep venous thrombosis, thrombophlebitis, pigmentation, matting, arterial injection, and lack of control. He asked important questions about who is in charge of treatment: the physician, the researcher, the purchaser, or industry; and who should treat the patients: the surgeon, the dermatologist or the phlebologist? He also highlighted patient expectations: quality of life, cosmetic results, and no complication store procedure.

At 5 years, surgery produces better results than foam treatment for people with confirmed varicose veins and truncal reflux. Foam is not usually Prof Van Rij treatment of choice.

Further reading:

Rigby KA, Palfreyman SSJ, Beverley C, Michaels JA, Surgery for varicose veins: use of tourniquet (Review)*Cochrane Database of Systematic Reviews*. 2004; Issue 4.

Foam sclerotherapy in elderly patients with severe and disabling chronic venous insufficiency (C4-C6 of the CEAP) Pier Luigi Antignani, Italy

This study presents the results of a study performed in 73 elderly patients (68-85 years old), suffering from severe chronic venous insufficiency (C4-C6). The results showed that foam sclerotherapy was an effective, safe, and well-accepted treatment for improving the clinical conditions in patients suffering from chronic venous insufficiency by reducing the symptomatology (assessed with venous clinical severity score [VCSS] and venous disability score [VDS]), and by improving quality of life (SF-12 questionnaire).

Transdermal echoguided foam valvuloplasty. Rationale, technique and preliminary results in 20 cases Paolo Casoni, Italy

The aim of the foam in this technique is to induce sclerosis outside the vein rather than inside, in order to create a "perivenous fibrosis." The foam sclerosing effect is achieved in the lymphovenous layer and its extravasation in perivenous tissues is well tolerated. In addition, as the groin region is rich in veins or lymphatic-venous anastomosis; foam treatment around puffy or aneurysmal veins can induce the vein to regress to normal caliber.

Inclusion criteria for this treatment are patients with clinical varicose veins contraindicated for surgery, with great saphenous vein terminal reflux and aneurismal junction (>10 mm). An echo-guided evaluation was performed before and after foam was injected at two points, above and below the saphenofemoral junction.

The treatment was performed in 20 patients with no complications, but with poor results. Varicose veins disappeared in two patients, and in seven patients vein caliber decreased, but reflux remained although it was decreased.

In the authors' opinion, perivenous injection is useful only in 35% of cases, and probably only in those in whom real adventitia injection is achieved.

Ultrasound-guided foam sclerotherapy of recurrent varices at the long and short saphenous vein: 5 years follow up Patrizia Pavei, Italy

When should recurrent varicose veins be treated? In the author's experimence t two reasons for retreatment are the appearance of symptoms and complications. All recurrent varicose veins can be separated into two general types. (a) *Neovascularization*. These varicose veins are usually fragile, and easy to treat with foam sclerotherapy (0.5%-1% concentration using 4-10 ml per session). The author's success rate in 142 patients was 91%*R*(b)*rrences at saphenofemoral or saphenopopliteal junctions* Reperforming surgery is associated with a 70% recurrence rate. Thus, in these cases, ultrasound guided foam sclerotherapy is a better option. If the varicose vein diameter is larger than 8 mm, treatment may require 1-3 sessions of 4-10 ml of 1%-3% STS foam. The results at 1 year are 87% complete occlusion, with complete occlusion remaining in 85% of patients at 2 years, and 80% at 3and 5 years.

In conclusion, for varicose recurrence, foam sclerotherapy is the treatment of choice for neovascularization, and can be considered for recurrences emanating from junctions, where it may be combined, if necessary, with phlebectomy.

LAFOS: holmium laser-assisted foam sclerotherapy

Alessandro Frullini, Italy

LAFOS is an office-based procedure, which is painless and does not require anesthesia, and which can be an alternative to isolated endovenous laser ablation (EVLA) or foam sclerotherapy (FS).

Holmium laser does not affect the intima. It only acts on the media, where its thermal effect causes shrinkage of tunica media type III collagen fibers. Thus, complementary sclerotherapy to reduce lumen size by laser action can enhance the results of FS and the amount of foam required compatible classical FS.

In our experience with 100 cases (38 great saphenous [GSV] and 12 small saphenous vein [SSV]), 100% were successful at the first follow-up examination. Two veins needed direct injection of foam because they were not fully ablated.

There are not enough data on late follow-up outcomes, but LAFOS could be a good option for GSV/SSVs resistant to foam sclerotherapy for several reasons: less expensive (office-based, faster, no anesthesia); makes sclerotherapy more technological; vein shrinkage results in a requirement for less foam volume; media pretreatment could be feasible in large veins, and fewer postoperative recurrences.

ENdoTHeF: endovascular treatment of hemorrhoids with foam

Maurizio Ronconi, Italy

It is estimated that 5% of the population is affected by hemorrhoids. Surgical treatment is aggressive and has a high rate of recurrence. Foam sclerotherapy can improve outcomes.

The technique is performed without sedation, an oxypulsometer is the only monitoring required. The patient is placed in the left lateral decubitus position and the puncture is made after rectal endoscopic exploration. The amount of foam in each globe is 3 ml, up to a maximum of 8 ml in each session. If required, a ne session is performed after 3 weeks. The mean number of sessions required is three.

In the author's experience with 290 patients with rectal bleeding, 210 were treated with 765 procedures (mean.& procedures per patient), with a median followup of 12 months. There was disappearance of bleeding in 83% of cases and local complications were found only in 5% of cases.

Foam sclerotherapy of hemorrhoids is a simple, painless and feasible treatment with good results. The recurrence rates are not yet known.

d. Varicose vein ablation

Invited lecture

Comparative effectiveness in the treatment of venous disease

Alun Davies, UK

The treatment of patients with superficial venous reflux has changed in recent years following the widespread acceptance of minimally invasive, endovenous modalities including ultrasound-guided foam sclerotherapy (UGFS), endovenous laser ablation (EVLA), and radiofrequency ablation (RFA). The treatment of symptomatic varicose veins has been demonstrated to improve quality of life (QOL), alleviate symptoms of depression and treat the complications of venous disease. Current evidence suggests that the treatment of varicose veins in all stages of symptomatic diseases is cost-effective.

The first point to consider when comparing the effects of the different therapeutic options is that the wide range of clinical situations in chronic venous disease (CVD) can make us think we are always treating the same disease. In CVD there are multiple different anatomical and clinical pathways.

The second point is the variable methods used to measure outcomes: anatomical, hemodynamic, clinical, or functional, or based on combined criteria; a situation that increases the heterogeneity of reporting standards. Problems encountered when comparing treatments in a series are the mix of different patients and different outcomes. For this reason, in the majority of recent studies (Rasmussen,

Davies), excluded subjects comprise nearly 50% of patients in order to achieve homogeneous results.

Most of the reported results for patients treated with different techniques are similar, with no significant differences, or only slight ones.

QOL appears to be an objective tool, but differences between treatments are slight, and populations with CVD have worse Q@bres than other diseases. There is also no significant difference in QOL in one technique over another. Thus, differences between techniques may have slight variations, and some may be more related with reimbursement issues than with real patient preferences (eg, local anesthesia, office-based treatment).

Occlusion rates at 1 year are similar for the different options, but RFA seems to be associated with less postprocedure pain and a faster return to work, and therefore a better cost-effectiveness analysis compared with surgery and EVLA. UGFS remains the cheapest option, but is associated with a significantly higher recurrence rate at 1 year.

The suggested options for varicose vein treatment by the NHS guidelines in the UK (NICE) are, in this order: RFA, laser, foam, and open surgery as a last option. The options may be different in other situations and other countries.

Varicose veins have a multitude of treatments options and all can provide excellent improvements in QOL at a cost-effective level. Overall costs have fallen dramatically despite material requirements, and no patient should be without a treatment option. This idea can be summarized as "different treatments are different in different patients".

Saphenous sparing procedures

Theoretical considerations in CHIVA and ASVAL

Fausto Passariello, Italy

Both ASVAL (Ambulatory Selective Vein Ablation under Local Anaesthesia) and CHIVA (Ambulatotory Conservative Haemodynamic Management of Varicose Veins) are conservative strategies for the treatment of chronic venous insufficiency (CVI). ASVAL involves ambulatory phlebectomy of all varicoskeutaries with preservation of the great saphenous vein and small saphenous vein, irrespective of their competence. The principle of CHIVA is to decrease the superficial venous pressure. The aim of CHIVA is not only to preserve the greater saphenous vein for use as a future vascular graft, but also to maintain its drainage eliminating reflux points.

