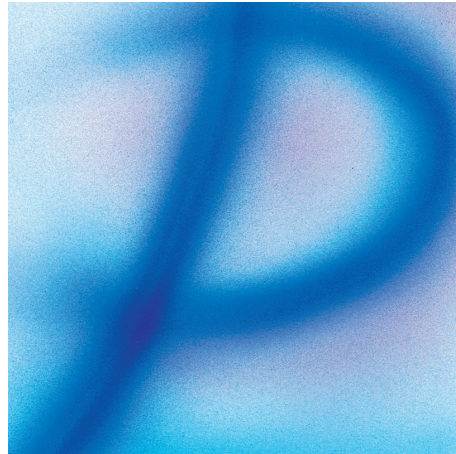


# PHLEBOLOGY

ISSN 1286-0107

## *Special congress issue*

*XVIth World Meeting  
of the Union Internationale  
de Phlébologie (UIP)  
Principality of Monaco  
August 31-September 4, 2009*



Vol 17 • No.1 • 2010 • p1-74

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# LYMPHOLOGY

## AIMS AND SCOPE

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

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

*Phlebology* is scientifically supported by a prestigious editorial board.

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

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

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Indexed in EMBASE, PASCAL,  
Index Copernicus and Scopus.

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# Phlebology

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# Preface

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The 16<sup>th</sup> World Meeting of the *Union Internationale de Phlébologie* which celebrated the 50<sup>th</sup> anniversary of the Union founded in Meyrargues, near Monaco, closed a year of many new activities started in the UIP. One major activity was the inauguration of consensus groups, working towards a worldwide curriculum of phlebology. The reinforcement of the UIP Fellowships with a new supportive sponsor is in line with the aim of the UIP to encourage studies and research on disorders of venous origin. In addition, the UIP started a big epidemiological project in cooperation with Servier, the **Vein Consult Program**, which will enable us to have a snapshot of chronic venous disease in many countries worldwide and to collect a huge database from nearly 80 000 patients. The only objective of these activities is to help towards more effective communication between phlebologists worldwide.

Meetings like the 16<sup>th</sup> World Meeting in Monaco are among the most important ways of transmitting information and knowledge. This is a unique occasion to summarize the latest progress, to update our knowledge, to devise new research and, above all, to meet and exchange with colleagues from all parts of the world. But outside the congress venue, there is the far greater number of would-be delegates, clinicians, and basic scientists for whom venous disease may also be a core interest, but who are unable to attend for a variety of reasons, like clinical commitments, funding, or administrative constraints.

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 aims to facilitate communication between them and, at the same time, to offer 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 thanks to the *Medical Reporters' Academy* for the task they have done in updating venous disease specialists' skills.

Happy reading.

**Eberhard RABE**  
President of the UIP

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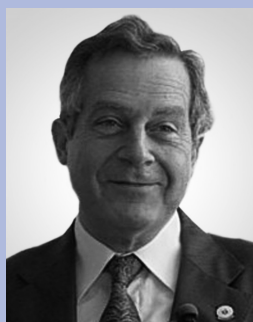
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# I UIP consensus, UIP fellowships



**XVIth World Meeting  
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# 1 - UIP Consensus, UIP Fellowships

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## Introduction to the UIP Consensus Project

By E. Rabe

Scientific and educational progress in phlebology in recent years has led to a higher demand for communication between phlebologists worldwide. At the same time specialization in phlebology by medical associations and the setting up of master degree programs in phlebology are increasing. For these reasons the Executive Committee of the UIP decided to establish a common platform to promote phlebology worldwide.

The first steps in this direction were taken by means of the consensus papers of the UIP on anatomy, definition of terms in the CEAP classification, evidence-based compression treatment and duplex consensus documents. In a further step, a number of consensus groups worked hard over several months to prepare a curriculum in phlebology and to finish various consensus papers in time for the World Congress in Monaco. These consensus papers define the accepted standards in phlebology.

Each group of 5-12 members worked mainly by the Internet with one chairman per group who coordinated the discussion in the consensus group in cooperation with the President and the Executive Committee of the UIP. Each paper has the same structure with definition of the topic, diagnosis, and treatment. The proposals made in the different documents are evidence-based with an evaluation of the literature according to the ACCP grading system.

## UIP Consensus. Venous symptoms and clinical assessment

Chairperson: B. Eklöf

Moderator: P. Carpentier

### **Venous symptoms: evolution of the concept**

P. Carpentier

Symptoms traditionally ascribed to chronic venous disease (CVD) include aching, heaviness, a feeling of swelling, cramps, itching, tingling, and restless legs. Prolonged standing, high temperature, and sexual hormones usually enhance them. Venous symptoms are associated with reduced quality of life. The proportion of patients presenting with venous symptoms increases with increasing CEAP class. Nevertheless, there are no strong correlations of venous symptoms with CEAP classes. New techniques for the objective evaluation of venous symptoms are necessary for international epidemiological studies and assessment of treatment modalities.



## **Pathophysiology of pain in chronic venous disease**

N. Danziger

Current hypotheses on pain mechanisms in venous disease are focused on a local inflammatory origin, related to venous stasis. The starting point for this mechanism is probably local hypoxia associated with capillary stasis. Hypoxia induced by capillary stasis has the effect of activating endothelial cells. Such activation is manifest in the synthesis of proinflammatory mediators (bradykinin, prostaglandins E2 and D2, PAF, and leukotriene B4). Some proinflammatory mediators can activate nociceptors located in the venous wall (between endothelial cells and smooth muscle cells of the media). The pathophysiological mechanisms involved in venous pain are now better understood, but the causal relationship between venous disease and pain remains difficult to explain by experimental methods.

## **Our obligation to monitor clinical outcomes in venous disease**

M. Vasquez, J.J. Guex

The Venous Severity Scoring (VSS) system was derived from the CEAP classification to provide for evaluation purposes. The VSS comprises the venous disability score (VSD), the venous segmental disease score (VSDS), and the venous clinical severity score (VCSS). The VCSS responds to features of venous disease that change with treatment. Each of these scores has been validated, and each has strengths and weaknesses. Maintaining the dynamic nature of assessment with periodic review and revision is the way forward for generating universal applicability. VCSS is in the process of revision in order to incorporate quality-of-life tools. Although the choice of instrument is debatable, our obligation is to improve treatment outcomes by examining our results and sharing them in a meaningful way.

## **CEAP classification: what is the future?**

B. Eklof

The CEAP classification is accepted and actively used around the world by venous experts in America, Asia, Australia, and Europe. It was originally intended that it should be amended progressively in the light of experience with its use. After the first 10 years, the CEAP classification underwent critical review with the aim of revision in 2004 by a new international subcommittee of the American Venous Forum (AVF). In this revision the fundamental structure of the CEAP categories was affirmed and retained. There are several conditions that are not included in the CEAP classification but that can influence the management of patients with chronic venous disease: combined arterial and venous etiology, postthrombotic lymphedema, ankle ankylosis with atrophy of the calf, venous aneurysms, venous neuropathy, corona phlebectatica, pelvic congestion syndrome, and morbid obesity. They can be incorporated into the CEAP classification in the future.

## UIP Consensus in Varicose Veins

Chairpersons: P. Gloviczki , H. Neumann

P. Gloviczki presented the guidelines of the AVF on diagnosis and treatment of varicose veins. Varicose veins have a high prevalence in the general population (more than 20% in the Western population). Varicose vein evaluation, grade C2 of the CEAP classification, can be done correctly by clinical and physical examination complemented by duplex sonography. Duplex scan determines vein patency, valvular competency, presence of incompetent perforators, the varicose map and evaluates the complications and efficacy of therapy. Duplex scanning is recommended as the first diagnostic test for patients with suspected valvular incompetence or obstruction (AVF grade recommendation 1 - grade of evidence A). Venous management of varicose veins can be conservative, with compression garments, correction of lifestyle and risk factors, and phlebotrophic drugs, or invasive with open surgery, minimally invasive endoscopic surgery, or endovenous procedures like sclerotherapy, radiofrequency ablation, and endovenous laser therapy. Great saphenous vein (GSV) high ligation and vein stripping have several disadvantages: invasive procedure, pain, delayed return to work, deep vein thrombosis (DVT) in 5.3% and recurrence rate of 6% – 66%. For treatment of the incompetent GSV high ligation and inversion stripping of the saphenous vein to the level of the knee is recommended (AVF grade recommendation 1 - grade of evidence B). Endovenous ablation of GSV has some advantage compared with open surgery: minimally invasive percutaneous access, no incisions, ambulatory procedure under local/tumescent anesthesia, and rapid return to full activity with a low complications rate (paresthesia 3%, thrombophlebitis 1.87%, skin burns 0.5%, DVT 0.27%, and pulmonary embolism [PE] 0.023%). Radiofrequency ablation results in less pain, earlier return to work, and reduces costs to society when compared with conventional surgery. Endovenous laser therapy and surgery were comparable in abolition of GSV reflux and in disease-specific quality of life, but return to normal activity following endovenous laser therapy was earlier than after surgery. Radiofrequency and EVL are safe and effective and have a better patient acceptance than conventional surgery. Foam sclerotherapy is an effective, safe, and minimally invasive endovenous treatment for varicose veins with a low rate of complications. Polidocanol microfoam was non-inferior to surgery or conventional sclerotherapy. Foam caused less pain and was followed by earlier return to work than surgery. Radiofrequency ablation of the GSV is safe and effective and we recommend it for treatment of saphenous incompetence (AVF grade recommendation 1 - grade of evidence A). Endovenous laser therapy of the GSV is safe and effective and we recommend it for treatment of saphenous incompetence (AVF grade recommendation 1 - grade of evidence A).

Finally, P. Gloviczki stressed that the use of guidelines is essential to practice evidence-based medicine and play a major, but not unique, role in determining the best management of patients with varicose veins, because as William Mayo recalled in 1910 *“The best interest of the patient is the only interest to be considered”*.

## UIP Consensus in Venous Edema and Skin Changes

Chairperson: J. Strejcek

Moderator: I. Staelens

This session was dedicated to the UIP Consensus on venous edema and skin changes. Particular attention was paid by the UIP to reaching a consensus on common definitions for venous disease, and on common tools to evaluate the burden and severity of disease, for both patient care and clinical research.

### Development of a questionnaire to evaluate the burden of venous disease in daily life

J-J. Guex

J-J. Guex presented a new questionnaire aimed at evaluating the burden of venous disease in daily life. The objective was to provide a tool able to explore and measure the overall disability of patients with venous disease, and the burden of the disease in their daily lives. Authors followed the recommended methodology for questionnaire construction. After a literature review and exploratory face-to-face interviews, they defined 5 possible dimensions to explore: pain, daily life, interpersonal relationship, work, psychological aspect. They eventually included 36 questions and three visual analogue scales in the ABC-V questionnaire (ABC-V standing for 'Assessment of Burden in Chronic Venous disease). In the discussion, J-J. Guex stressed the difference between quality of life questionnaires and the ABC-V, the goal of the latter being to take into account all aspects of disability caused by venous disease.

### Recommendations for evaluation of outcomes after treatment of C0s-C4 patients

A. Davies

In the same quest for common and reproducible tools for evaluating venous disease, A. Davies gave recommendations for the evaluation of outcomes after treatment of C0s to C4 chronic venous disease patients. The outcomes range from absence of reflux to improvement of symptoms or clinical signs, and to patients' and/or physicians' satisfaction. It is important to reach a consensus on reporting standards for publication, comparing treatment modalities, and eventually determining the best patient care. A. Davies described several possible ways of assessing venous disease: 1) anatomy, which can be explored by ultrasonography, 2) hemodynamics (plethysmography), 3) clinical evaluation, including CEAP or VCSS scoring systems, and 4) functional evaluation, using either generic (SF-36, SF-12, EQ-5D) or disease-specific (AVVQ, SQOR-V, CIVIQ-2, VEINES) questionnaires. However, there are some issues when using these tools. For example, reflux does not always correlate with symptoms and quality of life, and changes in hemodynamics do not correlate with other parameters. A. Davies also reminded the audience that CEAP is only a classification scale, is not sensitive to improvements following interventions and therefore can not be used as a follow-up tool. Finally, in the context of increasing competition for health care resources, these scales could be used by insurance companies to identify patients eligible for treatment, though the cost-effectiveness of interventions is hard to assess accurately.

The take-home message was that beside ultrasonographic assessment, current recommendations to assess outcomes in venous disease are the use of VCSS score, and of both generic and a disease-specific quality of life questionnaires.

### **UIP consensus in diagnosis and treatment of venous edema**

A. Scuderi

### **UIP consensus in diagnosis and treatment of CVI-related skin changes**

A. Cornu-Thénard

The two subsequent talks by A. Scuderi and A. Cornu-Thénard reported on the work currently conducted by the Union Internationale de Phlébologie on the diagnosis and treatment of C3 (edema) and C4 (skin changes) classes of chronic venous disease. Precise definitions will be provided for edema (C3), eczema and pigmentation (C4a) and lipodermatosclerosis and atrophie blanche (C4b). Recommendations for diagnosis include assessment of the full CEAP score. Three levels of diagnostic investigations have been defined: level 1 comprises office visit, medical history, and clinical examination, and hand-held ultrasound; level 2 includes color duplex ultrasonography, whereas level 3 refers to additional more invasive and/or complex testing, phlebography, varicography, magnetic resonance imaging, intravascular ultrasonography, computed tomography, etc. which are not required in all patients. Reflux and obstruction should be searched for. The best method for measuring edema is water displacement volumetry, though perimetry may be used in routine practice. Treatment options are: 1) Basic recommendations: change in habits, postural drainage; 2) Physical treatments: manual drainage, compression therapy (elastic stockings, bandage, intermittent pneumatic compression); 3) Pharmacological treatments (venoactive drugs, topical treatments). The underlying venous disease should also be treated. These therapeutic strategies are used in C3 and C4 patients, although as stressed by the second speaker, the level of evidence is low in C4 patients, for whom more research is needed.

## **UIP Consensus Curriculum in Phlebology**

Chairperson: S. Raju

Moderator: K. Parsi

### **UIP Consensus Curriculum in Phlebology**

K. Parsi

Recently, the UIP has made a considerable effort to define an inaugural training curriculum in phlebology which should be implemented and incorporated in the future in a training program by member countries. This document was presented in summary by K. Parsi who was the chairman of the Curriculum Committee, together with S. Zimmet. The Committee consisted of several international experts. The document is a guide to be adopted and modified to suit local needs. We need a training curriculum in phlebology to define phlebology, to set minimum training standards across the globe and to help practitioners identify gaps in expertise. It

addresses the needs of future trainees in phlebology and existing practitioners who need to acquire extra skills/expertise. Phlebology was defined as a specialty with surgical, interventional, and medical activity to help patients with acute and chronic venous disorders. Therefore, phlebology covers not just varicose veins, but skin manifestations, venous malformations, superficial thrombophlebitis, DVT, and PE. Phlebology is an evolving specialty and a phlebologist is a medical specialist competent in the diagnosis and management of all aspects of venous disease. Phlebology may have roots in surgery in many countries, but has evolved beyond its traditional origins. There is no “super-phlebologist” competent in everything covered in this curriculum. The standards have been set mainly for the future. The UIP Training Curriculum has 8 sections with many subsections including: anatomy (core venous anatomy and broader topics), basic sciences (physics, rheology, venous physiology, genetics, embryology, vascular histology, vascular biology, coagulation system, inflammation, detergent biochemistry, lymphatic biology), pharmacology (general principles, vascular pharmacology), clinical sciences (core clinical phlebology, pediatric phlebology, other venous conditions, vascular malformations, phlebology in other disciplines, lymphology), diagnostic evaluation (basic modalities, duplex ultrasound, venography, venous function tests, other imaging and laboratory investigations), treatment modalities (patient education and referrals, conservative interventions, nonsurgical treatment of CVI, surgical treatment of CVI, treatment of venous thromboembolism [VTE], other treatments), additional education (laser and safety, life support, research design, venous outcome assessment, infection control, legal issues), and reference reading (textbooks and journals). This training handbook was developed on a model based on the Australian College of Phlebology Training Handbook 2009 and with inspiration from the following documents: Australian College of Dermatologists Training Handbook 2009, American College of Phlebology, Phlebology Fellowship Curriculum, Phlebology education in France, proposed Phlebology Training Curriculum University of California, San Diego and the Vein Institute of La Jolla, 2008.

## **UIP consensus on diagnosis and treatment of deep venous insufficiency**

F. Lurie

A Consensus Group on Deep Venous Disease was created on behalf of the XVI World Congress of UIP. The summary document was presented by the chairman of this Group, F. Lurie. Deep venous disease includes primary and/or secondary pathological changes in the deep venous system. These may consist of valve insufficiency, complete or incomplete vein obliteration and/or functional impairment. Regarding pathophysiology, it was emphasized that the deep veins constitute the outflow track of the lower extremities. In healthy individuals the blood flow is unidirectional from the superficial into the deep veins. This is possible due to pressure gradient directed towards central veins, low resistance of deep veins and the muscle pump in the presence of competent valves. Recent studies have revealed substantial deficiencies in current understanding of venous physiology regarding pressure changes in veins during muscle activities, regarding relationships between the flow in major veins and their tributaries and additional functional roles of venous valves. Disruption of the venous blood flow plays the key role in

the natural history of venous disease, which includes one or more of the following: incompetence of venous valves, acute or chronic occlusion of the vein, and increased resistance to blood flow as a result of stenosis, synechia, or increased rigidity of the venous wall. A cascade of biological reactions results from interaction of disturbed flow and endothelium. Changes in collagen in patients with chronic venous disease appear to be systemic and not limited to the venous wall. Management of chronic deep vein disease requires accurate objective diagnosis of the venous tree from the lower calf to the diaphragm. Segment by segment diagnosis of reflux and obstruction is the standard and is achieved by means of duplex scanning. Venography is required for definitive diagnosis in the iliac and inferior vena cava vessels. Physiologic studies with pressure and volume methods are useful to evaluate global function and differentiate dominant obstruction from reflux. These studies are all complementary. New diagnostic modalities (B-flow ultrasound, intravenous ultrasound, MRI) provide information that is potentially useful for identification and evaluation of venous abnormalities. The CEAP classification is necessary for the definitive workup. Partial correction of venous defects may have enormous influence on the clinical state, allowing the extremity to achieve a clinically compensated state consistent with improved or normal function for the future. In advanced disease, unfortunately, the veins can seldom be restored to a totally normal state. Concomitant axial reflux in the superficial veins is poorly tolerated by the skin and must be corrected surgically. Axial deep vein reflux need not be corrected as the initial step when deep and superficial refluxes co-exist. In the short term, deep axial reflux appears to be better tolerated than superficial axial reflux. There is limited data indicating that correction of deep reflux can improve clinical outcomes and if not corrected can contribute to recurrence of varicose veins. Failure of the extremity to thrive following correction of superficial reflux is an indication for deep vein reconstruction. Correction of deep venous reflux in primary disease can be accomplished by internal and external repair. Correction of postthrombotic reflux can be achieved by direct repair when the valves have not been destroyed. When the valves have been deformed, transposition or transplantation of a competent valve may be successful. The long-term durability of these repairs is less than internal valve repairs in primary disease. Recent reports of open surgical creation of an autogenous valve (creation of a flap by dissecting the vein wall) provide the alternative of long-term success in the postthrombotic extremity with reflux. While not impeding the normal flow of blood, this method is able to withstand the reflux. Early restoration of iliac vein patency at the time of acute iliofemoral DVT has shown improved long-term results and is becoming the norm for treatment in the acute phase. Iliac vein obstruction is often present in silent form in the general population. Such lesions are present in >90% of symptomatic primary and postthrombotic CVI patients when examined with intravenous ultrasound. Iliac vein obstructive disease has been treated effectively with balloon angioplasty and stenting, which has replaced most of the attempts to bypass iliac obstructions, with good medium-term results, minimal morbidity, less than 5% restenosis, and significant improvement of pain, swelling, and quality of life. The indications for deep vein reconstruction are limited at this time to cases in which simpler forms of venous repair have failed to control the problem and the patient is healthy enough to benefit from the correction. The risk of vein surgery has proven to be surprisingly low. Mortality has been rare throughout the 40-50 year history of reporting from around the

world. The morbidity of operating inside the veins includes several considerations. Thromboembolic complications are rare in primary disease, and more frequent in postthrombotic disease. Several questions remain unanswered: relationship between changes in deep, superficial and perforator veins in the natural history of chronic venous disease, the impact of the presence, severity, and extent of reflux and obstruction on venous function and their interaction when present in the same extremity.

### **DAPS-dalteparin in patients with superficial leg vein phlebitis in addition to compression treatment - a placebo-controlled phase III study**

E. Rabe

E. Rabe talked about the results of a randomized, double-blind, multicenter, phase III trial which assessed the efficacy and safety of dalteparin in patients with superficial leg vein phlebitis (SVP). A total of 276 patients with SVP used compression stockings (30 mm Hg) for 3 months and either dalteparin 10 000 IU (group A) or placebo (group B) for 14 days. The primary end point was progression of the thrombotic process during the treatment period as confirmed by compression ultrasound. Sonographic assessment was planned in all patients on days 1, 7, 14, and 90. Secondary end points were pain assessment by visual analogue scale (VAS) and calculation of symptom scores (tension, heaviness, swelling). In each treatment group, 138 patients received at least one dose of study medication. Progression of the thrombotic process after 14 days was detected in 8% (95% CI: 4%-13.8%) of patients in group A and in 17.4% (95% CI: 11.5%-24.8%) of patients in group B. DVT rates were 0.7% in each group. No symptomatic PE occurred during the treatment period. Progression rates during posttreatment follow-up were 3.1% (A) versus 7% (B) ( $p=0.168$ ). One patient in group A (0.7%) and two patients in group B (1.5%) developed symptomatic DVT during follow-up. Another patient in group A experienced PE (0.7%). Symptom scores decreased in both groups without significant differences. During the first 14 days adverse events were reported in 7.2% (2.2% serious) of patients treated with dalteparin versus 13% (6.5% serious) of patients treated with placebo. The author concluded that combined dalteparin/compression therapy in patients with SVP is safe and results in a decreased progression rate of the thrombotic processes. No rebound phenomenon was observed after cessation of dalteparin. Comparing this study with others (STENOX study in 2003 with enxaparin, and Prandoni's study with nadroparin in 2005), the speaker remarked that in these studies there was no strict compression applied and no differentiation between varicophlebitis and SVP of other origin. That's why the comparison of data is difficult.

### **Updated terminology of chronic venous disorders: the VEIN-Term transatlantic interdisciplinary consensus document.**

Michel Perrin for the transatlantic interdisciplinary group

A transatlantic interdisciplinary faculty of experts under the auspices of the *Union Internationale de Phlébologie*, together with the European Venous Forum, the American Venous Forum, the American College of Phlebology, the International

Union of Angiology, and the Society for Vascular Surgery met in order to provide recommendations for fundamental venous terminology. The above organizations have endorsed these recommendations, which were recently published in the VEIN-Term consensus document.

The raison d'être of such recommendations came from the many terms that still pose problems of interpretation, highlighting the need for a common scientific language in the investigation and management of chronic venous disorders. Venous terms related to the management of chronic venous disorders of the lower extremities that are widely used and recognized to vary in applicability and interpretation in reports in the venous literature were summarized.

Terms previously defined in CEAP documents<sup>1-3</sup> and prior venous nomenclature refinements,<sup>4-5</sup> and those pertaining to a congenital etiology, were excluded. The terms selected for inclusion in the VEIN-Term consensus document are divided into three different groups: clinical, physiological, and descriptive.

Regarding clinical terms, a definition of *chronic venous disease* is, "morphological and functional abnormalities of the venous system of long duration manifested either by symptoms and/or signs indicating the need for investigation and/or care", *Chronic venous insufficiency (C3-C6)*, "a term reserved for advanced chronic venous disorders, which is applied to functional abnormalities of the venous system producing edema, skin changes, or venous ulcers", or *venous symptoms*, "complaints related to venous disease, which may include tingling, aching, burning, pain, muscle cramps, swelling, sensations of throbbing or heaviness, itching skin, restless legs, leg tiredness and/or fatigue. Although not pathognomonic, these may be suggestive of chronic venous disease, particularly if they are exacerbated by heat or dependency in the day's course, and relieved with leg rest and/or elevation". Besides these frequently used terms, thirty others were defined.

The whole set of terms is published in *J Vasc Surg*, (Eklof B, Perrin M, Delis KT, Rutherford RB, Gloviczki P et al. Updated terminology of chronic venous disorders: the VEIN-TERM transatlantic interdisciplinary consensus document. *J Vasc Surg*. 2009;49:498-501.)

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## UIP News, Awards

Chairpersons: E. Rabe, J-J. Guex

### BAUERFEIND Fellowships

#### **How to utilize compression therapy after ultrasound-guided sclerotherapy (USGS) with foam for the treatment of varicose veins – a randomized controlled trial**

R. Ceulen (Austria), winner 2007-2009

##### Main conclusions:

- Obliteration is achieved in >80% of all patients
- Compression does not influence the outcome of USGS
- Compression prevents the development of side effects, but:
  - When compression is completed, phlebitis will arise
  - It does not reduce the incidence of hyperpigmentation
- Patients suffer from less pain when phlebitis occurs and compression is applied
- This suggests that for the patient's comfort compression therapy should be recommended at least to reduce pain after phlebitis

#### **Compression therapy for superficial vein thrombophlebitis**

K. Bohler, S. Stolkovich, H. Kittler (Austria), winners 2009-2011

##### Main outcome variables:

- Reduction of spontaneous pain measured using a VAS
- Reduction of induced pain (modified Lowenberg test)

##### Additional outcome variables:

- Reduction of erythema in square cm
- Duplex sonographic change of thrombus length
- Duplex sonographic confirmation of new DVT
- Influence of treatment on quality of life SF-36
- Number of analgesics needed (pill counting)

### KREUSSLER Fellowship

#### **Catheter-directed foam sclerotherapy of varicose veins under tumescent anesthesia**

N. Tetsch, B. Kahle (Germany)

##### Objective:

to investigate whether intrafascial tumescent anesthesia (TA) around the insufficient vein treated by duplex-guided catheter-directed foam sclerotherapy (DGCDS) improves therapeutic outcome.

## SERVIER Fellowships

### **Erythrocyte diapedesis during chronic venous insufficiency**

C. Rosi (Italy), UIP/SERVIER winner 2007/09

#### Considerations:

Erythrodiapedesis is currently considered the cause of the abnormal iron deposition occurring in legs with CVI. Historically, Myers (1965) was the first to affirm that stasis pigmentation around venous ulcers is due to deposition of hemosiderin (Fe<sup>+++</sup>) resulting from disintegrated red blood cells.

#### Methods:

The author evaluated the occurrence of erythrocyte diapedesis in 110 skin biopsies from legs with CVI at different clinical stages of the CEAP classification.

#### Results:

Erythrodiapedesis was NEVER found in samples of apparently normal skin, even in cases of long-lasting and severe CVI.

Erythrodiapedesis was found in biopsies from: skin overlying varicophlebitis, skin with acute dermatitis, skin around the ulcer and in the ulcer base.

#### Preliminary conclusions:

1. In most cases skin iron overload is not due to erythrodiapedesis (cellular mechanism)
2. Skin iron overload is likely to occur by means of a molecular mechanism

### **The role of soluble uPAR fragments in venous ulcer healing**

A. Ahmad (UK), UIP/SERVIER winner 2009/11

#### Hypothesis:

The cleavage of uPAR into its fragments (D1 and D2-3) is an important mechanism in ulcer healing. Preliminary studies have shown a positive effect of suPAR in keratinocyte migration towards the ulcer wound that might help in venous ulcer re-epithelisation

#### Aims:

1. To compare levels of suPAR fragments in healed venous ulcers with these of poorly healed ones.
2. To examine pattern of distribution of uPA, uPAR, PAI-1 & PAI-2 in healing and poorly healing ulcers.
3. To determine the effect of suPAR D1 & D2-D3 fragments and wound exudates on *in vitro* keratinocyte migration.

# II Epidemiology



**XVIth World Meeting  
of the Union Internationale  
de Phlébologie (UIP)  
Principality of Monaco  
August 31-September 4, 2009**



## 2 - Epidemiology

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### Varicose Veins

Chairperson: M. Perrin

Moderator: J. Barrett

#### Epidemiology of varicose veins

E. Rabe

E. Rabe commented on the epidemiological results of Bonn Vein Study part I and remarked on the absence of epidemiological studies with long follow-up. This was one of the reasons for designing the second part of this study. The Bonn Vein Study part II includes the same population and procedures as in the previous phase, with a follow-up of 6.6 years. The objectives of this study were to analyze the incidence of venous disorders in the general population, progression of chronic venous disease and risk factors related to CEAP classification.

Chronic venous disease, like varicose veins and venous insufficiency, is one of the most frequent diseases in the Western population due to demographic changes, increase in body weight, and increase in sedentary life. Age and a family history of venous disease increase the incidence of new varicose veins. The main risk factors for CVI are age and obesity. The prevalence of this pathology may increase in the future.

#### Servier Vein Consult Project

Chairpersons: E. Rabe, J-J. Guex

With the participation of V. Bogachev, J-J. Guex, D. Milic, A. Puskas, E. Rabe

The VEIN CONSULT Program is being carried out under the auspices of the International Union of Phlebology (UIP), supported by an unrestricted grant from the Servier Research Group.

The program is an international educational survey to highlight the need for early detection and management of this chronic disease specifically amongst primary care doctors. Chronic venous disease is an extremely common condition that has a significant impact on both the individuals affected and health care systems. It is estimated that 30-35% of the general population are categorized as C<sub>0s</sub> and C<sub>1</sub> of the CEAP classification system. This includes people with venous symptoms but no visible or palpable signs of venous disease (C<sub>0s</sub>) and those with telangiectasias or reticular veins (C<sub>1</sub>). Despite being an expensive disease to manage which results in poor quality of life for its sufferers, few people recognize that early diagnosis and early patient monitoring can prevent complications of chronic venous disease.

The VEIN CONSULT Program's main objectives are the following:

- To assess the prevalence of chronic venous disease and provide a picture of the typical adult patient and the management of their disease, in different geographical areas
- To evaluate how GPs and venous specialists manage patients with chronic venous disease and to understand better at which stage of the disease specialists take over from GPs in the management process
- To improve GPs' and venous specialists' education about the need for early detection and management of chronic venous disease, with the goal of improving management of this chronic disease
- To assess the impact of chronic venous disease on the quality of life of patients, health care resources, and the economy

What is the VEIN CONSULT Program? The program is an observational, multicenter, descriptive survey of chronic venous disease. In Step 1, doctors in the primary care setting will complete a case report form assessing their patient's history, listing any chronic venous disease risk factors, screening for chronic venous disease symptoms, and performing a routine leg examination. If the patient shows signs of having any chronic venous disease symptoms and the GP considers him or her to be eligible to participate in Step 2 of the program, the patient will be asked to complete a CIVIQ questionnaire. The GP will then recommend a follow-up consultation with a venous specialist. Step 2 is the follow-up consultation with a venous specialist, who will complete a questionnaire to assess whether treatment is required.

Many countries will take part in the VEIN CONSULT research. The Program will run in participating countries in Europe and Latin America during 2009. A second batch of countries will then join the program in 2010. Many patients and doctors will be involved, as 3000 selected GPs will participate in Step 1 of the Program, screening approximately 70 000 patients. Around 400 selected specialists will follow up with Step 2, potentially seeing 7000 patients.

The VEIN CONSULT Program is unique in that it uses the same questionnaire worldwide and the same classification ( the "universal" CEAP classification) for description of patients. It will give a snapshot of the management of patients with chronic venous disease and reflects the reality in each country that performs the program. Finally , the VEIN CONSULT Program will be useful in:

- Establishing the prevalence of chronic venous disease
- Comparing the VCP epidemiological data with these of previous surveys
- Performing comparative analyses between countries and with previous surveys in the same country
- Evaluating resource requirements thanks to the assessment of the impact of chronic venous disease on patients' quality of life and costs
- Building a simplified screening questionnaire for earlier detection and management of chronic venous disease
- Preventing progression of chronic venous disease by intervention on environmental / behavioral factors



# Pathophysiology



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# 3 - Pathophysiology

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## Guest lecture

Chairperson: M. Malouf

### Why do varicose veins develop?

N. Labropoulos

N. Labropoulos gave an overview of current knowledge and theories on the pathophysiology of varicose veins. He reminded the audience of the high prevalence of this disease, particularly in developed countries, and its specificity to humans, which renders investigations on animal models impossible. The talk focused on primary venous disease, hence excluding postthrombotic syndrome, in which obstruction and valve destruction occurs. Venous hypertension plays a major role in the progression of the disease. It provokes vein dilatation and inflammation. Vein dilatation leads to distortion, leakage, and altered shear stress, which is responsible for inflammation. The inflammation may cause vein valve and wall changes responsible for the reflux, which further increases the venous hypertension. Several theories have been developed to explain initiation of the disease: 1) Primary valve failure leading to its incompetence, with retrograde progression through the venous system; 2) Existence of multiple arteriovenous fistulae; 3) Turbulences above the valve leading to secretion of noradrenaline, hypoxia, secretion of free radicals, and inflammation.

Current theory focuses on weakening and dysfunction of the venous wall due to changes in collagen and elastin structures. A deficiency in type 3 collagen is observed that could be due to its destruction by overexpressed matrix metalloproteases. Contrary to what was previously thought, reflux does not always extend in a retrograde fashion from a primarily damaged vein. In a longitudinal study of 31 patients with GSV reflux, follow-up examination revealed either local extension of the reflux in 17 patients (7 retrograde, 7 anterograde, and 3 two-directional extensions) or appearance of reflux in a new vein segment in 14.

The role of genetics remains unclear, even if a family predisposition is often reported. Whether venous disease is a local or systemic disease is also debated. Vein wall pathology may have not only local effects. On the other hand, normal venous segments adjacent to varicose veins share the same biochemical properties, suggesting that wall changes could precede biological abnormalities. The increased hydrostatic pressure could provoke increased vein wall tension and endothelial cell injuries, leading to inflammation and modification of matrix metalloprotease expression. This could eventually lead to vein dilatation and valve dysfunction through an altered collagen structure.