CHIVA, technical aspects and evidence

Erika Mendoza, Germany

The four principle aspects of the technique were explained: interruption of the venovenous recirculation, fragmentation of the hydrostatic column, preservation of the reentry perforators, and deletion of the incompetent tributaries. Several studies have been published on the long-term results achieved wHIVAC and a Cochrane review has been published – the CHIVA method reduces varicose vein recurrence and produces fewer side effects than vein stripping. However, these conclusions are based on a small number of trials with high risk of bias. New, randomized controlled trials are required to confirm these results and to compare CHIVA with other methods.

ASVAL, technical aspects and evidence

Paul Pittaluga, Fance

The ASVAL method is based on the concept of an ascending evolution of varicose disease. The theory has two presumptions: early treatment of varicose veins is useful to prevent spreading to the saphenous vein (if there is no saphenous reflux), and therapy should include ablation of the varicose reservoir, and not the ablation of the saphenous vein itself in which reflux is potentially reversible (saphenous stripping would only be indicated in cases where saphenous reflux is irreversible). Medium-term results (303 lower limbs) with ASVAL showed a major improvement in saphenous hemodynamics in 90% of cases compared with preoperative values at up to 4 -years of follow-up. Two other prospective studies have shown a significant effect of phlebectomy on reduction of the diameter of the saphenous vein. However, the indications for ASVAL treatment need to be refined with longer follow-up and randomized controlled trials.

Do we need to spare the saphenous vein?

Pro - Massimo Capelli, Italy Con - Fedor Lurie, USA

PRO: Massimo Capelli advocated sparing the saphenous vein not only for future use as a conduit for arterial bypass, but because preserving the saphenous trunk leads to a reduction of varicose recurrences over time. He pointed out that because the average age of the population is increasing as well as the incidence of arterial pathology, the probability of using veins as grafts will also likely increase.

CON: Fedor Lurie stated that the great saphenous vein (GSV) should be spared only in a very few selected cases of patients with existing severe peripheral arterial occlusive disease. The rate of coronary revascularization has decreased by 38%, and currently GSV is used in less than 10% of coronary artery bypass graft operations. Furthermore, less than 1% of patients with arterial disease need revascularization.

Discussion

Arkadiusz Jawien, Poland

The discussant pointed out that the preservation of the saphenous trunk is not the basis, but only one of the results of CHIVA or ASVAL. He also noted that only 0.3% of surgeons performed CHIVA as shown in a survey among 675 surgeons of the French speaking *Va*ular Surgery Society.

<u>Reference</u>

1. Perrin M, Guidicelli H, Rastel D. Surgical techniques used for the treatment of varicose veins: survey of practice in France [in Frence *Mal Vasc* 2003;28:277-286.

Controversy of the day

Both theoretical concerns and clinical evidence support a hemodynamic approach to superficial venous reflux Pro - Massimo Capelli, Italy Con - Fedor Lurie, USA

One of the most controversial subjects in phlebology is saphenous sparing procedures, of which there are two: CHIVA and ASVAL. Their supporters do not ablate or remove the great or small saphenous vein. CHIVA is based on certain principles referred to as the "hemodynamic approach" by it supporters.

PRO: The "pro" speaker Massimo Cappelli (Italy) defined a hemodynamic approach. It is a correction of the pathological changes caused by superficial venous reflux with simultaneous preservation of the saphenous trunks and tributaries. This can be achieved by ligation of trunks and branches in certain crucial points. M. Cappelli's arguments were: (1) we need to spare saphenous trunks for possible future arterial bypasses; (2) a ligated but preserved trunk serves as an effective draining system, which prevents recurrences; and (3) in case of future deep venous thrombosis, the spared trunk can become a collateral pathway. The most contradictory argument is the second one.

In summary, a hemodynamic approach to ablation of saphenous trunks leads to enlargement of other veins to drain tissues, and dissection of perforating veins results in opening of new ones to evacuate blood from outside to deep veins.

CON: The "con" speaker, Fedor Lurie (USA) challenged **dba i i** freferring to hemodynamics itself. He drew the audience's attention to the many contradictions in our knowledge of hemodynamics: reflux does not always cause varicose veins, reflux does not always cause symptoms and signs, and correction of hemodynamics does not always eliminate symptoms, reverse skin changes or edema, neither does it prevent progression of disease. He stated that there **isnica** ævidence to support a hemodynamic approach. A further point of discussion was the lack of data on what happens in the venous system in reality, ie, while not performing duplex ultrasound. The theory that ambulatory drops in deep venous pressure cause changes in blood flow in the superficial veins may not stand. The different changes that occur in the deep and superficial valves in primary disease cannot be explained by current data. The remodeling of the venous wall is not an adaptation to hemodynamic changes, but a nonreversible phenomenon. F. Lurie's conclusion was that hemodynamic changes are the result, not the cause of the disease. Therefore, while treatment is necessary, it cannot stop process.

Take-home message: The hemodynamic approach is an original and often effective treatment strategy with some contradictory principles. We are still lacking the data to explain the origin and peculiarities of hemodynamic changes in primary chronic venous disease.

Treatment of bilateral saphenous vein reflux and associated varicose veins in one session under local anesthetic without sedation: 5 year experience with 12-month follow-up

Haroun Gajraj, UK

In this study, the author investigates the outcome of a policy of treating bilateral saphenous reflux and varicose veins in one session, under local anesthetic without sedation, by a combination of endovenous thermal ablation, phlebectomy, and foam sclerotherapy.

The author treated 207 patients with bilateral saphenous reflux with C2-C5 clinical conditions from February 2007 to January 2012. The medium operating time was 90 minutes, treating in some cases very large varicose veins.

At 12-months follow-up, 185 patients (92%) had successful treatment of bilateral saphenous vein reflux and associated varicose veins in a single session, and 95% of the patients were very satisfied with the results. The time in hospital was 4 hours for the majority focases. The author indicated that it is possible to treat patients with bilateral saphenous reflux with local anesthesia without sedation.

Comparing endovascular laser ablation, conventional stripping and ultrasound guided foam sclerotherapy for great saphenous varicose veins

Lotte Engels, The Netherlands

The results of the MAGNA study comparing endovascular laser ablation (EVLA), conventional stripping (CS) and ultrasound-guided foam sclerotherapy (UGFS) for great saphenous varicose veins concluded after 1 year of follow-up that EVLA is as effective as CS, and superior to UGFS, according to occlusion on ultrasound duplex. Quality of life significantly improved after treatment in all groups.

Complications of venous ablations: a report from the MAUDE database

Nicos Labropoulos, USA

MAUDE (MAnufacturer and User facility Device Experience) is an open, voluntary national US database and was used in the current study to analyse the complications of endovenous ablation. A total of 349 adverse events relating to laser or

radiofrequency ablation reported between January 2000 and June 2012 were analyzed. Outcomes of interest were pulmonary embolism, deep vein thrombosis, death, and device failure (42% of reported events). More complications were related to radiofrequency compared with laser. There were 7 (2%) periprocedural deaths, all from pulmonary embolism. The author concluded that risks of endovenous procedures tend to be overlooked, and that the reported events represent only a fraction. Further investigation is warranted.

Endovascular laser ablation follow-up study (ELAFOS). A prospective trial to assess long-term EVLA results Demetris Kontothanassis, Italy

Long-term endovascular laser ablation results from the ELAFOS study (59 patients with a minimum of 5 years of follow-up) showed a low recurrence rate and good occlusion rates. There were 2 (3.4%) partial, and 3 (5.1%) complete recanalisations at the last follow-up. Residual disease was detected in 7 (11.9%) patients, and new disease developed in 20 patients (33.9%), but only a few patients were symptomatic.

One-year follow-up of the European multicenter study of cyanoacrylate embolization of incompetent great saphenous veins Thomas Proebstle, Germany

The first results of the eSCOPE study (prospective multicenter observational cohort study) on the efficacy of a novel greater saphenous vein ablation technique based on cyanoacrylate adhesive were presented. A total of 70 patients were included and the primary end point at 6 months was duplex ultrasound-proven vein closure with a lack of pathological reflux (anatomical success). At 2-day follow-up, 70 patients showed complete occlusion. Partial recanalization was reported at 3 months in three cases, and in one additional case at 6-months follow-up. Average venous clinical severity score improved from 4.3 ± 0.3 at baseline to 1.3 ± 0.16 at 6-months follow-up. The method proved to be feasible, safe and effective without the use of sedation, tumescent anesthesia, or compression stockings. No paresthesia was observed, but midterm results are expected.