Much work still needs to be done to better understand the pathophysiology of venous disease. Data from epidemiological studies need to be combined with clinical studies, genetics, cellular and wall matrix investigations, and studies of flow dynamics and wall mechanics.

When asked by the audience if these new concepts should have an impact on patients' clinical management, N. Labropoulos came back to the debate on whether

or not patients with chronic venous disease should be treated as early as possible to stop or at least delay the progression of the disease. It also appears that some venoactive drugs may have a favorable modulating action on metalloproteases.

## Satellite workshop

Tissular repair in phlebology

P. Sansilvestri-Morel presented her investigations on venous disease. She focused on vein wall distensibility, elasticity, and contractility. In patients with varicose veins, disorganization of the vessel media extracellular matrix is observed. Collagen plays a major role in the structure of vein wall. She compared collagen characteristics in cellular cultures obtained from varicose veins (vein stripping specimens) and from control veins (healthy veins removed for arterial bypass). The main result was a significant quantitative increase of collagen 1 in smooth muscle cells, and a decrease in collagen 3. An overexpression of collagen 1 was observed by RNA analysis, but no difference was seen in the expression of collagen 3 gene. Overexpression of collagen 1 could be due to collagen 3 deficiency. In fact, adding collagen 3 to the cell culture provoked a decrease in collagen 1 expression. Since expression of collagen 3 is normal, the hypothesis of an enhanced destruction of collagen 3 was raised, supported by the fact that adding matrix metalloproteases (responsible for collagen destruction) increased the levels of collagen 3. Similar results were obtained when comparing skin biopsies of patients with venous ulcer with biopsies obtained in healthy subjects.

Discussion with the audience raised the question of a possible systemic disease since the same pattern is seen in the skin and in the vein wall. Note that skin biopsy specimens were taken from the groin, which could partly account for the results. It would be interesting to compare data from skin biopsies taken from other parts of the body, the perivenous derma, and from arteries close to the diseased veins.

J-C. Kerihuel reported on his research on healing, which comprises four phases: coagulation, inflammation, proliferation, and remodeling. The healing process is altered in patients with chronic wounds. As compared with acute wounds, fewer mitoses are seen in the derma, fibroblasts tend to be in apoptosis, metalloproteinases are increased, the inflammation process is not controlled, and the extracellular matrix is damaged. Metalloproteinases play a role in the different phases of the healing process. They have proteolytic and angiogenic properties, interact with immunoglobins, cytokines and chemokines. They could become a major target for intervention in patients with vein ulcers. The micronized flavonoid fraction might exhibit a regulatory action on metalloproteinases, which could at least partly account for its efficacy in the treatment of venous ulcers.

## Venous pathophysiology

Chairperson: V. Blazek

Moderator: F. Boccardo

### **Unmyelinated C fibers and inflammatory cells are present in the wall of human varicose veins. A clinicopathological study**

A. Vital

The work by A. Vital is based on current hypotheses that pain in chronic venous disease has a local inflammatory origin. Over the last five years, indicators suggesting an inflammatory reaction in varicose veins have accumulated dramatically. However, little is known about the nociceptors, likely to be C fibers, their innervation and their relationship with inflammatory cells in human blood vessels, and particularly in veins. C fibers have yet to be found in human varicose vein samples.

In addition, the precise mechanisms governing the interaction between the mediators of inflammation and venous nociceptors, which may account for the variability of pain in venous disease, remain to be clarified.

The aim of the study presented was to localize C fibers and define their relationship with inflammatory cells in varicose vein wall. The material examined consisted of segments of the great saphenous vein harvested during saphenectomy from patients with documented chronic venous disease and venous pain scored  $\geq 4$  on a visual analogue scale.

Five segments per patient were immunostained with anti-S100 protein and anti-CD45 to identify nerve fibers and inflammatory cells, respectively. Light microscopy was completed by electron microscopy.

Immunostaining indicated that most sections had a low density of nerve fibers. CD45-staining showed a low density of inflammatory cells. At microscopy, most nerve fibers appeared scattered in the media and some were identified in the vicinity of the vasa vasorum, close to the adventitia, while mast cells were mainly located in the media, often close to the adventitia, but not in close contact with C fibers. Inflammatory cells were mainly macrophages, rather than neutrophils and lymphocytes, which were not observed.

The presence of unmyelinated C fibers in the wall of varicose veins suggests the existence of a neurological component able to diffuse pain signals from the vein into the spinal chord and finally to the brain. Inflammatory cells and particularly mast cells that could be responsible for activation of those C fibers were also found in the pathological vein wall.

C fibers and mast cells may form a functional unit that could contribute significantly to mechanisms of venous pain arising at earlier and/or later stages of chronic venous disease.

### **Proteomic comparison of varicose veins in humans and in those that develop in a new porcine model**

A. Van Rij

A. Van Rij and his team have developed and characterized a pig-based model of superficial varicose veins by means of femoral arteriovenous fistulae fashioned in the right thigh. Animals were examined at postoperative times up to 15 weeks to determine the development of varicose veins and the associated protein

expression. Protein expression associated with varicose vein disease was examined both in humans and the porcine model.

Gel electrophoresis and mass spectrometry were used to identify proteins expressed in the varicose porcine model and in control animals. The same process was used to compare human primary varicose and control superficial thigh vein samples. In humans and the pig model, cytoskeletal and contractility-related proteins were upregulated (actin, tropomyosin, desmin, and vimentin), as well as some heat shock proteins (in particular HSBP1). These profiles suggest a similar process of mild inflammation and tissue remodeling in both human and porcine varicose veins. Superficial varicose vein formation in this porcine model, which mimics human venous disease, may represent a considerable advance in the development and assessment of phlebotropic pharmacological agents.

### **Venous ulcer: the final stage in chronic venous disease - Managing it in 2009 (Pierre Fabre Symposium)**

Chairperson: P. Carpentier

In this symposium, the speakers summarized the latest information regarding to pathophysiology, clinical evaluation, and therapeutic management of chronic venous disease and venous ulcers.

As an introduction P. Carpentier emphasized that painful and disabling venous ulcers, which occur at high incidence and generate huge costs, remains a major public health issue. Understanding the pathogenetic mystery of end-stage chronic venous disease is crucial since its management is based mainly on this knowledge. A. Nicolaides gave us a useful summary of what we know about pathophysiology and about the levels of clinical evaluation in CVI. Changes in the superficial and/or deep veins are the starting events at the level of macrovasculature. Primary varicose veins occur in the absence of previous DVT; secondary ones are the consequence of DVT or superficial thrombophlebitis. Recanalization may give rise to relative obstruction and incompetence of deep, superficial, and perforating veins. Relative obstruction means that the affected vein becomes rigid, losing the ability to dilate in the case of effort. In 30% of patients with deep venous reflux, the etiology is primary valvular incompetence. Spontaneous lysis occurs in 50-70% following DVT and early thrombus resolution is associated with a higher incidence of valve competence. Postthrombotic syndrome (PTS) is the result of venous hypertension arising from deep valve incompetence and/or outflow obstruction after a previous episode of DVT. Venous hypertension leads to skin capillary damage, lipodermatosclerosis, and ultimately ulceration. The prevalence of PTS is variable and depends on the extent and location of thrombosis and on the results of treatment. The risk of PTS is lower in patients who have adequate and early anticoagulation therapy, and early mobilization with continuous compression. Patients with both chronic obstruction and reflux have the highest incidence of skin changes or ulceration. The risk of PTS is higher in patients with recurrent thrombosis and in the presence of thrombophilia. Incompetent perforating veins (IPVs) usually occur in the presence of superficial and/or deep venous reflux. The number and diameter of IPVs, and the volume and velocity through them increase linearly with clinical severity of CVI. Superficial and perforating vein incompetence with normal deep veins is found in 40% of patients with skin changes and ulceration. In the pathogenesis of primary varicose veins the leukocyte-

endothelium interaction plays a key role inducing chronic inflammatory process and remodeling in the venous wall and venous valves, generating reflux and venous hypertension. Leukocytes also play an important role in edema formation. The speaker emphasized that there is no single test that can provide all information needed to make clinical decisions and plan a management strategy. Understanding the pathophysiology is the key to selecting the appropriate investigations. For reflux and obstruction several questions need to be answered: are they present or absent, where are they (anatomic extent) and how, many are there (quantitation)? For the demonstration of reflux, the CW hand-held Doppler is frequently sufficient. However, to determine the anatomic extent we need duplex ultrasound or descending venography. Air plethysmography is best for quantitative measurements of reflux. There are three levels of investigations regarding the CEAP class of the disease. In class C0/I, level I investigations (history, clinical examination, which may include hand-held Doppler or duplex) are sufficient. In class 2, level II (duplex scanning with or without plethysmography) should be used in the majority of patients and is mandatory in those being considered for intervention. In class 3 or more, level II investigations are utilized to determine whether or not reflux or obstruction in the deep veins is responsible for edema or skin changes. If obstruction is demonstrated or suspected as a result of a noninvasive test, level III studies (invasive investigations or complex imaging studies) to investigate the deep venous system should be considered.

Later on P. Blanchemaison briefly presented the therapeutic options in the management of venous ulceration. Compression (four-layer bandage, short stretch bandages), dressings (wet dressings and hydrocolloids), physiotherapy (structured exercise improving calf muscle pump function, aquatic physiotherapy), venotonic (Daflon 500 mg, Cyclo 3) and other drugs (pentoxifylline, stanozol), sclerotherapy, surgery (stripping, laser, radiofrequency, deep venous surgery, skin grafts) vacuum-assisted closure therapy, hemodilution, autohemotherapy, hyperbaric oxygen, larval therapy (application of maggots –*Lucilla sericata* – to a necrotic lesion) all have a more or less evidence-based role in the management of venous ulcer. The main risk factors for chronic ulceration in patients with varicose veins are: heredity, age, obesity, diabetes, history of DVT, fixed ankle joint and impairment of the calf muscle pump. Regarding the role of superficial venous surgery and compression therapy in the management of venous ulcers, a systematic review by Howard et al (*Eur J Vasc Endovasc Surg*, 2008) and the ESCHAR randomized controlled trial conducted by Gohel (*BMJ* 2007) concluded that the surgical correction of superficial venous reflux in addition to compression therapy does not improve ulcer healing, but reduces the recurrence of ulcers at 4 years. Deep venous surgery (venoplasty, stenting, by-pass procedures, valvuloplasty, vein transposition, vein transplantation, neovalve formation, external cuff) might be effective and can be clinically beneficial, but there is a lack of evidence. The speaker concluded that conservative treatment should precede surgery. Compression therapy should consist of 4-layer bandages, class 3 stockings, or an Unna boot. The nutritional status of the patient, elevation of the leg and mobilization are also important factors. Venotonic drugs are always indicated and microcirculatory and hemodynamic follow-up is recommended

# IV

## Investigations



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# 4 - Investigations

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## Acute venous disease

### Guest lecture

Chairperson: M. de Maeseneer

### Asymptomatic deep vein thrombosis

W. Blättler

The term "asymptomatic" could in fact have several meanings – the symptoms (pain or edema) can be truly absent, unrecognized, misinterpreted or masked by another problem. The intensity and character of signs and symptoms depend on how fast the thrombotic process develops and on the location and extent of DVT. The sensitivity of DVT signs and symptoms is much lower in bed-ridden patients than in outpatients. During clinical probability assessment, not only signs and symptoms but also risk factors of DVT should be taken into consideration.

Even ilioacaval thrombi might be asymptomatic. Case reports have documented acute massive PE as well as severe PTS as a consequence of preceding undiagnosed DVT. However, larger studies have not demonstrated a high risk of poor outcome in patients with undiagnosed DVT. For example, if the exclusion of the diagnosis of DVT was based on clinical probability assessment solely, some cases of asymptomatic DVT were missed, but the prognosis of the patients was not poor. The problem is whether to screen some at-risk patient groups for asymptomatic DVT and which method should be used. In one study, complete duplex ultrasound had a poor sensitivity for asymptomatic DVT (compared with bilateral venography). Several studies have assessed the prevalence of asymptomatic DVT in various patient groups, eg, in surgical patients. The results have proven the occurrence of DVT despite prophylaxis (the prevalence of 10% and 8% after major abdominal and major orthopedic surgery, respectively), in the great majority of cases DVT was asymptomatic, mostly untreated, but the prognosis was good. Another study has searched for asymptomatic DVT in cancer patients and found the prevalence of 10%.

As to possible long-term sequelae, the published literature has not been conclusive so far. The epidemiological data on PTS prevalence are quite consistent with the known incidence of (diagnosed) DVT, thereby suggesting that PTS as a consequence of a possible prior undiagnosed DVT is probably not too frequent. However, a meta-analysis has found the prevalence of PTS after asymptomatic DVT to be 17%.

In a trial assessing the prophylaxis of VTE after the surgery of a ruptured Achilles tendon, 34% of cases of DVT occurred despite prophylaxis – mostly asymptomatic and most peroneal. The patients were given standard therapy (anticoagulation, compression) and in follow-up no significant clinical consequences were found (though sonographic changes – reflux and/or obstruction – were present).

In conclusion, DVT can occur without any symptoms and asymptomatic DVT may disappear without sequelae, but may cause serious complications as well. If the suspicion of asymptomatic DVT is high (based on clinical probability assessment), further tests should be used (D-dimer, ultrasonography, and even CT



if necessary). In cancer patients, routine screening for asymptomatic DVT is discouraged (long-term DVT prophylaxis is recommended). Once asymptomatic DVT has been diagnosed, it should be treated.

## Chronic venous disease

### Duplex of the deep veins - tips and tricks

N. Labropoulos

It is important to define the distribution and extent of reflux and obstruction for the treatment of chronic venous disease. The author summarized various aspects of detection with duplex ultrasound in chronic venous disease. The author reported that reflux was primary in 65% of patients, secondary in 27%, primary and secondary in 8%, and congenital in <1%. The prevalence of skin damage increased with the extent of reflux and obstruction. Reflux plus obstruction increased 3.5-fold the risk of signs and symptoms. The author highlighted that anatomic variations are very frequent. In a survey of 1000 limbs examined by duplex he observed 834/1000 (83.4%) had anatomic variations. The femoral vein was double in 261 limbs, triple in 12, hypoplastic in 2, and absent in 1, with reflux in one vein in 4% and thrombosis in 5%. Persistent sciatic vein was present in 3 limbs. The popliteal vein was double in 374 limbs and triple in 26, with reflux in one popliteal vein in 7% and thrombosis in 6.1%. The posterior tibial vein was triple in 82 limbs, single in 16, and absent in 3. The peroneal vein was triple in 11 limbs and single in 11. In another study (327 patients with DVT 122 chronic venous disease), a significant asymmetry rate of 84.4% was present.

The author showed the criteria for defining significant central vein stenosis with duplex: peak vein velocity  $V_2/V_1$  across the stenosis, poststenotic mosaic color, abnormal Doppler signal at the area of stenosis, contralateral asymmetry, vein dilation prior to the stenosis. He indicated the reflux cut-off values: superficial veins > 500 ms, perforator veins > 350 ms, calf veins + deep femoral > 500 ms, femoropopliteal veins > 1000 ms. Finally, he discussed the ultrasound findings in acute thrombosis: noncompressible vein dilation, filling defect on color Doppler, absence of signal, smooth borders, homogenous texture, echolucent. Chronic: decreased diameter, wall thickening, rough borders, heterogenous texture, echogenic, intraluminal webs, reflux. During question time the author suggested several sites to better visualize the calf veins.

### Guest lecture

Chaiperson: G. Jantet

### Chronic Venous Insufficiency - Think Obstruction!

P. Neglen

P. Neglen of River Oaks Hospital, Flowood, Mississippi, started his presentation by defining the problems experienced by patients with CVI: leg pain, swelling, discoloration, dermatitis, lipodermatosclerosis, and venous ulceration. Although CVI is recognized to have several contributing pathophysiological factors (failure

of calf muscle pump, stiff joints, vein wall stiffness, vein lumen geometry, calf venous volume, etc.), the main emphasis has so far been on valve reflux. CVI has almost become synonymous with venous reflux.

intravascular ultrasound-guided endovenous stenting of iliac venous obstructions or stenosis has resulted in major clinical improvement, even in the presence of remaining reflux, suggesting that chronic proximal obstructions are an important pathophysiological factor in the clinical expression of CVI. Generally speaking one should initially investigate the patient (duplex scanning, venography, magnetic resonance venography, CT-V or intravenous ultrasound) in order to define the classification of venous dysfunction (advanced CEAP) and afterwards combine conservative treatment with invasive procedures if necessary. P. Neglen emphasized that duplex ultrasound is only a qualitative method: duration of detected reflux does not correlate with clinical severity, peak reflux velocity is better but its high variance prevents clinical use and it is not possible to assess the contribution by individual segment reflux to global hemodynamics. Therefore, duplex findings alone are not enough for targeting and correction of a multi-level and multi-system disease. There is no method of quantifying reflux at a single valve site and in the superficial, perforator or deep system separately. Nor is it known how to quantify hemodynamically venous outflow obstruction (to what degree a venous obstruction is hemodynamically significant, for instance). There is no reliable noninvasive test and here invasive pressure measurements are insensitive. Duplex ultrasound is a test for segmental reflux and obstruction. It is the initial choice for determining morphologic criteria for obstruction and is able to define the severity of reflux and obstruction. Existing routine tests (eg, outflow air or strain-gauge plethysmography, duplex ultrasound and femoral or other pressure tests) can not be used to exclude significant venous outflow obstruction. When venous outflow obstruction is suspected, ultrasound scanning of the lower extremity has to be complemented by transfemoral venography, magnetic resonance venography, CT-venography or intravenous ultrasound in selected cases. Intravenous ultrasound is superior to all other imaging techniques for diagnosis of the degree and extent of obstruction. It is essential for adequate stent placement in the femoral-iliac-caval venous outflow.

Why do we have to think of obstruction in our practice? Because venous outflow obstruction plays an important role in the clinical manifestation of chronic venous disease, particularly pain. Ulcers occur rarely in the presence of isolated obstruction (4%) and more often in association with reflux (30%). Treatment of obstruction results in impressive clinical relief of pain, swelling, healing of ulcers, venous clinical severity score, venous disability score and quality of life, even when associated reflux is left untreated. Pelvic outflow obstruction is observed frequently following acute DVT, because only 20-30% of the veins completely recanalize. In cases of chronic iliofemoral obstruction, more severe symptoms are present than in femoropopliteal disease. Venous claudication is present in 15-44% of cases, and ulcer in 15% of cases within 5 years. Interestingly, in 80% of proximal postthrombotic cases an underlying compression-type lesion (May-Turner/Cockett syndrome, or iliac vein compression syndrome, intraluminal congenital lesions-webs, spurs, chords) can be identified. Stenting of the underlying stenosis after clot removal improves patency from 27-44% to 86-93%! These "primary", nonthrombotic iliac vein lesions (NIVLs) (more frequently on the left side) may be more pathogenic than previously thought. In the author's experience of stenting

more than 1000 obstructive limbs, approximately 40% had nonthrombotic blockage. Intravenous ultrasound–positive NIVLs are frequently present in “primary” reflux cases! NIVLs are frequently seen in asymptomatic populations (intraluminal lesions in 22-23% and external compression in 66-88%)! These primary lesions might not become clinically significant until other components of the venous system fail (and reflux is added) and the extremity becomes decompensated. Correction of these permissive iliac lesions alone often results in remission, even when the secondary pathology is not addressed. Intravenous ultrasound should be used in patients with clinical features (pain out of proportion to lesion, proximal postthrombotic disease, no detectable lesions explaining symptoms) and in the presence of positive indicators of obstruction (stenosis/occlusion on imaging techniques, presence of collaterals, positive pressure tests). Intravenous ultrasound–verified stenosis of greater than 50% is considered for stenting. Postprocedural thrombotic complications are rare (1.5-3%), the cumulative primary and secondary patency rate of stenting is quite good and the rate of in-stent restenosis is 1-10%.

As a key message of this exciting presentation we can summarize the following: a comprehensive workup and classification is mandatory prior to treatment; in the case of CVI think of obstruction; an obstructive NIVL on intravenous ultrasound is a frequent finding; complement ultrasound scanning of the lower extremity with transfemoral venography, magnetic resonance venography, CT-V or intravenous ultrasound; venous stenting is an evolving method which is the primary choice in the treatment of ilio caval obstruction; a more aggressive approach to diagnosis and treatment of venous outflow obstruction is justified; attempt minimally invasive procedures before surgery; iliofemoral obstruction should be treated before axial deep reflux in combined disease; superficial reflux should be treated before axial deep reflux; combine iliac venous stenting and endovenous ablation of superficial reflux even in the presence of axial deep vein reflux; deep valve repair should be considered when the above measures fail; percutaneous artificial valve placement may change this paradigm, but at this moment this is not the case.

## Venous malformation

### Diagnostic approach to venous malformations

B-B. Lee

The author stressed the importance of distinguishing correctly between hemangiomas and venous malformations (VMs). Hemangioma is a “self-limited” vascular tumor of endothelial cells that appears in the neonatal period. Hemangioma has a characteristic initial rapid growth, proliferation phase, followed by a phase of involution with a slow regression before the age 5-10 years, in the majority of cases. The differential diagnosis between VMs and hemangiomas is in general easy on the basis of the clinical history and a careful physical examination. Occasionally, a simple test such as an ultrasound study can confirm the clinical diagnosis.

The Hamburg classification based on the ISSVA (International Society of the Study for the Vascular Anomaly) workshop held in Germany in 1988 was created to classify congenital VMs according to their pathogenesis and clinical course, which

are essential for different treatment choices. The classification distinguishes between predominantly arterial malformations, venous, lymphatics and capillary lesions or a combination of them. Every congenital VM is divided into two embryological subtypes (extratruncular or truncular). The identification and confirmation of this embryological subtype is the first step towards proper management, because their prognosis is completely different.

In the second part of the presentation, B-B. Lee emphasized the correct differentiation between VMs and arteriovenous malformations, both being congenital VMs, but with very different prognoses. Congenital VMs present at birth as a vascular defect and continue growing at a rate proportional to the growth of the body. Congenital VMs may be a mix of several vascular defects with several characteristics and behaviors, involving more than one vascular component (arterial, venous, lymphatic, or capillary). Congenital VMs may present as a single predominant component (eg, venous malformations) or a combination of two or more types (eg, hemolymphatic malformation). Arteriovenous, lymphatic, and venous malformations are different forms with different clinical courses and prognoses.

VM is the most common form of congenital vascular malformation. In the majority of cases, a VM presents as an independent lesion but, sometimes, as a combined form with other congenital VMs (eg, Klippel-Trenaunay syndrome; Parkes-Weber syndrome). The identification of the embryological subtype of the VM (extratruncular or truncular) is of pivotal importance. The extratruncular form of VM is characterized by a single alteration: retention of mesenchymal cells (angioblast) during early embryological development. This lesion tends to progress with an unpredictable prognosis and a high rate of recurrence. The defect in the truncular VM appears during the vascular formation of the trunk during later fetal development. It remains as a truncal fetal malformation without a normal involution (eg, sciatic vein, marginal vein), or as a defective vessel trunk formation: obstruction/dilatation of the formed vessels (eg, venous aneurysm), or aplasia, hypoplasia, and/or hyperplasia of the vessel development (eg, agenesis/rudimentary deep vein). Truncular VM has, basically, a hemodynamic effect with better prognosis and less frequent recurrence than extratruncular VM. Unless there is any serious morbidity or complication, the truncular lesion in general should be closely monitored, with conservative/supportive management.

Finally, B-B. Lee explained the management of one VM. Following careful history taking and physical examination, the diagnosis must be confirmed with a noninvasive test such as ultrasound or MRI. More invasive studies (eg, arteriography) can be reserved for the more advanced cases and when surgical/endovenous therapeutic measures are being considered. Because of the high incidence of co-existing lesions, when one congenital VM is confirmed, the presence of others should be checked for.

## Miscellaneous

### Chronic Cerebrospinal Venous Insufficiency: diagnosis and treatment

Chairperson: P. Zamboni

Moderator: B-B. Lee

What we heard in this session has the potential to be a revolution in medicine. The hypothesis of P. Zamboni is the following. Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system of unknown pathogenesis. Magnetic resonance venography and postmortem studies have shown a topographic correspondence between MS plaques and an impaired cerebral venous system. Could impaired cerebral venous outflow, with delayed venous drainage and reflux to the brain, be at least partly responsible for MS?

### Chronic cerebrospinal venous insufficiency and multiple sclerosis: theoretical and practical issues

M. Simka

M. Simka further described this hypothesis, suggesting that chronic cerebrospinal venous insufficiency could lead to venous reflux toward to the brain. This might provoke a breakdown of the blood-brain barrier, extravasation of erythrocytes and immune blood cells, and trigger the inflammatory process of MS. The main abnormalities found at ultrasonography in patients with chronic cerebrospinal venous insufficiency are stenoses of the internal jugular veins, inverted valves, absence of flow in the internal jugular or vertebral veins, reflux in internal jugular and vertebral veins, as well as in the deep cerebral vein on transcranial ultrasonography.

### Cerebral veins and iron deposits explored by advanced MRI-SWI

M. Haacke

M. Haacker reported his use of venous magnetic resonance angiography (MRA) to evaluate iron deposits in the brain. This susceptibility-weighted imaging (SWI) MRA can visualize medullary veins and iron content in the gray matter. He observed a concordance between areas where iron tends to be deposited and venous drainage areas. As compared with controls, MS patients have increased amounts of iron in basal ganglia and the thalamus. In young patients, evaluation of iron content at SWI-MRA had the potential to discriminate between MS and control patients.

### Imaging and endovascular treatment of chronic cerebrospinal venous insufficiency

R. Galeotti

The imaging and endovascular treatment of chronic cerebrospinal venous insufficiency was presented by R. Galeotti. He reported on a series of 65 MS patients with ultrasonographic criteria for chronic cerebrospinal venous insufficiency who all underwent phlebographic examination of main extracranial

and extravertebral venous pathways: left femoral access, and imaging of the iliac, iliolumbar, renal, and azygous veins, as well as bilateral imaging of internal jugular and vertebral veins. They found multiple lesions: significant stenoses, annulus and septum, valve malformations, membranous obstruction, vein hypoplasia or agenesis. Uni- or bilateral internal jugular vein stenosis was found in 91% of patients, and azygous lesions were found in 86%. None of the 235 control patients included in the same study had ultrasonographic criteria for chronic cerebrospinal venous insufficiency.

All venous lesions were treated by percutaneous transluminal angioplasty. After 18-month follow-up, 95% of treated azygous veins remained patent, versus only 50% of internal jugular veins. A different distribution of lesion types between the two territories may account for this difference in the long-term success rate. Patients with internal jugular vein restenosis might benefit from redilatation with high pressure and cutting balloon, or open surgery.

### **Treatment of chronic cerebrospinal venous insufficiency: clinical results on associated multiple sclerosis**

F. Salvi

F. Salvi described the clinical progression of these 65 MS patients who underwent percutaneous transluminal angioplasty for chronic cerebrospinal venous insufficiency. Whereas those with secondary progressive or primary progressive MS had little change in their MS severity score after 18 months, patients with relapsing-remitting MS exhibiting significant improvement: 50% of them were relapse-free after 18 months. All patients with relapsing-remitting MS who had persistent vein patency at 18 months were relapse-free, whereas all patients with restenosis experienced disease relapse.

The authors concluded that chronic cerebrospinal venous insufficiency and MS might be closely related, and that endovascular treatment may alter the course of MS, though more studies are needed to confirm these results.

### **Max Ratschow Medal Session (Collegium Internationalis Angiologiae)**

Chairperson: E. Rabe

#### **Pelvic venous disorders: the desperate plea of women with the nutcracker syndrome**

J-L. Villavicencio

The *Max Ratschow Medal Session* (organized by the Collegium Internationalis Angiologiae) was introduced by the UIP president E. Rabe, who presented the main speaker – J-L. Villavicencio, an internationally known vascular surgeon. After paying tribute to M. Ratschow (the first German angiologist), J-L. Villavicencio proceeded to the lecture.

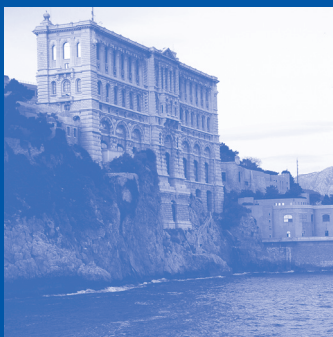
The main symptoms of pelvic venous disorders are chronic diffuse pelvic and flank pain, dyspareunia, dysmenorrhea, dysuria, vulval, intrapelvic and lower extremity varices, hematuria, and proteinuria. The possible etiology is: gonadal

vein insufficiency, insufficiency of internal iliac vein and its tributaries, combination of both these – “dumping syndrome”, and nutcracker syndrome.

Nutcracker syndrome is caused by the compression of the left renal vein between the aorta and superior mesenteric artery producing obstruction of the gonadal and left renal venous outflow leading to retrograde flow toward the pelvis and subsequent pelvic congestion, formation of periureteral tortuous collaterals and dilatation of gonadal veins. The diagnosis should be based on clinical and laboratory evaluation (hematuria, chronic left flank pain, proteinuria) and imaging methods – noninvasive (multi-slice 3D CT angiography, duplex ultrasound, MRI) and invasive (direct varicography, retrograde selective renal and gonadal phlebography, retrograde video-angiography with renocaval gradient measurement – normal is 0-1 mm Hg). The differential diagnostics should exclude other gynecologic pathology and urinary or bowel diseases. Treatment options comprise surgical and endovascular procedures: nephropexy, gonado-caval bypass, external Gore-Tex renal vein stents, balloon angioplasty with intraluminal renal vein stenting, left renal vein transposition to a lower caval site, spleno-renal bypass, and gonadal vein embolization alone or with the embolization of internal iliac vein tributaries. The treatment modality should be tailored to the type and severity of symptoms, the patient’s age, and hemodynamic findings.

# V

## Treatment



**XVIth World Meeting  
of the Union Internationale  
de Phlébologie (UIP)  
Principality of Monaco  
August 31-September 4, 2009**





# 5 - Treatment

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## Acute venous disease

### Deep venous thrombosis - how to treat in daily practice?

A. Comerota

In the first part of his presentation, A. Comerota dealt with the high prevalence of postthrombotic syndrome (PTS) in patients with iliofemoral DVT and defended the American College of Chest Physicians (ACCP) guidelines recommending thrombus removal, including venous thrombectomy and catheter-based procedures designed to eliminate clots, in patients with iliofemoral DVT. Following venous thrombectomy, patients should receive the same intensity and duration of anticoagulation as those patients who are treated with anticoagulation alone (ACCP recommendation Grade 1 C). In the author's opinion, catheter-directed thrombolysis is the preferred method of managing patients with iliofemoral DVT, but anticoagulation alone without thrombus removal is indicated in the majority of patients.

In the second part, the author presented the principles that should be adopted for successful anticoagulation of patients with acute DVT. The principal therapeutic objectives in DVT must be to reduce thrombus extension and recurrence, avoid PE and reduce PTS incidence. For this reason, sustained adequate therapeutic anticoagulation is necessary from the onset of therapy. Early subtherapeutic anticoagulation is associated with a 15-fold increase in the risk of recurrence. Initial anticoagulation with a heparin compound or fondaparinux should continue for at least a five-day overlap with vitamin K antagonist (VKA) and the international normalized ratio (INR) should be  $>2$  for 24 hours before heparin is discontinued. Subtherapeutic VKA doses increase DVT recurrence and does not protect against bleeding complications. Supratherapeutic VKA doses do not reduce DVT recurrence and increase bleeding risk. Patients must be stimulated to ambulate early wearing a 30-40 mm Hg ankle-gradient compression stocking during their waking hours to speed recovery and reduce postthrombotic morbidity (ACCP recommendation Grade 1 A). Duration of anticoagulation and risk of recurrence were other aspects discussed. Patients with a transient risk for DVT must be anticoagulated with VKA for a minimum of three months. In the author's opinion, in case of unprovoked DVT, patients should receive VKA for at least three months and then reevaluated for long-term (indefinite) therapy. Reevaluation must analyze patient status, ultrasound study, and D-dimer activity. Thrombus presence and D-dimer higher than 250 ng/mL increase the risk of recurrence of DVT. In these cases, patients are anticoagulated indefinitely and reviewed every six months. Patients with isolated calf DVT should be treated with three months of anticoagulation (ACCP recommendation Grade 1 A). For unprovoked recurrent DVT, indefinite anticoagulation is superior to six months of anticoagulation, but carries a higher bleeding risk. Patients with malignancy are best treated with low-molecular-weight heparin (LMWH) rather than a VKA. LMWH should initially be given for the 3-6 months, after which the patient should be reevaluated. Subsequent therapy with VKA or LMWH should continue indefinitely or until the cancer is resolved.

## Thromboembolic Disease

Chairperson: W. Blättler

Moderator: M. Meissner

### Current status of thrombolysis and thrombectomy in iliofemoral deep vein thrombosis

A. Comerota

Iliofemoral DVT, if treated with anticoagulation alone, carries a very high risk of postthrombotic syndrome (PTS), as well as a significant risk of recurrence. The strategy of thrombus removal – venous thrombectomy or a catheter-directed procedure – results in better outcome (better venous patency, preserved valve function, less PTS) with acceptable safety. Nevertheless, the lack of randomized controlled trials comparing this strategy with anticoagulation alone has not allowed a strong recommendation so far. In the last ACCP guidelines on antithrombotic therapy (2008), the recommendation for venous thrombectomy and catheter-directed thrombolysis in the case of extensive proximal DVT is graded 2B; the recommendation for pharmacomechanical thrombolysis is 2C. There is a strong recommendation for the same intensity and duration of anticoagulation as for the patients treated with anticoagulation alone (grade 1C). Two large randomized trials of thrombus removal strategy are underway (CAVENT, ATTRACT).