Patient follow-up after varicose vein interventions in the UK – the views of surgeons, general practitioners, and patients. Hayley Moore, UK

Patient follow-up practices after varicose vein interventions are changing in the UK as general mathematical provides (GPs) are now seeing many of these patients. In this study, the authors completed an online survey program among patients, surgeons, and GPs before the interventions were performed to assess how, where, and by whom they feel the intervened patients should be followed up.

The survey was conducted in 2012 and answers were obtained from 47 patients, 110 surgeons (65% vascular surgeons), and 21GPs. Only 19% of patients did not expect a routine follow-up by someone; moreover, the vast majority of them anticipated a postoperative visit to a member of the surgical team, compared with

only 36% of surgeons and 51% of GPs. Meanwhile, when complications occurred, both patients and medical professionals almost unanimously agreed that the surgical team should follow those patients up. Among the GPs, 42% felt confident about following up patients, assuming additional funding was provided; 21% felt they needed more training; and roughly a quarter did not wish to follow up these patients at all.

These UK survey results highlight that if follow-up practice after varicose vein procedures is moving toward GPs, or even no follow-up, additional patient and GP education measures should be considered to ensure safety and patient satisfaction.

12-month follow-up of a randomized study comparing endovenous occlusion of the incompetent great saphenous vein with radial EVLA (1470 nm) versus RFA closure fast

James Lawson, the Netherlands

The author compared the effectiveness of endovenous laser ablation (EVLA) (1470) versus radiofrequency ablation (RFA) in the treatment of great saphenous vein reflux. A prospective study was performed by the author between October 2010 and August 2012, in a single center. Three hundred and fifty great saphenous veins in 312 patients exer randomized for EVLA (174) or RFA (177).

No difference in visual analog score for pain was observed during the first 14 days. Partial recanalization was observed in one patient after an RFA procedure and total recanalization in one patient after an EVLA procedure. Clinical and quality-of-life improvements were similar after 2 weeks and 12 months for the two treatments.

e. Secondary venous diseases

Treatment of superficial venous thrombosis

Natural history of superficial venous thrombosis

Mark Meissner, USA

In the author's opinion, the historical view of superficial venous thrombosis (SVT) may not be entirely accurate. Many colleagues believe that SVT is a benign disease with a spontaneous resolution. But in fact there is at least a 20% incidence of concurrent deep venous thrombosis and/or pulmonarynbolism. In addition, 43% of them are noncontiguous. There are many areas to be determined, from risk factors to treatment strategies and optimal end points.

Role of thrombophilia

Russel Hull, Canada

Not many studies have been published on this subject. What we know today is that the risk of SVT is six times higher for FV Leiden mutations, four times higher for the FII G20210A mutations, and 13 times higher for the combination of ATIII and protein C and protein S deficiencies. Routine testing for thrombophilia should not be considered for SVT in varicose patients, but in cases of spontaneous onset of the thrombosis there should be a lower threshold for such testing.

Use of elastic compression and NSAIDs

Ted King, USA

The presentation was mainly based on the European Consensus Statement on SVT published in 2012. Despite a lack of randomized controlled trials, the document recommends the use of both compression anotheteroidal anti-inflammatory agents in patients with SVT.

<u>Reference</u>

1. Kalodiki E, Stvrtinova V, Allegra C, et al. Superficial vein thrombosis: a consensus statement. *Int Angiol.* 2012;31: 203-216.

Anticoagulation in superficial venous thrombosis

Suman Rathbun, USA

Many use anticoagulation agents in daily practice with good results. However, there is still no high quality scientific evidence on which agents and regime should be used. Only six studies have been performed allargest was CALISTO, which proved the efficacy of fondaparinux for 45 days. Whether it can be extrapolated to low molecular weight heparins is unknown. The cost-effectiveness of this treatment should also be questioned.

Discussion

The current place of surgery for SVT remains controversial. Carlos Simkin (Argentina) and Imre Bihari (Hungary) attempted to formulate clear indications for the ligation of saphenous trunks. A protrusion of the thrombus from the saphenofemoral or saphenopopliteal junction into the deep vein system can be regarded as mandatory. Other indications, such as location of a thrombus near the saphenous trunk junctions were questionable. This was also confirmed by Sylvain Chastanet (France) in a concluding presentation. He described recent data from a posthoc analysis of the CALISTO study, which found no difference in deep venous thrombosis/pulmonary embolism in patients with a thrombus at 3 cm or less from the saphenofemoral junction. What needs to be addressed in the future are criteria for identifying higher risk populations that could result in more targeted

and thus cost-effective treatment of acute SVT. The role of new anticoagulants should also be studied.

Anticoagulants appear to be effective in SVT, but this needs to be demonstrated in more large randomized controlled trials. Surgery is indicated in some situations, but currently has a limited role in SVT.

Resolution of VTE: natural, anticoagulant and pharmacomechanical

The natural resolution of venous thrombosis

Peter Henke, USA

The incidence of deep venous thrombosis (DVT) is high and is estimated to be between 250 000 to 900 000 patients/year in the USA.

At the vessel wall level there is a balance of thrombosis/resolution. DVT resolution is dependent on a number of factors. The primary natural driver of venous thrombosis is the urokinase plasminogen activator (uPA)-plasmin system. The plasmin axis is involved in local modulation of venous thrombosis and enrolls mostly uPA, driving DVT resolution, and tissue plasminogen activator (tPA). A cellular factor is also important and involves activation of leucocytes (neutrophils and monocytes).

The matrix metallo-proteases MMP-2 and MMP-9 play an important role in midterm DVT resolution. Thrombus neovascularization occurs with time, and is cellular driven from the periphery inward. The modulation of the neovascularization is via local hypoxia: a low level 20 drft ves HIF-1a and secondarily neovascularization. Thrombus fibrosis contraction also occurs, but the mechanism is unknown. The use of normal iron metabolism for determining thrombus age and lysability potential could be useful.

The natural history of thrombus resolution in patients on anticoagulation: an ultrasound analysis

Anthony Comerota, USA

The author focused on several areas including deep venous thrombosis (DVT) ultrasound resolution frequency and speed, differences between patient groups and between iliofemoral, femoro-popliteal, and calf DVT, characteristic changes in thrombus echogenicity, resolution vs valve fuction, and recurrent venous thrombembolism. Interesting data about prognosis of ultrasound normalisation (luminal obstruction less than 40% of a noncompressed vein) were presented. Postoperative DVT has a better prognosis than idiopathic DVT, and cancer-free outpatients have a better prognosis than cancer patients. Single-segment DVT also has a better prognosis than multisegment DVT. In a study by Baut, the left leg had a greatenthombus burden, but resolution rates were similar in left and right legs, and iliac veins had significantly less thrombus regression. According to this study, ultrasound characteristics cannot be used to age a thrombus (after 30 days in 70% of cases because of unchanged echogenicity). Slow clot resolution

with persistent venous luminal abnormalities is associated with a high risk of recurrence.

Thrombus resolution with lytic therapy

Niels Baekgaard, Denmark

In the last two decades, the principle of catheter-directed thrombolysis (CDT) has become an alternative treatment modality for some types of deep venous thrombosis (DVT). Dealing with iliofemoral DVT is important because the iliofemoral segment is the outflow tract, responsible for the run-off from the entire leg, and this segment has the poorest chance for recanalization with anticoagulation alone. For the author, this issue is much more important than only « thinking of valves ». CDT treatment is limited to the thrombus alone, thereby minimizing the effect of a systemic anticoagulation treatment, and it permits placement of stents to abolish the obstructive lesions in the iliac vein during the procedure. The method should be applied for acute episodes of iliofemoral DVT with a thrombus not older than 14 days. Treatment with recombinant tissue plasminogen activator (tPA) for a few days is commonly used, and no deaths have been reported in 10 years of follow-up. The CDT is introduced through the popliteal vein and allows precise manipulation. The goal of treatment is to obtain patent veins with functional valves leading to a decreased occurrence of postthrombotic syndrome (PTS). Several randomized controlled trials comparing CDT and anticoagulation have reported good resultsbut with a short follow-up. In the Copenhagen study, there was a patency of 82% without reflux at 6 years, and the PTS rate was 61% with good quality of life. Only two major cases of bleeding occurred, with no deaths. In conclusion, CDT is a simple and safe technique that requires only a few days of treatment, and which has been proven to reduce the rate of PTS. Unfortunately, in a recent study only 15% of patients eligible for CDT were referred for treatment.

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Does pharmacomechanical thrombolysis speed thrombus resolution compared with catheter-directed thrombolysis alone? Suresh Vedantham, USA

Several methods are available of thrombus removal:

- Infusion only for a mean duration of 53.4 hours through a catheter-directed thrombolysis (CDT).
- Infusion-first pharmacomechanical catheter-directed thrombolysis (PCDT) (refers to the combination of CDT with percutaneous mechanical

thrombectomy): the infusion time and the drug doses are reduced by 40% and 50%, respectively, compared with CDT, with greater efficacy.