### Catheter-directed thrombolysis in deep vein thrombosis

N. Bækgaard, R. Broholm, LP. Jensen

Review of the recent literature demonstrates the good outcome and acceptable safety of catheter-directed thrombolysis of proximal DVT in selected patients, but this method is still underutilized. The possible indications are sudden onset of symptoms, no contraindication, good clinical reserve, anatomical cause of DVT, iliofemoral location, acute leg compromise, failure of standard anticoagulation therapy, and high risk of PE. So far, few publications have documented the long-term results of catheter-directed thrombolysis. The results, however, are not fully comparable due to different inclusion criteria and methodological differences (doses of thrombolytic drug, doses of heparin, techniques - catheter-directed thrombolysis alone, pharmacomechanical thrombolysis, angioplasty, and venous stenting). In the study of the Oslo group, there was a significantly better patency rate compared with anticoagulation alone, but disappointingly no difference in the presence of reflux in the common femoral vein. In the study from Copenhagen, 89% patients were without reflux. The study of the authors' institution was finally presented (highly selected population, 103 legs treated for DVT, median follow-up 50 months). The results were very satisfactory – no mortality, low morbidity, no venous claudications or skin changes, 87% preserved venous patency 6 years after DVT.

### Endovascular deep vein thrombosis interventions

S. Vedantham

Because of the endovascular “evidence gap” (lack of randomized controlled trials comparing endovascular procedures with anticoagulation alone in DVT), these

methods are currently underutilized in clinical practice. The objections to their use could be the invasiveness and potentially higher risk, possible medicolegal issues, and higher costs. There is also a lack of skilled interdisciplinary networks of physicians and of a standardized DVT lysis protocol.

ATTRACT is a phase III, open label, randomized, controlled, multicenter trial in the USA, comparing anticoagulation alone with pharmacomechanical catheter-directed thrombolysis. It is planned to enroll 692 patients with acute symptomatic proximal DVT (inferior vena cava, common femoral vein, femoral vein). The primary objective is to prove the efficacy of interventional methods in preventing PTS (evaluated 24 months after DVT with the Villalta score, design planned to prove 33% risk reduction). Secondary questions in ATTRACT will be the effect of invasive treatment on PTS severity, quality of life, early symptom relief, safety, cost-effectiveness, valvular reflux.

ATTRACT is interdisciplinary and includes representatives of diverse medical specialties participating in the investigators network as well as in the steering committee.

## **New anticoagulants in the treatment of venous thromboembolism**

H. Decousus

The reference therapy for acute VTE includes initial therapy with heparin or LMWH or fondaparinux followed by long-term warfarin administration. The disadvantages of this therapy should be overcome by new anticoagulants.

Idraparinux is an indirect factor Xa inhibitor with a very long half-life allowing once weekly dosing without the need for laboratory monitoring. The initial results have revealed an increased risk of bleeding. In the Van Gogh DVT and Van Gogh PE trials, idraparinux (for initial as well as for long-term treatment) was compared with standard anticoagulation therapy, with similar efficacy for DVT but worse outcome for PE (higher rate of early PE recurrence).

Idraparinux has been replaced by idrabiotaparinux, a biotinylated substance with available antidote. It has been compared with standard therapy in the EQUINOX study for DVT (results not yet published, but the efficacy of the two treatments was similar) and the CASSIOPEA study for PE (nearly finished; unlike Van Gogh PE, the initial therapy was enoxaparine in both groups).

Rivaroxaban is an orally available direct Xa inhibitor, administered once daily, without the need for laboratory monitoring. It has been evaluated in the EINSTEIN phase II study for proximal DVT and is currently being evaluated in the EINSTEIN phase III study for DVT and PE.

Apixaban is another direct Xa inhibitor. The main difference from rivaroxaban is predominant biliary/fecal metabolism and potential use in renal insufficiency. BOTTICELLI is a phase II study for proximal DVT and AMPLIFY is a phase III study for proximal DVT and PE.

Dabigatran is an oral, direct IIa inhibitor with prevalent renal metabolism, evaluated in RE-COVER 1 and 2 studies.

Rivaroxaban and dabigatran have already been approved in Europe for VTE prophylaxis in major orthopedic surgery.

## Calf vein thrombosis – how to treat?

J. Lohr

According to the author there are several reasons for routinely scanning calf veins in patients with suspected DVT: to detect superficial venous thrombosis, to detect DVT, to evaluate the propagation of thrombosis, to assess potential for embolism, to “look where it hurts”, and to exclude other pathologies, like Baker cysts, neoplasm, hematoma, etc. There are also several arguments for not scanning the calf veins: low incidence (not justified), rare for propagation or embolization, complicates and lengthens the examination. But the speaker emphasized that the ICAVL 2008 recommends compression imaging for both posterior tibial and peroneal veins and also for the gastrocnemius and soleus veins in the evaluation of possible thrombosis in symptomatic patients. There are several obstacles to distal ultrasonography, like obesity, epifascial edema, interstitial edema, inability of the patient to sit upright, but these are not so frequent in daily practice. A meta-analysis of studies comparing ultrasound in symptomatic patients with venography shows a sensitivity for distal veins of 73% and a specificity of 93%. The prevalence of isolated calf vein thrombosis (v. poplitea and below) is 5-12% in symptomatic DVT patients, but is much higher in asymptomatic DVT patients (15% after hip-knee surgery and 45% after CABG). Isolated calf DVT rarely causes symptoms, but in 20-30% of cases untreated symptomatic calf DVT extends to the proximal veins mostly within one or two weeks of presentation. Both symptomatic and asymptomatic calf DVT propagates with equal frequency. Isolated calf DVT is associated with about half the risk of recurrence of proximal DVT or PE. In more than 90% of cases of proximal DVT, there is associated calf vein involvement. Calf vein thrombi can embolize and cause symptomatic PE in 0.5-13% of cases, according to different studies. Taking these data into account, the American Society of Chest Surgeons recommendation in symptomatic calf DVT patients is at least 6-12 weeks of anticoagulation. The anticoagulation prevents further thrombus deposition, reduces the risk of interval recurrent thrombosis, the established thrombus undergoes stabilization or endogenous lysis, and after 3 months of therapeutic anticoagulation the frequency of extension of symptomatic isolated calf vein thrombosis is reduced from 29% to 0%. The natural history of untreated calf vein DVT involves a 20-29% recurrence rate within 3 months, 4-46% postthrombotic manifestations, 20% valvular incompetence, up to 32% propagation, and 33% silent PE on lung scan. In treated patients the recanalization is rapid, with 50% clot reduction in 1 month and with total clearing by 1 year. Reflux is present in 24% of cases at one year. Many trials (PREVENT, ELATE, THRIVE III) demonstrate that long-term anticoagulation in patients with idiopathic VTE, including those with isolated calf DVT, is a safe and effective strategy.

## TULIPA registry – recent practice in diagnosis and treatment of deep vein thrombosis

R. Bauersachs

In this presentation P. Bauersachs from Germany shared with us the results of the TULIPA registry demonstrating that the management of patients with suspected DVT has changed substantially over the past 15 years. The aim of this registry was to assess current real-world practice and performance of the diagnostic workup

of patients with suspected DVT in ambulatory care in Germany. A total of 4976 consecutive patients with suspected DVT were included by 326 ambulatory care vascular specialists in a nationwide, prospective DVT registry. Signs, symptoms, and preceding management were recorded and the patients were assigned to group A (DVT confirmed), group B (DVT excluded) or group C (diagnosis pending). Follow-up was performed at day 90 and VTE events and deaths were adjudicated centrally. The TULIPA registry results show us that the diagnosis work-up was done on the same day in 58% of patients, 15% had received treatment from their GP to bridge the time to diagnosis, while 14% received treatment for a different suspected disease. Diagnostic workup included mainly ultrasound (96%), D-dimer test (36%), venography (6%), and CT and MRI (0.5%). After the workup, 28% of the patients were in group A, 68% in group B, and 4% in group C. Men had a higher prevalence than women. Objective clinical findings were more common in men, and in more than half of the women an alternative diagnosis was more likely than DVT. DVT was distal in 61.7% of cases. The discriminative value of the Wells score was very high. 9% of DVT patients had combined DVT and superficial thrombophlebitis, 5% underwent testing for concomitant PE, and 85.3% received outpatient treatment. Secondary hospitalization was necessary in 2.2% of patients. In group B, 4 patients (0.31%) had confirmed symptomatic VTE (diagnostic false-negative rate <1%), compared with 18 in group C (9.1%). The author concluded that within the two-level ambulatory patient care system covered by the TULIPA registry, which is the largest German research project, diagnostic workup of patients with suspicion of DVT was performed in due time. GPs refer patients according to their risk factor profile. Pretreatment anticoagulation was applied appropriately. Almost all patients underwent imaging procedures, mostly complete compression ultrasound. Even though the guidelines-recommended pathway regarding D-dimer testing was followed in only 32% of cases, the diagnostic safety of excluding DVT in this real-world setting was excellent and as good as in prospective management studies. Long-term follow-up data of the TULIPA patients will be available next year.

### **Anything new in travel-related venous thromboembolism?**

B. Eklöf

The speaker started his presentation by enumerating the proven or supposed risk factors for air travel-related venous thromboembolism (ATVT), which include patient-related internal factors (age more than 60 years, overweight, previous VTE, recent surgery/injury, pregnancy/postpartum, malignancy, cardiorespiratory diseases, thrombophilia, varicose veins, other chronic diseases, etc) and cabin-related external risk factors (immobilization, coach position, low air pressure, relative hypoxia, dehydration). Based on alarming previous reports of ATVT, the WHO organized a consultation in Geneva in 2001 where the experts agreed that there is probably an association between air travel and VTE, but such an association is likely to be small and mainly affects passengers with additional risks for VTE. Similar risks may exist for other forms of travel, but the available evidence does not permit an estimation of the actual risk and therefore public recommendation cannot be made at present. It was the unanimous view of the participants that further multicenter, epidemiological, international, pathophysiological and

preventive studies regarding ATVT should be undertaken as soon as possible. For this purpose the WRIGHT project (WHO Research Initiative on Global Hazards of Travel) was created. The project has received partial funding, so in Sydney in September 2005 four preliminary results were reported. The conclusions were as follows: air travel is associated with an increased risk of VTE and the risk is slightly higher after exposure to a succession of flights; thrombin generation occurs in some individuals after an 8-hour flight, suggesting that more than just immobilization causes ATVT; the risk of developing VTE seems to be lower in Dutch airline pilots than in the Dutch population; hypobaric hypoxia is not associated with prothrombotic alterations and is unlikely to contribute to the risk of ATVT; traveling for more than 4 hours by any transportation mode increased the risk of VTE two-fold; this was more apparent with air travel, suggesting flight-related factors that are absent during travel by other modes. In summary, the WRIGHT project tells us that air travel is associated with an increased risk of VTE. This increased risk applies to other forms of travel where travelers spend long periods seated. Obesity, height, use of contraceptives, and the presence of prothrombotic abnormalities increase the risk. The results of the WRIGHT project suggest that over 150 000 of two billion air passengers per year will develop ATVT, of whom 7500 will suffer fatal PE. For this reason it is essential that the prevention study proposed for phase II of the WRIGHT project is carried out and that future passengers are adequately informed about their risk and the optimal mode of prevention. It is hoped that the suggested research projects will answer these questions within the next few years. While waiting for the outcome of the research, at this moment we can also report the conclusions of a Conference on Traveler's Thrombosis organized in Hall, Austria, 2006, the updated version of which was published in VASA 2008, resulting the following consensus: cabin-related risk factors can be remedied by drinking plenty of nonalcoholic fluids, moving feet and legs and taking deep breaths several times every hour; passenger-related risk factors that can trigger any of the factors in Virchow's triad may be potentiated by the cabin-related risk factors; awareness of this problem has to be increased among the public as well as among doctors. Each person should be advised before flying by a physician, based on the individual level of risk (low, medium, high). In high-risk patients, prevention consists of general measures, compression stockings, and pharmacological methods (LMWH or pentasaccharides).

### **How to treat superficial thrombophlebitis?**

M. de Maeseneer

In the introduction of her presentation, the speaker stressed that the clinical diagnosis of superficial thrombophlebitis (ST) seems to be easy, but often underestimates the real extent of the disease and also often overlooks the presence of associated DVT or PE. That's why ST is a serious illness as it may lead to DVT and even PE in certain cases. The thrombus could directly extend through the saphenofemoral (SF) junction or saphenopopliteal (SP) junction often with a "free floating tail" or appear as non-contiguous ipsi- or contralateral DVT. The incidence of VTE in ST ranges from 5% to 32%, depending on the study. Therefore, duplex scanning is mandatory to evaluate the extent of the thrombus and to detect any associated DVT. A wide variety of therapeutic measures have been

described: local applications (cold pack, gel, cream, spray, etc.), local incision with expression of clot, immediate mobilization with compression bandages or stockings, NSAIDs (no antibiotics), and anticoagulation with heparin (LMWH or unfractionated heparin) or oral anticoagulants. The main practical problem is to find out which particular treatment will be appropriate for each single patient. Some cases of ST are clear-cut and there is no doubt regarding the appropriate therapeutic option. For instance, a limited ST in a varicose tributary can be treated with simple local measures, mobilization with compression bandages or stockings, and specific treatment of underlying disease in a later phase, whereas an ST associated with DVT will be treated as DVT. However, there is less consensus in the literature regarding non-clear-cut cases, such as extensive ST of the main trunk of the great or small saphenous vein. Several recent papers (The Stenox Study Group, Marchiori et al., The Vesalio Investigators Group, Cochrane Database Systematic Review by Di Nisio et al. And the ACCP guidelines 2008) suggest the use of intermediate or high doses of unfractionated heparin or LMWH for at least 4 weeks. In cases where ST is close to the SF or SP junction, anticoagulation with VKA for 1-3 months might be indicated. Surgery is recommended long after the acute ST episode. Future studies are needed to optimize our strategy in patients with extensive ST.

## Interaction of detergent sclerosants with the coagulation system: an update

K. Parsi

Two sclerosing agents – polidocanol, a nonanionic detergent, and sodium tetradecyl sulfate (STS), an anionic detergent, have been tested for their interactions with the hemostatic system. Several in vitro assays have evaluated the effects of these substances on various components of the coagulation system.

The tests assessing coagulation reactions – thrombin time (TT), prothrombin time (PT) and activated partial thromboplastin time (APTT) – revealed a different effect of these agents: the coagulation times were minimally affected by polidocanol, but significantly prolonged after STS at higher concentration (>0.6%). The two further tests (factor Xa clotting time and surface-activated clotting time) are phospholipid-dependent, ie, influenced by platelet count and function (while platelets provide their surface with phospholipids for coagulation reactions). These two tests again revealed little effect of polidocanol, but surprisingly the effect of STS differed between low concentrations (0.1-0.3%)—shortening of coagulation time—and high concentrations—prolonging of coagulation time. This would suggest activation of platelets at lower concentrations and destruction of platelets at higher concentrations.

The activity of respective coagulation factors was then measured after incubation of plasma with both sclerosants. The results demonstrated little effect of polidocanol, but a significant decrease of the activity of some coagulation factors was seen after STS (especially of the factors V and VII), which could be explained by proteolysis of these factors.

Further tests showed that at high concentrations both agents caused platelet lysis. The release of prothrombotic, platelet-derived microparticles was proven with both agents at low concentration.



The effect of sclerosants on the natural anticoagulant system was then assessed by the measurement of protein C, protein S, and antithrombin levels and by performing a functional test of activated protein C (APC) resistance. STS at high concentration significantly decreased levels of protein C, protein S and antithrombin, while polidocanol at high concentration had some effect on protein S only (moderate decrease). However, polidocanol induced APC resistance to some degree.

In a comparison with heparin (the effect on APTT), STS acted as an anticoagulant (similar but much weaker than heparin). Moreover, when added to heparin, STS potentiated the anticoagulant effect of heparin (such an effect was not observed after polidocanol).

To summarize the result of all these heterogeneous tests, *STS at high concentration* had some antithrombotic as well as prothrombotic properties, but the net effect can be characterized as *antithrombotic*. The effect of *polidocanol at high concentration* is *probably neutral*. Conversely, both *STS and polidocanol at low concentrations* have a *net prothrombotic effect*.

Finally, the effect of sclerosants on red blood cells and endothelial cells was tested, as well as the interaction with plasma components, including albumin. Both sclerosants caused the *lysis of erythrocytes and endothelial cells*. However, the *neutralizing effect of albumin* on the sclerosants was protective.

The practical implication is the suggestion to increase the concentration and reduce the volume of sclerosants and to inject rather than infuse them.

## Chronic venous disease

### A - GENERALITIES

#### Servier Symposium: Management of chronic venous disease: therapeutic recommendations

Chairpersons: A-N. Nicolaidis, E. Rabe

#### What's new in guidelines?

A. Comerota

Guidelines for patient care offer recommendations to physicians for diagnosis and management of common diseases that generally apply to the typical patient. The presentation addressed some of the newer guidelines to help clinicians manage patients with chronic venous disease of the lower extremities.

The method of determining the strength and quality of the recommendations deserves mention. Recommendations are generally accompanied by a number, which refers to the *strength* of the recommendation, and a letter, which refers to the *quality of the evidence* supporting the recommendation. The guidelines for chronic venous disorders use three levels of strength: Grade I is a strong recommendation, Grade II a moderate, and Grade III a weak recommendation. The recent ACCP guidelines use only two levels for the strength of their recommendations: Grade 1 for strong and Grade 2 for weak.<sup>1</sup> They further indicate

that statements accompanied by a Grade 1 level are “recommendations” and statements accompanied by a Grade 2 level are “suggestions.”

The quality of evidence upon which the strength of the recommendation is based ranges from “A” for high quality, which is consistent evidence from randomized trials, to “B” for moderate quality, which is evidence from nonrandomized trials or inconsistent evidence from randomized trials. Level “C” is low quality, which is suggestive evidence from nonrandomized trials, observational reports, or expert opinion.

Classification and severity scoring of chronic venous disease are important to consider when building guidelines. A widely accepted, objective, and standardized classification system is crucial for accurate and reproducible description of patients. Lack of precision in diagnosis and description leads to conflicting reports of disease distribution and a poor understanding of the management of specific venous pathology. A standardized classification facilitates improved precision of communication and serves as a foundation for accurate reporting of the severity of disease and response to treatment. The CEAP classification (Clinical, Etiology, Anatomy, Pathology) was proposed and subsequently adopted worldwide as a basis for improved patient description.

Understanding the pathophysiology of a disease state is a prerequisite to effective treatment. Results from studies that demonstrate treatment efficacy lead to guideline recommendations. The apparently simple concept of venous hypertension being responsible for chronic venous disease belies the complex cellular and molecular processes set in motion by the abnormal venous hemodynamics. Ambulatory venous hypertension is the hemodynamic pathology, with its underlying components being venous valvular incompetence, luminal obstruction, and failure of the calf muscle pump. The seminal role of leukocyte activation as a result of venous hypertension was recognized following basic animal experiments and human research. Animal models of venous hypertension demonstrated increased numbers of leukocytes in the skin of extremities with venous hypertension.

What’s new in guidelines?

The recent ACCP guidelines<sup>1</sup> have added important new recommendations and suggestions for the treatment of iliofemoral venous thrombosis, venous thrombectomy, catheter-directed thrombolysis, early ambulation and compression, Intermittent pneumatic compression, pentoxifylline, and micronized purified flavonoid fraction (MPFF; Daflon 500 mg). This last compound is the only mentioned phlebotropic drug in the ACCP guidelines

#### Reference:

1. Kearon C, Kahn SR, Agnelli G, Goldhaber SZ, Raskob G, Comerota AJ. Antithrombotic therapy for venous thromboembolic disease: ACCP evidence-based clinical practice guidelines (8th ed). *Chest* 2008;133(6):454S-545S.

## Management of chronic venous disease: the example of Daflon 500 mg

A-A. Ramelet

Among the pathological processes involved in the development of chronic venous disease, the sequence of leukocyte adhesion, endothelial interaction, activation, and migration, and its association with valvular damage have focused attention on available molecules with known activity on this chain of events. MPFF (Daflon 500 mg), consisting of 90% diosmin and 10% other flavonoids, reduces leukocyte interaction with the endothelium in acute venous hypertension and inflammation, reinforces venous tone, reduces abnormal capillary permeability, and increases lymphatic drainage.

Chronic venous disease may be associated with a wide range of lower limb symptoms, which may be present in any class of the CEAP classification: leg heaviness, discomfort, itching, cramps, pain, paresthesia, sensation of swelling, and edema.

Venoactive drugs may be indicated as a first-line treatment for chronic venous disease-related symptoms in C0s to C6s patients. In the most recent guidelines for the management of chronic venous disease, three agents, including Daflon 500 mg, received a Grade A level of evidence for their effects on venous symptoms. Daflon 500 mg is effective from the earliest stages of chronic venous disease. Symptom relief is achieved rapidly, as demonstrated in three randomized controlled studies. Three further studies have also demonstrated beneficial effects of Daflon 500 mg on edema, and a significant correlation between the improvements in the symptom score of sensation of swelling and a decrease in ankle circumference.

Postoperative recovery after venous surgery is enhanced by Daflon 500 mg, as established in 2 recent studies. Mean pain scores in women with pelvic congestion syndrome are significantly lower in Daflon 500 mg-treated patients than in patients receiving placebo.

The efficacy of Daflon 500 mg in promoting venous ulcer healing has been demonstrated in a meta-analysis of 723 patients. As a result, Daflon 500 mg was assigned a Grade 1B as adjunctive treatment in ulcer healing in the recent guidelines of the American Venous Forum.

## Unmet needs in assessment of symptoms and signs

A. Jawien

Chronic venous disease, which is highly prevalent among populations of Western countries, induces pain and discomfort and significantly reduces quality of life, but lacks specific and consensual instruments for adequate assessment of its signs and symptoms.

For vascular specialists who strive to find something better for their patients and are willing to change based on what they find, outcomes must be analyzed and presented in such a way as to be shared and compared. Needs are still unmet regarding the tools currently available for the assessment of the therapeutic efficacy of drugs, in particular Daflon 500 mg, in reducing symptoms and signs.

*Tools available to physicians to assess the efficacy of treatments in reducing symptoms and signs:* The CEAP classification, a universally adopted classification of chronic venous disease signs, has facilitated meaningful communication about the disease. The

adjuncts to the CEAP that are likely to show the greatest score change in response to therapy are a useful complement to the CEAP classification, and should be used for research. Besides these physician-generated tools, previous methods remain valid for objective measurement of symptoms and signs of chronic venous disease. For symptoms, practitioners may use visual analogue scales such as the 10-cm VAS. For assessment of venous edema, leg volume can be assessed simply by ankle and calf circumferences. Other methods reported are water displacement volumetry, optoelectronic methods, CT scanning, MRI, and dual X-ray absorptiometry. For leg ulcers, the parameters most frequently used to measure a wound are the lengths of the principal axes, the projected surface area, and the perimeter. Most methods have been used for the study of Daflon 500 mg's efficacy. *Tools adapted to patient-reported outcome:* Patient-reported quality-of-life assessments are valuable adjuncts to both clinical observations and physician-generated assessments. At least seven specific scales adapted to chronic venous disease (Aberdeen Varicose Veins Questionnaire, Charing Cross Venous Ulceration Questionnaire, Tübingen, Franks, Freiburger, VEINES-QoL, and CIVIQ) have been developed until now, pointing to the need for a single scale applicable to a wide spectrum of diseases and validated in many languages. Most of these tools are validated in a single language, while thirteen linguistic versions of the CIVIQ were validated according to the forward/backward methodology. CIVIQ has been extensively used as a means of assessment in the treatment of chronic venous disease patients at all stages of the disease.

### **Recent guidelines in chronic venous disease: the place of Daflon 500 mg**

A-N. Nicolaides

Because chronic venous disease is common in Western populations and because both specialists and general practitioners have to deal with it, there is a need for practical support in its daily management and more particularly for evidence-based guidelines.

Regarding chronic venous disease management, recent guidelines have reviewed the place of venoactive drugs in the treatment of symptoms, edema, and venous leg ulcer.

*Guidelines on chronic venous disease-related symptoms:* A group of 14 experts, chosen to be representative in the fields of angiology, dermatology, and vascular surgery, from countries in which venoactive drugs were available and who had experience of their clinical use, published in 2005 the Siena consensus paper on the efficacy of venoactive drugs in relieving symptoms. Data from randomized, controlled trials were selected according to the predefined criteria of evidence-based medicine and were classified as Grade A (randomized controlled trials with large sample sizes, meta-analyses with homogeneous results), Grade B (randomized controlled trials with small sample size), or Grade C (other controlled trials, non-randomized controlled trials). Outcomes included only symptoms at any stage of the disease. The experts agreed that venoactive drugs were indicated to relieve venous symptoms CEAP clinical class C<sub>0S</sub> through to painful venous ulcers (C<sub>6S</sub>). MPFF (Daflon 500 mg) was assigned a Grade A in this indication.

*Guidelines on venous edema:* International guidelines on the management of chronic venous disease used the same grading system as that of the Siena experts. Outcomes

included not only symptoms but also edema and venous ulcer healing. When considering venoactive drugs, the guidelines largely summarized and endorsed the positive findings of the recent Cochrane reviews and highlighted the evidence of efficacy of several venoactive drugs in chronic venous disease–related edema. Daflon 500 mg was assigned a Grade A recommendation in venous symptoms and edema, and as an adjunct to standard compression treatment in the healing of venous ulcers.

*Guidelines on venous leg ulcer:* Based on the GRADE system described by Guyatt et al, the recent guidelines (2008) of the American College of Chest Physicians recommended Daflon 500 mg to be added to compression (Grade 2B) in the treatment of venous leg ulcers in patients with venous thromboembolic disease. In the last edition of the Handbook of Venous Disorders (2009), the use of Daflon 500 mg in combination with compression in longstanding or large venous ulcers was recommended (Grade 1B).

## Conclusion

A-N. Nicolaides

This symposium provided a clear and comprehensive review of the latest advances in the field of chronic venous disease. Major advances in the management and prevention of chronic venous disease have occurred in the last few years. The stimulus has been the realization of the magnitude of the problem and the better understanding of the pathophysiology of the condition in terms of the macrocirculation and microcirculation and at the molecular level. It should be remembered that DVT might be responsible for some of the most severe forms of chronic venous disease and prevention of acute venous disease is part of the management of the chronic venous disease.

The most important advance in understanding the pathophysiology has been the realization that changes in blood shear stress, with activation of leukocytes and endothelial adhesion followed by subendothelial migration, stimulation of proteolytic enzymes such as MMPs, and accumulation of extracellular material have a key role in the development of chronic venous disease. With this as background knowledge, drugs like Daflon 500 mg can ameliorate the above mechanisms.

The development and availability of appropriate tools to assess the severity of symptoms and the objective determination of treatment efficacy in improving signs such as edema, venous ulceration, and quality of life have enabled us to embark on appropriate randomized clinical trials. The results have provided level I evidence and grade A recommendations for therapies: compression, medication, and surgery. Medications such as Daflon 500 mg have now a proven place with grade A recommendations for the whole spectrum of chronic venous disease, ie, early disease, as an adjunct to surgery in moderate and advanced disease, and in the treatment of leg ulcers. Recommendations are now available in guidelines for the management and prevention of chronic venous disease developed both in North America and Europe.

## B - CONSERVATIVE TREATMENT

### Special issue in Phlebology

Chairperson: J. Cabrera

Moderator: A-A. Ramelet

#### **Recovery of vein dilatation by photochemical-induced collagen cross-linking**

A. Frullini

The author proposed a new treatment to recover valve function and original vein diameter. Riboflavin combined with UV-A light generates a photo-polymerizing effect with formation of new links in the collagen structure. The same treatment is used in an ectatic disease of the cornea (keratoconus). This method is not operator-dependent, does not cause endothelial or nonvalvular lesions or damage to surrounding structure, and does not generate inflammation. He reported his experience with human fresh GSV samples exposed to a light-emitting diode-blue led (L:450 nm-480 nm) for 15 min and supplied with vitamin B2 (riboflavin) or saline solution (control). Histological findings showed that the vein wall thickness almost tripled and the endothelium was unaffected. In conclusion, the author suggested that this treatment could be indicated in initial disease, deep vein insufficiency, telangiectasia and perhaps to recover ectatic veins for arterial bypass or for enlarged arteriovenous fistulas in dialysis patients. Clinical trials will be necessary to assess the method.

#### **A new pharmacomechanical method of endovenous ablation: Clarivein®**

S. Elias

The author presented a new endovenous device—Clarivein—consisting of a catheter for endovenous mechanical vein wall destruction and a device for the simultaneous infusion of liquid sclerosant to enhance venous ablation without tumescent anesthesia. His experience includes 30 limbs with varicose veins (GSV only) at C2 24 p, C3 2 p, C4 4 p. GSV medium size 8.1 mm. GSV length treated 36 cm. GSV treatment time 14 min. 30/30 closed at 1 month, 19/20 at 3 month, 7/8 at 6 month. He reported 3 subcutaneous ecchymoses, minimal pain, no DVT, no nerve injury, no skin injury. This method represents a simplification and advance in the treatment of varicose veins.

#### **Age-related macular degeneration and venous insufficiency**

F. Chleir

Age-related macular degeneration (AMD) includes two forms: wet AMD occurs when abnormal new blood vessels start to grow from the choroid, dry AMD occurs when the light-sensitive cells in the macula break down, gradually blurring central vision.

Duplex scanning was used to study ocular blood flow and so assess the relationship between varicose veins and AMD in 40 patients. Arteries showed the slowest speed

and low resistance particularly in wet AMD. Wet AMD indicated vasodilation with neovascularization and opening of arteriovenous shunts. Dry AMD showed dilation and blood stasis like varicose veins, but it was not clear whether the vessel abnormalities were the cause or consequence of venous disease.

## **My technique in compression treatment – bandages or stockings?**

H. Partsch

Compression must be tailored to individual needs, according different clinical conditions. Several patient-oriented factors should be considered, eg, the underlying disease (venous, lymphatic, arterial involvement), size and configuration of the extremity, age, walking ability, pain, and discomfort. The compression tools differ mainly in terms of the applied pressure, the elastic properties of the material, and the duration of wear.

There are several indications for compression therapy with bandages or stockings in therapy and maintenance phases. In the therapy phase, for severe stages of CVI (CEAP C4 - C6), after varicose vein ablation by different methods, and for the initial treatment of lymphedema, superficial and DVT compression devices providing a high massaging effect during walking (“high working pressure”) are preferred (inelastic bandages like Unna-boots, cohesive and adhesive bandages, multicomponent bandages with high stiffness). Such bandages applied with an initial pressure of more than 50 mm Hg need to be applied by trained personnel. The speaker emphasized that randomized and observational studies showed faster resolution of pain and swelling with early ambulation and leg compression compared with immobilization, and a similar incidence of new PE on routine repeat lung scanning after 10 days of treatment. These observations suggest that mobile patients with DVT should remain ambulant. In addition, intermittent pneumatic compression pumps may be beneficial, but this must be investigated. In the maintenance phase, medical compression stockings must be considered as the basic management in all patients with CVI in order to reduce pain and prevent massive swelling and ulcer recurrence. Except in cases of severe swelling of the thigh, knee-high compression stockings are usually sufficient. Compliance, which is the most important practical problem, can be improved by special aids to alleviate donning of stockings, by information and education of the patients, but also by special tricks like putting on two stockings, one over the other. With the use of compression stockings in venous ulcers one can expect a healing rate of 84% in 12 weeks, if ulcers are not too large (< 5 cm), not too longstanding (< 6 months) and frequently with the concomitant use of appropriate pressure pads.

## C - NON-CONSERVATIVE TREATMENT

### Guest lecture

Chairperson: J. Bergan

#### **Phlebology in the last 50 years: varicose veins and venous ulcers.**

K. Burnand, C. Jeanneret

Varicose veins are known from extreme antiquity, but only 50 years ago the early definitions emphasized the description of the tortuous dilated vein. The modern definition of varicose veins is "...subcutaneous, permanently dilated veins equal to more than 3 mm in diameter in the upright position...". Van Bemmelen et al introduced duplex measurements of venous reflux for estimation of CVI (1989). In 1995 Porter et al introduced the CEAP classification, which is routinely used in many countries now. Crossectomy and different types of stripping in addition to compression therapy have been the gold standard for more than 100 years. The high postoperative recurrence rate studied over a very long follow-up gave way to the development of new endovascular techniques. VNUS closure and endovenous laser therapy are new methods that eliminate reflux and large varicose veins without crossectomy. VNUS closure abolished reflux and varicose veins in 95.7% cases during 2-3 years of follow-up, and endovenous laser therapy has given similar results. Foam sclerotherapy is the method of a choice in the treatment of large varicose veins. In comparative studies, foam sclerotherapy was more effective than liquid. However, not all endovascular techniques have been studied in large randomized controlled trials with long-term follow-up. Venous ulcers are a more serious complication of CVI. It is generally estimated that 1% of the population will present with one or more episodes of venous ulcers during their lifetime. In the last 50 years there have been a number of new theories on the etiology of venous ulcers, but the mechanism of ulceration is still unknown. Venous ulcers are still managed by compression bandaging. Multilayer bandaging systems have been shown to be effective in healing 80% of venous ulcers within a year. Unfortunately, 20% of patients with C6 have recalcitrant ulcers requiring more investigation. Establishing which ulcers do not heal with compression would be very helpful so that more radical techniques such as tangential excision and mesh split skin grafting or the use of skin substitutes could be applied at an earlier stage. There is no evidence that abolishing superficial venous reflux by surgery enhances ulcer healing (the ESCHAR Trial), but it is clear that abolishing superficial reflux and regularly wearing compression stockings does reduce ulcer recurrence. In the last 50 years the management of venous ulceration has come a long way, with level one evidence now available for a number of investigations and treatments. It is, however, clear that a number of areas still require much more investigation. There are several important unsolved problems:

The cause of venous ulceration remains unknown

There is no diagnostic test for venous ulcers

The value of eradicating incompetent perforating veins has not been established

Deep vein obstruction is not quantifiable



Postthrombotic ulcers continue to recur despite adequate compression  
Postthrombotic veins cannot at present be returned to normal function

## **Sclerotherapy treatment of reticular and telangiectatic veins.**

J-J. Guex

Reticular varices and telangiectatic veins are serious cosmetic problems for large populations. These vascular abnormalities can be responsible for different symptoms such as heaviness, itching, tingling, burning, feeling of swelling, and pain. Therefore their treatment is not only for cosmetic but clinical reasons too. Sclerotherapy is most commonly used for the treatment of reticular varices and telangiectatic veins. Its technique is demanding and requires care, practice and knowledge. Clinical investigation (Level 1) and bilateral duplex scanning (Level 2) are necessary prior to treatment. Varicose veins must be treated before reticular varices and telangiectatic veins. Several devices such as Veinlite®, Syris®, and video projection can improve visualization of the pathological veins. Low-concentration sclerosing agent should be injected very slowly. Local compression with cotton balls and adhesive tape are sufficient in most cases. Light massage and anti-inflammatory cream may be recommended for prevention of bruising. Poor sclerotherapy can be divided into objective and subjective groups. Objective bad results usually include matting, discoloration, necrosis, scarring, and inefficiency of the procedure. Employment of sound techniques should avoid these problems. Subjective bad results are a usually problem of miscommunication between the phlebologist and the patient. Sclerotherapy of reticular veins and telangiectasias is not recommended in the case of deep venous incompetence with CVI.