• Fast PCDT: Treillis and Angiojet can be performed in one session and are better for acute upper extremity deep venous thrombosis (DVT) and acute lower extremity DVT with a good inflow. The procedure usually takes 1-3 hours.

The PCDT **d**chnique enables faster clot removal, but some important questions remain: is 50%-75% clot removal sufficient to obtain good long-term results? What about thrombosed nonaxial veins? Does use of the device increase recurrent DVT? More long-term randomized controlled trials are required.

The argument for early thrombus removal in all patients with iliofemoral DVT

Antony Comerota, USA

The goal of early thrombus removal is to decrease the rate of postthrombotic syndrome (PTS), to improve quality of life, and to decrease recurrent deep venous thrombosis (DVT). The most powerful predictor of PTS is iliofemoral DVT. By removing the clot, one can improve outcomes. It has been proven that PTS does not occur if the residual thrombus after treatment is less than 10%. PTS is directly associated with the patencyf the iliofemoral segment.

Preventing recurrent venous thromboembolism, the state of the art

Suman Rathbun, USA

The most important factor when assessing risk of recurrent venous thromboembolism (VTE) is the relationship of the initial episode of thrombosis to risk factors. When a major reversible risk factor such as surgery can be identified as the sole explanation for VTE, then the risk of recurrence atively low (3% in the first year). In contrast, the risk is high (10% in the first year) in patients with unprovoked ("idiopathic") VTE, and in those with persistent, irreversible, or other risk factors. Diagnostic testing is required because two-thirds of patients with a clinical suspicion of recurrent deep venous thrombosis (DVT) are subsequently shown to be free of acute thrombosis. All of the available diagnostic tests for DVT have limitations for excluding acute recurrent DVT: the results of compression ultrasonography may be persistently abnormal for 1 year in 50% of patients and longer in others, venography also has limitations for excluding the diagnosis of recurrent DVT due to obliteration and recanalization of the previously affected venous segment or nonfilled venous segment and rement of plasma D-dimer seems to provide a simple method for excluding acute recurrent DVT in symptomatic patients! The DASH score (D-dimer, age, gender, hormonal therapy), has been proposed as a method to assess the risk of recurrence, but is still in evaluation. Long-term anticoagulant treatment is highly effective in preventing recurrent VTE, but the optimal duration of this therapy remainertain. The

next step is to identify patients at low risk who may benefit from a short period of anticoagulation for recurrent thrombotic events in order to drive a management strategy for both the prevention of recurrences and the selection of a DVT: DACUS study,³ AESOPUS study⁴

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The ATTRACT trial: implications and update

Suresh Vedantham, USA

The ATTRACT trial addresses a major controversy among physicians regarding the best way of treating patients with proximal deep venous thrombosis (DVT). On the one hand, even when standard blood-thinning drugs are used, 25%-50% of DVT patients will develop post-thrombotic syndrome (PTS), a long-term condition that causes daily pain, heaviness, fatigue, and swelling of the leg. Small studies of thrombectomy, systemic thrombolysis, or catheter-directed thrombolysis suggest that early clot removal may prevent PTS. As new catheter-based devices appear to offer safer clot removal, many doctors are now using clot-busting treatment for DVT more often. However, the American College of Chest Physicians (ACCP) have long advised against the routine use of clot-busting treatment, citing safety concerns (mainly the risk of bleedingthwuse of the clot-busting drugs), and the lack of strong evidence in favor of these more aggressive treatments from large, well-designed clinical trials. The delivery of state-of-the-art clot-busting drugs into the clot through a specially designed device such as Treillis or Angiojet (known as pharmacomechanical catheter-directed thrombolysis or PCDT), the potential risks and costs of PCDT, and theck lof physician consensus on the treatment of proximal DVT provide a compelling scientific and ethical rationale for a welldesigned clinical trial to determine if PCDT prevents PTS.

The ATTRACT study is a multicenter, randomized, controlled clinical trial of 692 patients with symptomatic proximal DVT that involves the iliac, common femoral, and/or femoral vein. Patients are randomized to receive anticoagulation and compression, catheter-directed thrombolysis (CDT), or PCDT followed by anticoagulation and compression. The duration of follow-up isa2s.yThe study will answer five questions: Does PCDT prevent PTS? Does it improve quality of life? Is it safe enough? Is it cost-effective? And what is the mechanism by which PCDT prevents PTS? The results of this study are eagerly awaited, and if positive, could fundamentally change clinical DVT practice and improve health by enabling prevention of PTS, a common, morbid, and expensive conditionthousands of patients.

New oral anticoagulants and their role in venous thromboembolism

Oral direct thrombin inhibitors, oral Xa inhibitors, new anticoagulants in venous thromboembolism Kathleen Gibson, USA; Russell Hull, Canada; Stephanie Dentoni, USA

Three presentations summarized current data about the range of new oral anticoagulants (NOACs). K. Gibson talked about the advantages and disadvantages of dabigatran. R. Hull reviewed the current situation with rivaroxaban, apixaban, and edoxaban, and S. Dentoni discussed the indications on the basis of published randomized controlled trials. The main conclusion by all the presenters was that NOACs are easy to use and noninferior in comparison with low molecular weight heparins and warfarin. However, NOACs do not have antidotes and this is their greatest disadvantage.

New anticoagulants and the management of bleeding complications

Thomas Wakefield, USA

What to do if a patient bleeds while on NOAC therapy? There are some available data concerning reversal agents for NOACs. For apixaban and rivaroxaban, four-factor prothrombin concentrate complex (PCC) and activated PCC can be used; for dabigatran, activated PCC, hemodialysis and recombinant fact**Un V**an be used. In the future, targeted agents such as PRT4445, which is similar to native factor Xa may be developed. The approach for reversal of NOACs should be determined by the patient's clinical status. In the case of non-urgent reversal, the anticoagulant therapy can simply be withheld for 2-4 days. In the setting of major bleeding, withholding therapy is not sufficient and the above mentioned measures should be taken.

Anticoagulant strategies for reducing postthrombotic syndrome

Susan Kahn, Canada

In postthrombotic syndrome (PTS), subtherapeutic anticoagulation could result in suboptimal clot dissolution, leading to valvular damage and persistent venous obstruction. The results from the REVERSE study have shown that if a patient on warfarin has an International Normalization Ratio (INR) < 2 for more than 20% of the time the risk of PTS is significantly increased: OR 1.88 (95% CI 1.15-3.07) at 5-7 months.

Take-home messages: new oral anticoagulants are noninferior in comparison to low molecular weight heparins and warfarin. Effective reversal agents for NOACs are still to be found. Suboptimal anticoagulation leads to PTS.

The new oral anticoagulants: what is safe?

John Fletcher, Australia

The author focused on recent intensive activity in the development of new anticoagulants, which have demonstrated therapeutic benefit compared with low molecular weight heparin (LMWH) and warfarin. Four new oral anticoagulants (OA) are widely used - dabigatran, rivaroxaban, apixaban, and edoxaban. A simplified dosing regimen, no dietary restrictions, predictable anticoagulation, and no need for routine coagulation monitoring are their main advantages. Dr Fletcher described their dose, route of administration, possible interactions, and relation to surgery or, invasive interventions. OA should be stopped at least 24 hours before surgery, if possible. The time of treatment cessation should be based on benefit/risk, and should be earlier, for example in patients with a higher risk of bleeding or in cases of major surgery where complete hemostasis is required. Until now, we have had no specific agent to reverse the anticoagulant, and if the procedure cannot be delayed, the increased risk of bleeding should be assessed against he urgency of intervention. Dr Fletcher concluded that OAs represent a viable alternative for patients who have poor warfarin control or cannot be treated with warfarin. Studies show that patients well controlled on warfarin are less likely to benefit from switching to an OA.

What's new in the European Venous Forum's 2013 International guidelines on the prevention of venous thromboembolism?

Risk assessment

Joseph Caprini, USA

Individual risk assessment is an important tool to evaluate patient thrombosis risk, particularly prior to an intervention. The Caprini thrombosis risk scoring assigns a point value to each risk factor according to the relative risk of venous thromboembolism (VTE) based on the literature and validation studies. It balances the risks and benefits of anticoagulation according the relative probability of bleeding versus thrombosis, and accounts for all risk factors that could affect the outcome of a procedure or illness. A linear relationship exists between the score and the incidence of clinically relevant VTE. In a study of 2016 patients, those with a score of >8 suffered a >18.3% incidence of clinical VTE and were more likely to develop a VTE compared with patients with a Caprini risk scorePeto0.001.