## **Foam Sclerotherapy in 2009 (STD Pharmaceutical Symposium)**

Chairman: L. Tessari

### **Foam sclerotherapy- the state of the art**

P. Coleridge-Smith

P. Coleridge-Smith dealt with controversial issues of foam sclerotherapy and posed three questions: How well does foam sclerotherapy work? How safe is it? What do we do to optimize it?

The author reported his personal experience of an early occlusion rate of 100% in both GSV and SSV, GSV 88% SSV 83% at 1 year, GSV 88% SSV 91% at 5 years with a recurrence rate of 13%. As for adverse events, Henriot (1999) reported 9 visual disturbances/10 000 treatments, Guex (2005) 0.4% visual disturbance/12 173 treatments, and Morrison (2008) 8% with air foam (49 treatments), and 3% with CO<sub>2</sub> foam (of 128).

Hansen (2007) in 20 patients showed bubbles in the R atrium after 9-59 s in all patients, 13 of 20 showed bubbles in the L atrium: migraine + visual disturbance in 7 cases, 7 of 20 showed no bubbles in the L atrium: migraine + visual disturbance in 3. Regan (2008) studied 50 patients, treated by foam sclerotherapy - Varisolve, with transcranial Doppler and MRI. Transcranial Doppler showed a bubble rate

of 90% in the middle cerebral artery and in all patients MRI was normal 1, 7, and 28 days after treatment.

In conclusion, foam sclerotherapy is effective in obliterating veins with a recurrence rate of 10-20% at 5 years, which is no worse than surgical treatment. Larger volumes (> 10 ml) are more effective than small volumes (< 5 ml). Adverse events are more frequently reported with larger volumes of foam. Carbon dioxide foam is associated with fewer events. Varisolve - foam results in no MRI detectable cerebral lesions.

### **Foam sclerotherapy in Italy with postsclerotherapy compression**

A. Cavezzi

A. Cavezzi discussed some key points of foam sclerotherapy. The Tessari method has become the reference when forming the sclerosant foam. Bubble size depends on the type of drug and gas used. The CO<sub>2</sub>-O<sub>2</sub> mixture used to form the foam is less durable and has smaller bubbles. Low silicone syringes and large (21-25 G) needles are used to avoid foam degradation. As adjuvant measures: elevation of the limb during the procedure and post-injection immobilization without Valsalva delaying local compression + stockings. In the majority of cases foam sclerotherapy does not obliterate veins completely but transforms a high volume refluxing system in a low volume refluxing or antegrade flow system.

### **Recurrent varicose veins - foam sclerotherapy**

M. Perrin

M. Perrin reviewed the treatment of recurrent varicose veins, which after operative treatment are a common, complex, and costly problem. A new term PREVAIT (presence of varices residual or recurrent). The presence of PREVAIT is stated between 20 to 80%. Clinical diagnosis remains essential but does not allow a precise assessment of PREVAIT. Duplex scan is mandatory.

Interventional treatments for recurrent varicose veins include:

- non invasive treatment (drugs, compression) that may improve only symptoms.
- invasive treatment namely open redo surgery
- minimally invasive treatment including thermal ablation (endovenous laser, radiofrequency) and chemical ablation (liquid and foam sclerotherapy).

There is no data comparing sclerotherapy outcome after operative versus nonoperative treatment. Some data are available to estimate recurrent varicose vein operative treatment outcome. Open redo surgery provides variable results. Sclerotherapy is minimally invasive and repeatable and has provided good results. In asymptomatic patients without severe signs of venous insufficiency the decision to treat depends on the severity of the non invasive findings.

In symptomatic patients with recurrent varicose veins and hemodynamic anomalies or with varices at C4-C6 of CEAP interventional treatment must be considered. Although randomized controlled trials comparing outcomes of invasive and minimally invasive treatments are not available there is a large consensus for recommending ultrasound guided foam sclerotherapy as first line treatment in all patents except when the DS identifies a major reflux at saphenous femoral junction.

## Foam sclerotherapy treatment in varicose veins-results from 1200 cases

A. Bradbury

A. Bradbury reported his personal experience with over 1000 patients treated with ultrasound-guided foam sclerotherapy. Clinical and duplex follow-up was at 1, 6, 12, and 24 months. He reported a complete truncal occlusion rate of 83% and complete absence of visible varicose veins at a rate of 85% at 12 months. Rapid ulcer healing and low recurrence. Quicker return to normal activities and less pain, bruising and analgesia than after surgery. Statistically significant improvements in both physical (disease-specific) and nonphysical (relationships, appearance etc.) symptoms. A low level of side effects and complications: 2 DVTs (0.2%), 5 visual disturbances (0.5%), 2 migraine (0.2%), 1 allergy. In conclusion, ultrasound-guided foam sclerotherapy for varicose veins is extremely safe clinically and cost-effective.

## Closure Fast®, indication and procedure

T. Proebstle

The energy dosing problem that hampered radiofrequency ablation has been overcome with radiofrequency segmental thermal ablation Closure Fast. 100% immediate occlusion with an annual recanalization rate not exceeding 1-2% should be the benchmark. Sufficient energy dosing must be questioned in treatment of large veins with bipolar radiofrequency. Despite higher energy dosing, radiofrequency segmental thermal ablation has a good side effect profile.

## Varicose Veins

Chairperson: M. Perrin

Moderator: J. Barrett

### Tributary treatment in saphenous insufficiency – outcome after 4 years

P. Pittaluga

The author presented the midterm results of a retrospective study of varicose vein phlebectomy with conservation of a refluxing saphenous vein.<sup>1</sup> Clinical examination and duplex ultrasound were performed prior to the surgical procedures, 6 months and 1 year after, and then once a year. The study included 811 lower limbs operated on for first-time varicose veins with a preoperative a saphenous vein reflux >0.5 seconds. Surgery was of the GSV in most cases, and of the small saphenous vein in 2.3%. Saphenous vein reflux was reduced to < 0.5 seconds in approximately 70% of cases during the follow-up and at 4 years after surgery. Symptoms improved or disappeared in 80% during follow-up. Four years after surgery, the recurrence rate was below 88%. When ostiotruncal saphenous vein reflux extended to the malleolus preoperatively, the elimination of the saphenous vein reflux was less frequent. It was concluded that varicose vein phlebectomy with conservation of a refluxing saphenous vein can be an effective treatment in the midterm for the signs and symptoms of saphenous vein insufficiency and leads to nonsignificant saphenous vein reflux in more than two of three cases.

**Reference:**

1. Pittaluga P, Chastanet S, Rea B and Barbe R. Midterm results of the surgical treatment of varices by phlebectomy with conservation of a refluxing saphenous vein. *J Vasc Surg.* 2009;50:107-118.

**Do we need saphenofemoral junction ligation in endovenous procedures?**

B. Disselhoff

The author presented a randomized clinical trial to evaluate endovenous ablation (EVA) of the GSV with and without saphenofemoral junction (SFJ) ligation. 43 patients with bilateral varices were enrolled and treated in one limb with EVA alone and in the other limb with EVA +SFJ ligation. Follow-up with duplex scanning was performed at 6, 12, 24 months. After 2 years the recurrence rate was 17% in the EVA group and 13% in the EVA + SFJ ligation group. The occlusion rate was 88% in the EVA group and 98% in the EVA+SFJ group. Recurrences were caused by an incompetent SFJ (9%) and incompetent tributaries (8%) in the EVA group, while in the EVA + SFJ ligation group recurrences were due to neovascularization. There was no significant between-group difference in bruising, pain score, or tightness. In conclusion, the addition of SFJ ligation made no difference to the short-term outcome.

**Foam sclerotherapy – the challenge of neurological symptoms.**

N. Morrison

The author focused his presentation on the neurological symptoms during foam sclerotherapy. 59 patients underwent ultrasound-guided foam (CO<sub>2</sub>/O<sub>2</sub>) sclerotherapy for saphenous and nonsaphenous leg veins were studied with transcranial Doppler monitoring of the middle cerebral artery. The incidence of high-intensity transient signals was of 32% in all patients. 63% of asymptomatic patients had high-intensity transient signals compared with only 37% of symptomatic patients. The incidence of high-intensity transient signals was not significantly different between patients receiving <10 ml of foam and those receiving >10 ml. The incidence of symptoms in the low volume group was double that in the high volume group.

In conclusion the injection of CO<sub>2</sub>/O<sub>2</sub> sclerosant foam in superficial veins resulted in detection of emboli in the middle cerebral artery in 1/3 of patients treated. Silent emboli were frequent. Incidence of symptoms or high-intensity transient signals was not avoided by injecting less than 10 ml.

**Pathophysiology of visual disturbance occurring after foam sclerotherapy**

J-L. Gillet

A prospective multicenter study was carried out to validate the hypothesis that visual disturbances after foam sclerotherapy correspond to aura and are not transient ischemic cerebrovascular events.

20 patients (C2 in 16, C3 in 4) treated with foam sclerotherapy (volume of injected air 5 to 10 ml) were studied with MRI (T1, T2, T3, diffusion) within 14 days after

treatment. Visual disturbances occurred in 8 patients, dysphasic speech disturbance in 1, headache in 11. All MRIs were normal.

This study showed that visual disturbances occurring after foam sclerotherapy correspond to aura and suggested a pathophysiological hypothesis resting on the release of endothelin that would reach the cerebral cortex through a patent foramen ovale. Endothelin has been shown to trigger aura.

## Iliofemoral obstruction - how to treat the disease?

S. Raju, P. Neglen

This presentation was divided into two parts: S. Raju discussed the pathophysiology of iliac venous obstruction and P. Neglen gave the technical details of treating this underdiagnosed disease.

CVI has two main causes: postthrombotic syndrome, which produces obstruction and venous reflux, and primary venous insufficiency without previous DVT. Venous reflux may occur in both cases, but in the majority of patients there is an associated underdiagnosed iliac vein stenosis. Nonthrombotic iliac vein lesions, such as the webs and spurs described by May and Thurner, are commonly found in the asymptomatic general population. However, the clinical syndrome, variously known as May-Thurner syndrome, Cockett syndrome, or iliac vein compression syndrome, is thought to be a relatively rare contributor to CVI, predominantly affecting the left side of young women. In the author's opinion, intravenous ultrasound can detect iliac vein stenosis unseen in phlebographic studies. Ascending phlebography continues to be the gold standard for venous iliac stenosis, but must be done in different projections to detect iliac venous stenosis, which often does not appear in anteroposterior projection. Correction of iliac venous stenosis, without correction of associated reflux, offers a high rate of venous ulcer healing and improvement in pain/edema, with a low recurrence rate during long periods of follow-up.<sup>1</sup> S. Raju recommends treatment of iliac vein stenosis based on clinical considerations in patients with pain, swelling, skin changes, or ulcers with an iliac vein stenosis where previous conservative measures have failed.

In the second part of the session, P. Neglen presented the technical details of performing an iliac vein angioplasty. Arterial techniques are not necessarily transferable to veins. This technique must be done in a fully equipped endovascular/angiographic suite and intravenous ultrasound is mandatory to achieve optimal outcome. Stenting is mandatory in the treatment of venous obstruction because, if not stented, the venous stenosis will recur early. The authors recommend access to the femoral vein below the suspected obstruction under ultrasound-guided vein puncture. In cases of treating stenosis close to the confluence of the common iliac veins, especially when using Wallstents, the stent has to be placed well into the IVC to reduce proximal restenosis. The "double-barrel" stenting technique is recommended in cases of bilateral occlusion. Usually, large stents are employed (14-18 mm diameter). Incidence of vein rupture is low in spite of use high balloon pressures (more than 18 atm). The stent is redilated after insertion to achieve a good wall apposition as evaluated by intravenous ultrasound. The entire obstruction is covered as outlined by the intravenous ultrasound to ensure adequate in- and outflow, which is crucial for long-term patency. Overlap of stents more than 2 cm is essential and should be extended caudally to the

inguinal ligament when necessary. The patency rate is related to incomplete treatment or other factors, not to metal load. Patients are anticoagulated preoperatively with LMWH. After the surgical procedure, low-dose aspirin is used and, in patients previously treated with anticoagulant, oral anticoagulation is reintroduced. Sequential compression therapy is used postoperatively.

### Reference

1. Raju S, Neglen P. High prevalence of nonthrombotic iliac vein lesions in chronic venous disease: a permissive role in pathogenicity. *J Vasc Surg.* 2006;44:136-143; discussion 144.

## Lasers And Veins

R. Weiss

Use of the laser (light amplification by stimulated emission of radiation) was presented with a view to treating telangiectasias. The arguments in favor of the laser for leg veins were cited as easier technically, less bruising, easier for smaller vessels, and reduction of telangiectatic matting.

It was stated that one must always keep in mind a logical progression in the treatment of leg telangiectasias: 1- Begin with cut-off of reflux from SFJ/SPJ (surgery, endoluminal laser closure or radiofrequency); 2 – Ambulatory phlebectomy of tributary veins (usually > 4 mm); 3 – Sclerotherapy of remaining veins; 4 - Laser or intense pulsed light for remaining telangiectasias.

It was necessary to define optimal parameters for each procedure, as wavelength, pulse duration, fluence, spot size, and adequate cooling to avoid epidermal damage. Suggested types of cooling included gel (cold, refrigerated), contact cooling, dynamic cooling by spray, and air cooling. It was also explained why cooling is necessary: 1 – normal skin temp is around 33°C; 2 – a 15 msec pulse of 70 J/cm<sup>2</sup> heats the skin to 43-45°C; 3 – with contact cooling the skin cools to 15°C and after a laser pulse the skin heats to 25-30°C; 4 – with dynamic cooling the skin cools to 12°C and after a laser pulse the skin heats to 30°C.

The indications for use of the laser on leg telangiectasias were as follows: 1 – contraindications to sclerotherapy; 2 – inexperience with sclerotherapy; 3 – resistant matted telangiectasias; 4 – fine caliber, pink telangiectasias, which may be difficult to treat with any technique.

It was concluded that sclerotherapy for telangiectasias still remains the gold standard, in more than 95% of cases. However, in less than 5% of cases lasers can be used, in particular, long-pulse Nd: YAG 1064 lasers.

## Session of the American College of Phlebology

### **Preliminary results of low-energy density laser ablation treatment of incompetent truncal veins.**

J. Mauriello, E-J. Sanchez, J. White, W. Schroedter, B. White

J. Mauriello presented preliminary data on laser treatment using a low wavelength of 1470 nm and low linear endovenous energy density. 49 vessels (21 GSV, 27 SSV, 1 anterior accessory) in 24 patients were treated (6 C2, 12 C3, 5 C4, 1 C5 CEAP). Mean diameter of GSV at SFJ was 8.1 mm and of proximal SSV 4.9 mm. The veins were ablated using radial emitting fibers at 3 watts, delivering a mean low linear endovenous energy density of 25.6 joules/cm. Postprocedure follow-up with duplex was at 6 months. After the procedure only two GSVs remained patent but sclerotic with flow for 3.6 cm from the superficial epigastric vein, but were distally occluded. Minimal perioperative pain and bruising, no paresthesia or heat. At 6 months one SSV was recanalized. The same two GSV remained patent for 4-6 cm past the superficial vein and closed distally. Low-energy density laser ablation was effective in chronic venous disease treatment with minimal patient discomfort.