The Caprini score can be used to identify low-risk patients that may be spared the risks of anticoagulation, and also to identify those with high and very high risk, where extended prophylaxis should be considered.

Prophylaxis in orthopedic surgery

Russell Hull, Canada

<u>Elective hip replacement</u> Low molecular weight heparin (LMWH), fondaparinux, vitamin K antagonists (VKAs), rivaroxaban, apixaban, dabigatran are recommended (level of evidence (LE): high)

<u>Elective knee replacement LMWH</u>, fondaparinux, VKAs, rivaroxaban, apixaban, dabigatran are recommended (LE: high). Intermittent pneumatic compression (IPC) is an alternative option, and LMWH combined with IPC is more effective than LMWH prophylaxis alone and should be considered in all cases (LE: high).

<u>Hip fracture surgery</u> LMWH, fondaparinux, adjusted dose VKA, low-dose unfractionated heparin (LDUH) (LE high).

<u>Knee arthroscopy for simple diagnos</u>tica careful risk assessment should be undertaken. Routine prophylaxis is not recommended unless other risk factors are present (LE: low).

<u>Knee arthroscopy for surgery</u> LMWH starting before or after the surgery (LE: moderate) or IPC in the presence of contraindications to LMWHs are recommended (LE: low).

Prophylaxis in medical patients

Sam Goldhaber, USA

Pulmonary embolism (PE) is the first cause of preventable death among hospitalized patients, and survivors of venous thromboembolism (VTE) are at risk for recurrent deep venous thrombosis (DVT) or PE and postthrombotindsome (PTS).

In-hospital VTE prophylaxis halves the VTE rate without increasing major bleeding. After discharge, the VTE rate doubles and VTE-related death increases fivefold so there is also a need for prophylaxis in that situation. Those who will benefit the most from extended prophylaxis are female, elderly, and immobile patients. Among acute stroke patients with immobility, intermittent pneumatic compression reduced all DVT, symptomatic DVT, and overall mortality at 6 months.

The IUA 2013 VTE prophylaxis guidelines provide a roadmap for implementing « best clinical practice » among patients vulnerable to PE and DVT.

Prevention of postthrombotic syndrome

Bo Eklöf, Sweden

Despite appropriate anticoagulant therapy, about 50% of patients with deep venous thrombosis (DVT) will develop postthrombotic syndrome (PTS) sequelae, which can be severe in up to 20% of this population.

Although it is not possible to foresee the development and course of PTS in individual patients, clinical medictors of PTS are identifiable at the time of acute DVT. Proximal DVT involving the common femoral or iliac veins, elevated BMI, previous ipsilateral DVT, high Villalta score after 1 month, and older age are all associated with the development of PTS. Anticoagulation therapy alone will not protect against the occurrence of venous obstruction and valvular destruction, and initial insufficient anticoagulationreatment is associated with an increased risk of thrombus propagation, pulmonary embolism, and recurrent DVT. When elastic compression stockings are combined with early ambulation, the rate of PTS is decreased, but a lack of compliance will increase the risk. In a recent multicenter randomized controlled trial (SOX trial) of 800 patients, elastic compression stockings did not prevent the incidence of PTS after a first proximal DVT, and did not influence the severity of PTS or the rate of recurrent venous thromboembolism. Early thrombus removal, whatever the technique, has been shown to decrease rates of PTS, and stenting of remaining iliac vein obstruction seems to improve long-term patency. A chronic obstruction of the iliofemoral segment following an acute DVT is common as only 20%-30% iliac vein thrombi recanalize with anticoagulation alone. Proximal obstruction is the principle cause of PTS in approximately 30% of cases. Percutaneous endovenous angioplasty and stenting is the treatment of choice. A recurrent ipsilateral DVT is probably the most important etiologic factor in the development of PTS. Reducing the rate of recurrent DVT will therefore decrease the incidence of PTS.

The place of new oral anticoagulants

Jawed Fareed, USA

The new oral anticoagulants (NOAs) representing anti-IIa (dabigatran) and anti-Xa (rivaroxaban, apixaban) are effective in the management of postsurgical prophylaxis of deep venous thrombosis (DVT). Benefits claimed for these agents include ease of administration without the need for routine monitoring, and less drug and food interactions. Howevehey also have certain drawbacks including the lack of an antidote to neutralize bleeding.

Rivaroxaban is approved in Europe and the USA for the prophylaxis of DVT after orthopedic surgery, and for the treatment and prevention of recurrence of DVT/pulmonary embolism.

Apixaban and dabigatran are approved in Europe for postsurgical DVT prophylaxis, but not in the USA.

These agents should be used with caution in elderly patients, especially those with compromised renal or hepatic function or those prone to bleeding because of a greater risk of hemorrhagic complications. Due to the lack of an antidote, the management of bleeding episodes is difficult. Dabigatran is an absolute contraindication in patients with mechanical heart valves dais not useful in pregnancy. Clinical trials also reveal that these agents are relatively inferior to the standard of care in medical patients, especially in cancer, and cost considerations present an additional factor limiting their widespread use. For DVT prophylaxis, heparins and warfarin will remain the standard of care. However, in compromised patients, NOAs may be an option. Warfarin's low cost, efficacy and «track record » will prolong its life. In time its use may decrease, but it will remain a useful drug for years to come. Due to the risk of uncontrollable bleeding complications, NOAs are of no value for interventional and surgical indications.

f. Deep venous surgery

The Italian neovalve: techniques and results

Oscar Maleti, Italy

The author presented a new method to correct chromious insufficiency: the Italian neovalve. The purpose is to create an anti-reflux mechanism in patients with deep venous reflux when conservative treatments are not able to prevent dystrophic lesions (C4b-C6). Over the period January 2000 to May 2013, the author performed 602 procedures in the deep venous system: 352 open and 250 endovascular.

According to the author, the neovalve is indicated in pati**anss**ified as C3-C6 after failure of conservative treatments, and after previous treatment of the superficial system.

The author stated: "Equilibrium doesn't mean restoring normal anatomy and physiology, but acting in a strategic and progressive way on hemodynamic lesions, so that one can obtain a re-equilibrium of the leg."

The technique aims to create an anti-reflux mechanism in patients affected by deep venous reflux whenever valvuloplasty is not feasible. There are many options for reconstruction: bicuspid neovalve, monocuspid neovalve, monocuspid by parietal invagination, and enlargement of the flap to obtain a "sail effect."

Endovascular and surgical management options in chronic deep venous thrombosis

Kumudi Rai, India

According to the author, deep venous thrombosis (DVT) accounts for almost 10% of cases of chronic venous insufficiency. A retrospective study reviewed patients affected by chronic venous insufficiency following DVT who were managed with surgery or endovascular procedures during the period January 2010 to December 2012. Clinical assessment included history of venous claudication, physical

examination, duplex scan, and computed tomography (CT) venography. The outcome was based on technical success and relief of symptoms.

Forty-five procedures were performed (31 endovascular, 14 superficial femoral and popliteal veins). The author had technical success in 28 cases of endovascular procedures in iliac territory (93.5%), and in 13 surgical cases (92.8%). The follow-up was between 3-38 months (median 14 months) by clinical examination, duplex scan and CT venography.

The author concluded that endovascular and surgical management of chronic occlusive disease gives reasonably good results in selected cases.

Retrievable versus nonretrievable IVC filters: when to choose which

Paul Timperman, USA

The author stated that it had not yet been proved that the **sedety** fiacy of retrievable filters was equivalent to that of permanent filters.

A minority of filters must be removed, and the removal is associated with many serious complications.

Trauma is the commonest indication for temporary filters.

Inferior vena cava (IVC) filters are indicated when primary therapy cannot be started or when the patient has recurrent pulmonary embolism despite adequate anticoagulant herapy.

g. Chronic iliofemoral obstruction

Complications of iliocaval recanalization

Cees Wittens, The Netherlands

With the rising popularity of venous stenting, and the consequent increasing experience in these techniques, an increase in treatment complications is inevitable. The author discussed the potential complications and gave advice on how to prevent unnecessary mistakes. The most common complication is early occlusion (30 days) due to local thrombosis, and perioperative thrombosis prophylaxis is therefore critical. Recanalization and stenting procedures are usually performed under full anticoagulation therapy. Following intervention, the author's group usually places patients on therapeutic low-molecular-weight heparin until a therapeutic international normalized ratio (INR) $lev \partial l 0(-4.0)$ is reached with coumadin, which is then continued for at least 6 months. When no underlying coagulation disorders are present, these standard anticoagulation protocols have good results in preventing venous thrombosis. In contrast, platelet inhibitors like aspirin and clopidogrel appear less effective in preventing venous thrombosis Unfortunately, even though they are rare (3%), major hemorrhagic complications can occur. The author has had no cases of perioperative death or pulmonary

emboli due to recanalization attempts and subsequent stenting. Minor complications like hemorrhage at the access site (6%) or prolonged pain are more frequent, but are easily managed in the majority of cases. In regard to stenting in this specific location, there are several issues that can arise. Patency can be impaired by: an incorrect inflow (at femoral vein level**}temt**-related problem (fracture, kinking, non-alignment and tapering), or an inadequate outflow (at inferior vena cava level, much less common). Incorrect inflow can frequently be corrected by femoral endophlebectomy, stenting to this level, and an AV-fistula construction. The frequency of stent-related issues seems to depend on the stent design. In contrast with the arterial-designed stents initially used, more recent, vein-dedicated stents appear to have a higher flexibility and radial force, possibly leading to reduced stent-related problems, and thus permitting a better primary patency and a reduction in the number of reinterventions.

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Characteristics of the perfect venous stent: do we have it?

Peter Neglén, Cyprus

The perfect stent has not yet been designed because the theoretical characteristics of the stent that the clinician desires are difficult to match with the physical characteristics of the material.

An ideal stent would: be easy to place and replace, create an adequate flow channel, restore flow channel adequately, have long patency, be nonantigenic, have structural integration, resistance to kinking, prevent recurrent thrombosis, and be self-expansile while allowing repeated shortening and twisting.

Several of these characteristics (eg, radial force vs strength) are opposing, and if one is improved, the suitability of the other decreases. Most stents of modern design are not intended for use in the USA.

Crossing chronic iliocaval occlusions: tips for success

David Gillespie, USA

There are several "tricks" for crossing the iliac obstruction, and success can be achieved in most cases with:

- 1. Appropriate patient selection.
- 2. Multimodality image assessment (simple venography, multiplan venography, 3D computed tomography venography, duplex or intravasculaurasound [IVUS]). The more information you can obtain, the greater the success rate. Multiplane venography is more useful for visualizing and assessing a stenotic lesion than any other method. IVUS is the most accurate tool for assessing iliac vein pathology.

- 3. Critical evaluation of inflow and outflow.
- 4. Appropriate stent sizing.
- 5. Thoughtful treatment of bifurcation lesions.
- 6. Aggressive and continuous monitoring of the patient postoperatively.

Optimal treatment for bilateral iliocaval obstruction

Antonios Gasparis, USA

Isolated bilateral iliac involvement is rare and in the majority of cases there is also involvement b the inferior vena cava.

Double femoral access is required and the right jugular vein approach may be necessary in some cases. Lesion crossing can be achieved with a 0.35 inch guidewire with a 4F guide-catheter. In some cases, 0.18 and 0.14 crossing wires may be necessary. Oblique views should be used if there is any uncertainty about where the wire is going. If unable to cross... try anotherOdce crossed, dilate to create a channel using a high-pressure balloon prior to placing the stent. In cases of multiple stent placement, overlapping is necessary.

Ask the experts

How I treat iliofemoral obstruction. Pearls from the masters

Peter Neglen, USA

Stenting in the venous system is different to arterial stent placing for several reasons: (a) no kissing balloon is necessary to protect the contralateral side in venous confluences; (b) the different structure of the wall lesions in diseased arteries and veins (diffuse fibrosis in veins in contrast to layered plaque in arteries); and (c) diseased veins are stiffer and thus the angioplasty balloons must be able to inflate at high pressure.

Stenting venous iliofemoral stenotic lesions must be performed in a radiological suite with technical accuracy (infusion pumps, subtraction angiography), and under anesthesia in order to achieve long-lasting results.

Venous access is usually ipsilateral, but this approach may not be possible if the femoral vein is not patent. In such cases, popliteal (via selective canalization of branch communication with profunda) access can be achieved. However, the femoral contralateral approach is not possible with the patient in the prone position. Contralateral access navigation and stent deployment is more difficult. Femoral access is preferred by surgeons, but the internal right jugular access is preferred by some radiologists in certain circumstances.

1. Ultrasound-guided tight access

The puncture of the vein must be clean. Echo-guided puncture is desirable, as ultrasound can provide information on the vein, and help locate the vein as well as the needle. Sheath size is not important, veins have less tendency to hemorrhagic and thrombotic complications due to sheath size.

Systemic complete anticoagulation (5000 IU heparin) is performed after vein canulation.

The recanalization is made over 0.35 inch guidewires. It is sometimes necessary to change to stiffer wires if there is no support.

- 2. The use of intravascular ultrasound (IVUS) is essential. The procedure begins with phlebography, and crossing the lesion with a guidewire. Non-occlusive lesions and short occlusions are easy to cross, but true occlusions need recanalization with guiding catheters, guidewires, and quick-cross catheters. If the guidewire does not progress and reaches an extraluminal situation, the risk of bleeding is minimal, but this false lumen is likely to be followed by the guidewire in any subsequent attempts. It is therefore better to try again several days later. If recanalization is successful, one can ensure that the true lumen location ds been reached using IVUS.
- 3. Identify degree and extent of the lesion. No hemodynamic tools are available. It is accepted that more than 50% stenosis is a reason to treat. Remember that the lesion must be visualized in different projections. Positive pressure measurements support the presence of significant obstruction, but normal pressures do not exclude it. Use large sheaths and high pressiloors to pre-dilate the lesion; stiff guidewires may be necessary.
- 4. Always stent, balloon dilation alone results in recoil in most of the lesions. Use 14 or 20 mm stents, 6-20 mm length, flexible, and with radial force; wall rupture is not a major concern. Re-dilate the stent to ensure wall apposition. Stent all lesions without skipping any areas. Overlap stents generously to avoid separation (at least 2 cm). Ensure outflow and inflow by adequate stent extension.
- 5. Stent the inferior vena cava through occluded filters.

h. Venous malformations

The management of venous malformations

Ahmad Alomari, USA

Advances in the treatment of venous malformations (VMs) are still limited, despite progress in our understanding of its clinical and genetic aspects. VMs typically manifest as solitary blood-filled spongiform lesions that can be disfiguring in some cases, leading to poor quality of life. Pain may be caused by thrombosis, engorgement or involvement of joints. Different types of venous malformations such as phlebectasia, venous aneurysms, Bean syndrome, glomovenous malformations, and Klippel Trenaunay syndrome demand a specific treatment for each case.

High-resolution ultrasound and magnetic resonance imaging are the most helpful imaging modalities. Treatment indications and the management of patient expectations must be conducted with great clarity by the doctor in the first consultation based on patient history, a clinical assessment, and review of imaging status. It should be noted that none of the available treatments offer a cure for VMs.

Minimally-invasive approaches to VMs include sclerotherapy, laser, and photodynamic therapy, embolization of anomalous phlebectasia, and combinations of treatments.

Ultrasound guidance and angiography under anesthesia are used when treating VMs with sclerotherapy. The double needle technique is commonly used by the author. Sclerotherapy outflow control is not needed for most cases nor is a tourniquet for long periods of direct compression. In some cases, the author suggests the initial use of foam to block the flow, in combination with ethanol (0.5-1.0 mg kg, max 30-60 cc).

Extravasation is the most common cause of complications. Signs of extravasation are a geometric smooth or lenticular contrast collection around the needle tip. The author recommends follow-up at 1 day, 1 week, and 1 month, and an office visit at 2 months with photos.

i. Pelvic congestion syndrome

Invited lecture

The diagnosis and treatment of pelvic venous disorders Melvin Rosenblatt, USA

According to the author, the prevalence of symptomatic pelvic venous disorders is poorly studied in the literature. About 33% of the female and multiparous population will suffer from symptomatic pelvic venous disorders. In the USA, 15%-20% of women aged between 18 and 50 years complain of chronic pelvic pain, costing society about \$3.3 billion/year.

The author reports that 10% of lower limb varicose veins and 34% of nonsaphenous reflux are of pelvic origin. Pelvic or supra pelvic reflux are detected by duplex scan in 16.6% of patients with postoperative recurrences of varicose veins.

Patients with pelvic venous pathology often have confusing presentations and complex venous anatomy. Lower extremity ultrasound may only hint at the diagnosis. Patients with pelvic disorders can present with pelvic as well as lower extremity symptoms.

The pelvic symptom is pain during standing, after intercourse, and with menstruation. The lower extremity symptoms are: vulvar varicosities, generalized heaviness and achiness, varicosities, and swelling.

The sources of the varicosities are: gonadal vein insufficiency, internal iliac venous insufficiency, congenital vascular anomalies, and internal iliac hypertension (nutcracker syndrome, May-Turner syndrome, and inferior vena cava obstruction).

The initial treatment decision is symptom driven:

If symptoms are confined to the pelvis then focus treatment on supeffior r component.

If symptoms primarily involve the lower extremity, then focus treatment on the lower reflux components.

The secondary treatment decision is driven by two factors:

Recurrence of varicosities.

Persistent symptoms.

The images used for diagnosis are: ultrasound, computed tomographic venography, magnetic resonance venography, and venography.

The treatment of the inferior component when icosities are extensive is made with sclerotherapy, which can be used just as when treating the internal iliac vein reflux. It is important to reach the periuterine venous plexus.

The author recommends treatment of the superior component by approaching the jugular vein with cava and left renal injection, making a selective venogram from the gonadal veins. The use of coils plus sclerotherapy is recommended by the author to treat the gonadal vein reflux. An occlusion balloon can be used to trap the embolic in the pelvic varicosities.

The author reports initial success in 98%-100% of upper components treated; successful pelvic symptom resolution ranges from 50%-80% in published series. The author reports success in 57 patients with lower components: 80% required one treatment and 18% required an average of 1.5 sclerotherapy treatments; 2% of treatments required a second embolization.

In conclusion, pelvic-derived varicosities have many etiologies, but good abdominal ultrasound may often be enough to make the correct diagnosis. Management strategies are dependent on the patient's clinical presentation, not on the presence of disease. Minimally invasive treatment strategies for reflux disease may be very effective.

Further reading:

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j. Chronic cerebrospinal venous insufficiency

Chronic cerebrospinal venous insufficiency, multiple sclerosis, and the role of chlamydia pneumoniae Paul Thibault, Australia

This presentation focused on the etiology of multiple sclerosis. Epidemiological and geographical findings for the prevalence of this disease indicate the involvement of an infective agent. A number of agents have been suggested, but the respiratory pathogen *Chlamydia pneumoniae*has the most convincing evidence from a spectrum of medical disciplines. It is proposed that the pathogenesis of multiple sclerosis is initiated by this bacteria, which causes a specific chronic persistent venulitis affecting the cerebrospinal venous system. The theory proposes a mechanism by which an infective phlebitis could result in the specific neural damage, metabolic, immunological, and venous obstructions observed in multiple sclerosis. This approach provides a framework for further research and opens a pathway for alternative therapies.

Controversy of the day

There is a clear relationship between multiple sclerosis and CCSVI which has important implications for treatment Pro: Paolo Zamboni, Italy Con: Alun Davies, UK

The aim of this debate was to analyse the actual scientific evidence on chronic cerebrospinal venous insufficiency (CCSVI) and its association with multiple sclerosis (MS).

PRO: *Paolo Zamboni*: camined all published studies on the prevalence of CCSVI in MS patients, including ultrasound and catheter venography series, and the press release of the recent COSMO study.

According to Paolo Zamboni, the bibliography shows intraluminal obstruction in 72% of MS patients versus 17% of controls. Abnormal fibrosis and microdepositions and calcifications in the vein wall were observed by synchrotron-based XRF imaging. Evidence already exists for a reduced perfusion in MS, but there has been no attempt to correlate this with obstructed venous outflow. 2D MRI flow techniques demonstrate that flow in the internal jugular veins in humans is linearly related to global brain perfusion.

CON: *Alun Davies* referred to the absence of scientific data according to the Bradford Criteria (strength of association, consistency, specificity, temporal relationship, biological gradient, plausibility, coherence, and reversibility).

Ultrasound alone is not a reliable tool to define CCSVI. Alun Davies believes multimodal imaging, venography and intravascular ultrasound are required to move forward in terms of diagnostics.

VI. Emergencies

Emergencies in phlebology: anaphylaxis, intra-arterial injection, neurological and cardiac repercussions Kurosh Parsi, Australia

Even though emergencies in phlebology are rare, they can be life-threatening. Complications with foam sclerotherapy may be related to the drug and/or gas and can be localized or generalized. Significant complications include anaphylactic reactions (<0.1%), deep vein thrombosis (1%-3%), superficial venous thrombosis (4.4%), tissue necrosis, edema (0.5%), nerve damage (0.2%), pulmonary embolism, cardiac manifestations, stroke (0.01%), and other neurological events. Cosmetic complications include telangiectatic matting (15%-24%) and pigmentation (10%-30%).

Anaphylaxis is a sudden, severe hypersensitivity reaction. It occurs on reexposure to antigen, it is not dose-related, and is usually a type I hypersensitivity, IgEmediated reaction. Nonallergic anaphylactic reactions, formerly called anaphylactoid, are not immune mediated, are dose-dependent, and can happen with first exposure. Even though anaphylaxis can result in gastrointestinal, renal or hematologic manifestations, cutaneous (90%; flushing, pruritus, angioedema), respiratory (70%; bronchospasm, stridor, wheeze, cough), and cardiovascular (50%; hypotension and tachycardia) repercussions are the most common. Differentiation from other conditions such as vasovagal reaction (which is much more common) or acute anxiety should be made. Treatment requires: 1) keeping the airway secure; 2) giving oxygen; 3) gaining access for IV fluids; and 4) administering drugs. With regard to the latter, adrenalin is $e^{he}(k_3 \text{ to } 0.5 \text{ mg})$ intramuscular), although hydrocortisone and premathazine can also be administered. Calling for an ambulance should be done in parallel with initial patient support. The speaker stressed the importance of having a clear protocol established for these situations.

Tissue necrosis can arise either by direct arterial/arteriolar injection or by venoarterial reflex vasospasm. The lattesually occurs after a rapid dilatation of the vein and can be overcome by avoiding rapid injections especially in telangectasias and reticular veins.

Discussion

Jean-Luc Gillet, France (Discussant)

Dr Gillet reported that direct arterial/arteriolar injection is exceptionally rare. In fact, less than 70 cases have been described to date. Most of them have occurred after injection in the ankle area, and site of the perforating veins above the medial ankle. Ultrasound guidance has helped to minimize the occurrence of this catastrophic event, which most frequently results in amputation.

The most common neurological complication is visual disturbance usually associated with migraine. Stroke, a much less frequent event, is ischemic in 85% of cases and can result either from a paradoxical clot or a gas embolism. Patent foramen ovale (PFO) and other cardio-pulmonary right-to-left shunts are the most consistent risk factors. Meanwhile, screening for PFO should only be performed in patients at risk (history of cryptogenic stroke, recurrent classic migraine). During the procedure, movements that lead to Valsalva must be avoided, as well as rapid sitting or standing immediately after the procedure. The bubble load should also be minimized. Kurosh Parsi emphasized that saphenofemoral junction compression and release during foam injection does not prevent it entering the deep venous system, and can even induce a foam bolus to enter into the systemic circulation. Jean-Luc Gillet added that a small volume of injected foam (less than 10 ml) and its respective quality can further limit neurological events. It was also noted that polidocanol can lead to cardiac toxicity, which is dose-related.

In conclusion, sclerotherapy is an effective and safe treatment when used by trained and careful hands. Meanwhile, as with every medical treatment, side effects and complications may occur. Fortunately, most of them are benign, but physicians must be aware of the potentially serious events and should be trained to react adequately. Good technique, satisfactory imaging, general precautions and compliance with posttreatment instructions may help avoid some of the adverse events.

<u>Reference</u>

1. Hill D, Hamilton R, FungJ Wasc Surg. 2008;48:934-939

VII. Assessment Tools

Chronic venous disease and quality of life – the time has come to choose tool

Burden of venous disease: comparing worldwide and American findings

Armando Mansilha, Portugal

The prevalence and socioeconomic burden of chronic venous disease (CVD) are significant in the USA and Europe, and only increase with older age. The presence of venous symptoms has a marked effect on both htpsicpl and mental health of patients with varicose veins; findings that have been verified with generic and specific quality-of-life tools. CVD is not a cosmetic problem and patients with CVD deserve treatment. The long-term effects of CVD and their related cost are highly preventable, particularly if early diagnosis and treatment are made.

Specific quality-of-life questionnaires: a systematic review

Robert Launois, France

A systematic review of the literature concerning the quality-of-life (QOL) scales used in chronic venous disease (CVD) and leg ulcers was performed in February 2013 to identify the respective advantages and lacunae of existing tools. A research protocol was developed following the PRISMA statement and PICOS criteria. Three databases: EMBASE, CINHAL, and Cochrane were screened without a time window, and the identified references were chronologically ranked. Relevant systematic reviews, randomized trials, comparative studies and psychometric/linguistic validation studies were included. Inclusion criteria were met in 70 of the 511 references, in which nine scales were identified: three for leg ulcers, three for CVD, and three for both. The validation studies were based on face, construct, and group validity, as well as reliability, and responsiveness. Among the specific tools, CIVIQ and VEINES-QOL/Sym were the most validated scales and had the longest iterative validation process. The stability of the factorial structure of the CIVIQ-14 questionnaire was confirmed, as well as the effect of CVD on health-related quality-of-life.

Choosing a quality-of-life instrument to suit your needs

Michael Vasquez, USA

The author concluded that patient-reported outcomes and physician-evaluated clinical signs are complimentary tools, practical, valuable, and proven.

Quality-of-life tools for chronic venous disease: how reliable are they?

Amanda Shepherd, UK

Quality-of-life tools for chronic venous disease are reliable and consistent, well validated, and dependent on data quality and appropriate use. They can be used for evaluating quality-of-life, disease severity, outcomes following intervention, and comparison of treatment modalities. Their use for predicting treatment outcomes and rationing of resources is arguable.

Severity scores, quality-of-life scores, classifications, Villalta scores, etc; a critical review

Cees Wittens, The Netherlands

The main message from this presentation was that we still do not have a reliable instrument to assess the severity of venous disease, the efficacy of treatment, and to evaluate new techniques. Instruments such as the Clinical, Etiological, Anatomical, Pathophysiological (CEAP) classification, the Venous Clinical Severity Score (VCSS), and quality-of-life (QOL) scores have many advantages, but at the same time many important limitations. For example, CEAP is not sensitive to small changes over time, VCSS includes some items that are non-specific for venous disease, QOL tools have weak correlations with generic- and diseasespecific questionnaires, and with QOL and hemodynamic parameters. A truly all round combined QOL Score and clinical tool is still to be created. A reliable instrument to assess venous disease and the results of treatment is also still required.

The intuitive registry solution for Europe

Cees Wittens, The Netherlands

There are contradictions between the results **an**fdomized controlled trials and data from real-life practice. Selection criteria make populations included in randomized controlled trials different from those seen in daily practice. The author suggests that registries are the best tool for representing the real-life situation, for monitoring and improving healthcare, and for collecting epidemiological data. Unfortunately, existing registries such as the Electronic Health Record are imperfect. The author's team created the Maastricht Registry, which was designed especially for venous patients and allows research data to be obtained automatically from all clinicians. Venous registries such as this could be a good tool to obtain useful data on real-life practice.

Validation of VVSym^M, a new patient-reported outcome instrument for measuring symptoms in varicose vein patients Kathleen Gibson, USA

VVSymQTM, a new patient-reported outcome instrument for measuring symptoms in patients with varicose veins, was found to be easy to use, reliable, sensitive to changes in symptoms, and able to measure treatment success from the patient's perspective.



I. Second meeting of the Deep Venous Reconstructive Surgery Club (DVRS)



In the framework of the XVIIth World Congress of the Union Internationale de Phlébologie (UIP), 9-13 September 2013, Boston, MA, USA

The first meeting of the Deep Venous Reconstructive Surgery (DVRS) club was held in June 2012 and hosted by the 13th EVF Annual Meeting in Florence – see *Phlebolymphology*. 2013;20(1):68-82. Now in its second year, this year's DVRS club meeting took place during the XVIIth World Congress of the Union Internationale de Phlébologie (UIP), 9-13 September 2013, Boston,AMUSA.

The goal of the club is to promote the DVRS around the world via various support activities such as meetings, publications, websites, etc. This aim can be achieved through regular meetings of experts in reconstructive procedures for acute or chronic deep venous disease, during which they present innovative or as yet unpublished topics in the field. The format allows informal and free discussions between members of the club and results in more interactive presentations than those usually presented at conventions or meetings of learned societies. The last DVRS club meeting was attended by 19 world experts and chaired by Bob Kistner, the father of deep venous reconstructive surgery for reflux.

M. Perrin (France) began the meeting by reminding members of how and where the DVRS club was born. Hiscdssed present and future projects and proposed a database of publications on deep venous diseases. Such a database would be useful to those members of the DVRS club who require easier access to the medical literature. He also proposed that the literature be monitored for any new relevant publications.

O. Maleti (Italy) insisted that the DVRS club must remain a club and not become a scientific society. This was agreed by most of the attendees. Particularly appealing was his announcement of the creation of an Inter-University Center for Phlebolymphology, with the aim of increasing knowledge on the deep venous system. The center currently comprises six Italian universities and has been joined by the Inter-Departmental Mathematics Center for Technology, Medicine and Biosciences. O. Maleti has been appointedredotor of New Medical Products in Phlebology, a nomination that may be useful and beneficial for future DVRS club projects.

M. Lugli (Italy) presented the draft of the DVRS club website. This will include several sections and will include general information about the club, and a "Library" in which different content can be stored. Three levels of access will be provided: founder members, followers, and patients. Each founder member will have his/her own page.

The scientific session of the second DVRS club meeting comprised eight presentations.

A. Nicolaides (Cyprus) presented a new concept for measuring pathophysiological anomalies by promoting outflow resistance, which is in his opinion a neglected hemodynamic measurement. This new approach may be used in combination with other investigative procedures such as air plethysmography and duplex scanning to measure independently the importance of reflux and obstruction. As these factors frequently coexist in chronic deep venous disease this approach is crucial for determining its ideal management and the order of treatment. In
addition, the effectiveness of any operative procedure can be measured by combining the above-mentioned investigations.

F. Lurie (USA) an expert in venous ultrasound investigation, described the role of the venous valve in the circulation. He underlined that besides prevention of reflux, venous valves contribute to efficiency of outflow, and to the prevention of **h**rombosis. Consequently, valvular dysfunction results not only in reflux, but also in increased resistance, or physiologic obstruction.

P. Neglen (Sweden and Cyprus) presented the state-of-the-art in venous stenting. Imitating Donald Rumsfeld he divided his presentation into three parts: the known Knowns, the known Unknowns and the unknown Unknowns.

In terms of known Knowns, he reminded the expertseoft deterious effects of residual postthrombotic iliofemoral obstruction, the relationship between compression lesions and acute deep vein thrombosis, the underestimated importance of nonthrombotic iliac vein lesions, the safety and efficacy of iliac vein stenting, and the crucial role of IVUS.

For known Unknowns, he underlined that there is currently no accurate hemodynamic measurement for quantifying obstruction, and no knowledge about the degree at which a stenosis becomes permissive and requires correction. This is even more difficult when obstruction and reflux coexist, which is the most often encountered pathophysiological anomaly.

For unknown Unknowns, there was just a question mark, with a reminder of the design features of the ideal stent.

M. Lugli (Italy) presented a new concept of stent, specifically designed for venous implantation. The particular features that are required in the venous system, such as high radial force, flexibility, and calibre variation have all been considered in the design of this stent.

B. Eklöf (Sweden) discussed a controversial topic in depth: Is ablation of incompetent perforators (IP) in the presence of deep venous obstruction and/or reflux recommended? After malysis of a numerous and varied range of articles, his brief answer was NO. According to the anatomical and pathophysiological classification of the disorder, he recommended the following:

In C4-C6 patients with combined primary superficial and deep venous reflux, and IP:

- Start with ablation of superficial reflux
- Defer treatment of IP

If symptoms progress, or if healing is delayed or in case of ecantly ence, reevaluate the perforator and treat it if still incompetent

If problems remain: rule out iliac vein obstruction (May-Thurner). If negative, proceed with deep valve reconstruction

In C4-C6 patients with combined superficial reflux, IP and, secondary deep venous obstruction with/without reflux:

- Start with ablation of superficial reflux
- Defer treatment of IPV

If symptoms progress, healing is delayed or early recurrence, evaluate the iliac vein for possible angioplasty and stenting

If problems remain, consider deep reflux and deep vein valve reconstructive surgery

A. Rosales (Norway) presented the Oslo Pilot study on engineered allogeneic venous valves demonstrating the promising results of his research in this fascinating field, which could represent the future for correction of secondary deep venous reflux.

H. Moore (United Kingdom) works in the A. Davies unit for developing new venous valves and illustrated some interesting mathematic models concerning venous valve function.

E. Shaydakov (Russia) has demonstrated outcome improvements when using the Vedenski spiral for external support after valve reconstruction or transfer. Although the patients were not randomized in this series, external support appeared to offer better results when performed in association.

Each scientific presentation was followed by a discussion and a consensus was obtained in almost all cases.

R. L. Kistner (USA) ended the fruitful meeting with a keynote speech on the way ahead for the DVRS.



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