### **Compression therapy after phlebologic interventions: How Much? How Long? How High? A United States Perspective**

T. Morrison

T. Morrison reviewed the compression protocols used for cosmetic and medical vein procedures in the USA. There are five different classifications for compression: British, German, French, European, USA standard. The British standard Class one is 18-24 mm Hg, while USA Class one standard is 20-30 mm Hg. There is a need to refer to mm Hg instead of Class I or II. Compression stockings are classified on the basis of the pressure applied at the ankle. The survey supported the use in the United States of compression stockings after cosmetic and medical vein procedures. The majority (44%) used compression for 3 weeks after cosmetic sclerotherapy, and for 2 weeks (68%) after endovenous thermal and chemical ablation and phlebectomy. The majority (42%) used 20-30 mm Hg after cosmetic procedures. 15% used 20-30 mm Hg after medical procedures. The majority used thigh-high compression after cosmetic and medical vein treatments.

### **Effectiveness of single injection of sodium tetradecyl sulfate in predicting outcomes following ultrasound foam sclerotherapy using an ultrasound scoring system**

P. Raymond-Martimbeau

P. Raymond- Martimbeau showed the effect of different sodium tetradecyl sulfate (STS) concentrations on an ultrasound scoring system to predict outcomes following ultrasound foam sclerotherapy of the great saphenous vein (GSV). 64 sclerosed proximal GSVs in 42 patients with saphenofemoral junction incompetence were classified into four groups (A, B, C, D). The vein score was composed of vein wall thickness, lumen filling percentage, and vein diameter reduction.

Each group received a single injection of STS . Group A with 1% STS 4 ml, Group B with 1% STS 8 ml, Group C with 3% STS 4 ml and Group D with 3% STS 8 ml. The GSVs were analyzed at 1 month and 1 year post-injection.

The overall ultrasonic score was significantly affected by the STS concentration. Using the Tukey post hoc test showed that group A had a significantly lower overall score than group B . There was no significant difference in the ultrasonic score between any other groups . Time of scoring also had significant effect on the overall ultrasonic score, with the score being significantly higher at one year than at one month (except for group D). There was also significant interaction between concentration and time of scoring . In conclusion, the ultrasonic score was significantly affected by STS

concentration, time of scoring, and interaction between the two factors. Ultrasonic great saphenous vein sclerosis images can be differentiated by their characteristic features of wall thickness, endoluminal filling, and vein diameter reduction.

### **The complementary roles of surgery, endovenous thermal ablation, and foam sclerotherapy in the treatment of chronic venous insufficiency - the U.S. perspective.**

N. Morrison

N. Morrison gave a personal overview on the complementary role of surgery, endovenous thermal ablation in the treatment of chronic venous disease. The objectives of the various treatments proposed are the ablation of axial and perforator vein reflux, improvement of leg function and cosmetic appearance, and minimization of recurrence and complications.

In the U.S., minimally invasive, percutaneous, endovenous treatment methods have largely replaced the traditional surgical procedure. Adjunctive treatment is considered to avoid recurrences in saphenous vein and include ablation of incompetent accessory saphenous tributaries, persistently incompetent perforator veins, and incompletely ablated truncal veins. Incompetent distal saphenous vein, incompetent tributaries and persistently incompetent perforators must be eliminated.

Mid-term results of endovenous thermal ablation seem to be similar to those of surgical treatment, with fewer complications. Endovenous foam chemical ablation also appears to be effective, with infrequent complications, but with rare serious neurologic adverse events.

## **VNUS workshop**

Chairpersons: T. Proebstle, M. Vasquez

This workshop on the use of radiofrequency for ablation of varicose veins was organized by VNUS Laboratories.

### **Small Saphenous Veins with ClosureFAST**

J. Alm

The first speaker, J. Alm reported on the use of ClosureFAST in small saphenous vein disease. In this study, 603 limbs in 468 patients were treated. The mean length of the small saphenous vein treated was 24.9 centimeters, and the mean



procedure duration was 12 minutes. After one year of follow-up, 97.9% of treated veins were occluded. A low proportion of patients had paresthesia in the weeks following the procedure (2.1%), and this proportion further decreased after six weeks. J. Alm was asked by the audience how to minimize this complication, and in particular whether trying to localize nervous structure before the procedure would help. However, the use of tumescent anesthesia separates the catheter from adjacent structures, which minimizes such complications.

### **ClosureFAST, 3-year follow-up**

T. Proebstle

T. Proebstle gave the 2-year follow-up results of a multicenter multinational study using ClosureFAST for the great saphenous vein in varicose disease. The 225 patients included (female 74%, 295 limbs) were managed in an outpatient setting, under tumescent local anesthesia. Combined procedures were allowed, and 13% and 56% of patients underwent concomitant sclerotherapy or miniphlebectomy, respectively. Three days after the procedure, 99.7% of treated veins were occluded. After two years, the occlusion rate was still very high: 95.2%. Only 3 patients had clinically relevant recanalizations. Regarding the side effects, the rate of paresthesia was 3.4%, 2.0%, and 0.0% at 3 days, 3 months, and one year, respectively. No DVT was observed. Many questions were raised by the audience. As regards to how distally the vein can be treated, the answer was that typical treatment would go down to the upper calf, but could be limited to mid-thigh or conversely to lower calf according to the lowest level of vein incompetence. There are no recommendations about thromboprophylaxis, but such treatment should be considered in high-risk patients. When asked where to start the treatment, T. Proebstle reminded the audience never to start the treatment less than 2 cm from the saphenofemoral treatment, regardless of the epigastric vein insertion. Also, he stressed the importance of not immediately treating subcutaneous or extrafascial veins when they are not at least 1 to 1.5 cm deep under the skin.

### **Perforators with the VNUS RFS catheters**

M. Vasquez

M. Vasquez reported his experience in the treatment of perforators with radiofrequency catheters. He first discussed whether or not adjunct procedures to perforators are required when treating saphenous veins. In a longitudinal study of patients initially treated with radiofrequency, in which the one-year occlusion rate was 87%, there was no need for a new procedure during follow-up in 70% of patients. Among the 30% of patients who underwent complementary treatment, only 3% had perforator treatment. Thus, it is not recommended to systematically treat the perforators as an adjunct to the treatment of saphenous veins. If indicated during follow-up, treatment of perforators could be made using radiofrequency. The treatment should never be performed closer than 0.5 cm from the deep vein, and when an artery is seen adjacent to the perforator vein. The treatment should be performed under ultrasonographic control, and the lack of DVT should be checked by ultrasound 72 hours after the procedure. However, M. Vasquez told

the audience that he was not very happy with the results, with a success rate of only 50%. Concomitant foam sclerotherapy of the remote tributary behind the treated segment could be of interest. On the other hand, he had doubts that foam sclerotherapy could be used alone given the size and the very rapid washout of some of these vessels.

### **Closure vs Laser (Recovery Study)**

O. Goeckeritz

Finally, O. Goeckeritz presented the results of the RECOVERY study, a multicenter, multinational, single-blind, randomized trial that compared Closure versus laser for the treatment of saphenous veins. End points were the occlusion of the vein and the complications of the procedure. Of the 87 patients included, 46 were treated with radiofrequency and 41 with laser. At one month, all patients in both groups had satisfactory venous occlusion, and no between-group differences were observed at one month in terms of VCSS and quality of life score. However, statistically significantly fewer adverse effects were observed in patients treated with radiofrequency. Pain and tenderness scores at one week, as well as use of analgesic drugs, were less important in this group. On the other hand, more patients in the radiofrequency group developed an ecchymosis. No serious adverse events were seen in any group. Paresthesia was observed in 1 patient in the Closure group, and in 2 patients in the laser group. No DVT was observed in any group. The conclusion was that both methods are effective and safe for the treatment of varicose veins, but that post-procedure pain and tenderness could be less when radiofrequency is used.

## **Postthrombotic syndrome**

### **The Neovalve in Postthrombotic syndrome – Tips and Tricks**

O. Maleti

Postthrombotic syndrome after an episode of DVT is produced by the presence of an axial reflux uninterrupted from the groin to the calf. Until now, several valve repair techniques (valvuloplasty, valve transposition, or use of cryopreserved and bioprosthetic venous implantation) have been used, but all have several limitations: postoperative thrombosis, inadequate segments for transplant, incompetence of transplanted venous segments, etc.

Some noninvasive studies must be done before to indicate a neovalve construction. Duplex ultrasound and air plethysmography studies should be performed to determine the residual volume after calf contraction. In addition, ascending and descending venography are considered mandatory before valve venous reconstruction. The hemodynamic, morphological, and clinical parameters are of vital importance in deciding whether to perform such procedures. Cava and iliac vein patency, state of femoropopliteal venous segment, amount of deep venous reflux from cava to calf, presence of good calf contraction, and the presence of efficient deambulation are other aspects that must be considered before neovalve

reconstruction. Clinically, deep venous surgery is indicated in cases of severe CVI (grades C6 of CEAP). The speaker then discussed the details involved in neovalve reconstruction. The recommendation involved valve reconstruction in the mid-thigh segment thereby avoiding the proximal and distal thigh segments, as this is an easier location to tackle. Removal of all adventitial layers is recommended. Different kinds of venotomy can be used, but the author recommended longitudinal venotomy as a better option for reconstruction. After this, it is necessary to do an endophlebectomy to remove all the fibrotic intraluminal material that appears after a DVT. There are two different technical options to create a neovalve, depending on the parietal conditions (monocusp or bicusp neovalve). The author recommended flap fixation in the semi-open position to avoid flap collapse with venous reflux.

Postoperative therapy is based on anticoagulation, early physiotherapy, and elastic compression. Patients are anticoagulated with unfractionated heparin during the surgery and the day after. This is followed by LMWH for 2 days and oral anticoagulation for 6 months. Leg elevation (22°), pneumatic intermittent compression and physiotherapy, and short-stretch bandage are mandatory after the surgical procedure. Patient deambulation is restored the second postoperative day. Ulcers must be cleaned every day and bandaging maintained until the ulcer heals. The most common postoperative complications are hematoma and seroma, which can be avoided by careful preoperative surgical dissection and hemostasia. The indications of this technique are patients with severe chronic insufficiency (class C6 of CEAP) and some cases of C5 and C4b with severe reflux (Kistner class IV) in patients with good ankle movement and normal deambulation without peripheral arterial disease. Superficial venous reflux and calf perforator insufficiency must be corrected before any intervention. Before surgery it is necessary to reduce leg edema, improve the inflammatory process, and clean the ulcer. Severe thrombophilic diseases, heparin contraindication, previous PE with low residual breath capacity are contraindications to this procedure. Femoral, iliac, or cava stenosis is a relative contraindication that can be corrected.

Finally, the author presented a series of 51 procedures in 46 patients treated during the last 8 years with a follow-up of 42 months (1-96). The neovalve competence obtained with this technique was 86% with an ulcer healing rate of 91% and ulcer recurrence in only two cases. DVT appeared in 7.8% of the cases during follow-up.

In conclusion, neovalve constructions can be a good way to correct venous reflux after DVT in selected patients with severe postthrombotic syndrome.

## Deep Venous Insufficiency

Chairperson: O. Maleti

Moderator: N. Labropoulos

### Three-year follow-up of patients with deep vein thrombosis monitored in the TULIPA registry

H. Gerlach

TULIPA is a registry of DVT patients in Germany, established to monitor DVT management. A representative cohort of 310 patients (50.7% men, mean age

57.3 years) was followed up. Thrombosis was located in proximal veins in 49.4%, in calf veins in 36.1%, and in muscle veins in only 14.5%. The patients underwent follow-up examination 3 years later. The prevalence and severity of PTS were assessed clinically (Prandoni score). PTS was present in 34.7% in the total group, and was more frequent after proximal DVT. However, after isolated muscle vein thrombosis, mild PTS was relatively frequent and even the prevalence of severe PTS was not negligible. The modality of DVT treatment was also evaluated. Anticoagulation had lasted more than one year in only 25% of patients. Compression stockings had been used immediately after DVT diagnosis in 92.8%. One year later, 81.8% of patients still continued wearing compression stockings (80% of them persistently, mostly compression class II). In summary, the recent guidelines for DVT treatment have been followed quite adequately. One surprising result is the relatively high prevalence of PTS after isolated muscle vein thrombosis.

### **The time sequence of the development of axial deep reflux following lower limb deep vein thrombosis – A prospective study over 5 years.**

A. Van Rij

114 patients (122 limbs) with DVT underwent follow-up examination (clinical assessment, duplex ultrasound, and air plethysmography). The patients were divided into three groups – extensive (iliofemoral) thrombosis, thrombosis of the thigh, and thrombosis of the calf. Venous recanalization was similar and quite satisfactory in all groups and occurred mostly in the first year after DVT. There was an inverse relationship between reflux and clot load. 5 years after an iliofemoral thrombosis, 45% of patients had axial reflux as a consequence of segmental reflux progression, with continuing deterioration. Axial reflux was predicted by pathological venous filling index and impaired outflow at two years. If DVT was isolated at the calf, popliteal, or femoral region, only segmental reflux was present.

### **Iliac vein stenting – Indications and long-term results**

S. Raju

Iliac venous stenting is a low-risk procedure, with negligible mortality and minor morbidity. Moreover, venous stents have better patency and less in-stent restenosis than arterial stents. Following stenting, only aspirin therapy is needed (if no thrombophilia is present). Intravascular ultrasound is often needed to diagnose iliac vein obstruction.

The long-term results of iliac vein stenting were presented. 528 limbs with combined obstruction and reflux underwent this procedure. In follow-up, good stent patency was documented, as well as a substantial improvement of symptoms (pain, swelling), ulcer healing, and better quality of life. Reflux remained unchanged or improved.

In summary, correction of iliac vein obstruction by stenting can lead to substantial and lasting symptom remission and this procedure might be suggested even from stage C3 of the clinical CEAP classification.

## **Long-term results of stenting for iliofemoral vein obstructive lesions**

O. Hartung

98 patients (104 limbs) with obstruction of iliofemoral veins underwent venous stenting. All patients were symptomatic (venous claudication, pelvic congestion, venous insufficiency). The etiology of the obstruction was: May-Thurner syndrome, previous DVT, retroperitoneal fibrosis, congenital vein hypoplasia. The patients were examined with duplex ultrasound and CT or MR angiography prior to stenting. The procedure was performed via percutaneous access and self-expanding stents were used. There were no major complications; early complications were rare (early rethrombosis in 2 cases). During follow-up, 7 patients had restenosis and 4 cases of rethrombosis occurred. Long-term patency rates were satisfactory. Stenting as a treatment of choice for iliofemoral venous obstruction was further discussed and the following indications were suggested: patients symptomatic or disabled despite medical therapy; with no malignancy; with or without reflux. Thrombophilia, pregnancy, and the presence of an inferior vena cava filter or clip are not contraindications. After DVT, the procedure should be delayed for 6 months, but could be successful even many years after the event.

## **Prevention of postthrombotic syndrome by compression therapy – evidence from comparative studies.**

H. Partsch

Elastic compression stockings (ECS) and early ambulation are recommended in mobile DVT patients. Reducing the incidence of PTS with ECS is very well documented. Therefore, their use after DVT is recommended in the last ACCP evidence-based guidelines with 1A grade. ECS should be started as soon as possible and continued for at least 2 years. However, one survey documented limited adherence to these guidelines and great differences between respective countries in ECS use.

169 patients with proximal DVT were randomized to ECS versus no ECS use. During follow-up, skin changes occurred significantly more often in the non-ECS group. Symptom relief was significantly better in the ECS group during the first year, but not thereafter.

In conclusion, in DVT treatment, not only adequate anticoagulation (preventing recurrence) but also antistasis measures (preventing PTS) are necessary.

## **Impact of iliofemoral thrombosis on the development of postthrombotic syndrome**

N. Labropoulos

A prospective study of patients with acute first iliofemoral DVT was performed. The patients were divided into three groups (DVT above and below the inguinal ligament or both above and below the ligament). Patients with previous DVT, chronic venous disease, thrombolysis, short life expectancy, or interruption of oral anticoagulation were excluded. Finally, 301 limbs were included with a mean follow-up of 3.8 years.

In the long term, the thrombotic burden had a marked impact on the development of PTS. Isolated iliac DVT had a good outcome, but the number of patients was

too small for drawing firm conclusions. Iliofemoral DVT had the worst outcome (the most frequent progression to skin damage). These results suggest that more aggressive treatment (eg, pharmacomechanical thrombolysis) is probably appropriate for iliofemoral DVT. Two large randomized trials are expected to demonstrate the efficacy and safety of the interventional therapy (CAVENT, ATTRACT).

### **Neovalves in postthrombotic syndrome: long-term results.**

O. Maleti

Conservative therapy is often insufficient to control the symptoms of PTS. The valvular incompetence may occur due to partial or complete destruction of the valve. Neovalve construction is one possible technique for correction of valve insufficiency. The long-term results of 51 neovalve construction operations were presented. 51 consecutive patients with severe CVI underwent surgery, with a mean follow-up of 42 months. The technique was modified during the study leading to better neovalve competence. The clinical improvement following neovalve construction was substantial (cumulative ulcer healing 91%, significant improvement in patients of class C5), and safety was satisfactory (mortality 0, minor complications in 17.5%).

The results suggest good efficacy of this technique in patients with PTS. However, symptoms may recur due to the natural evolution of venous disease.

### **The future of artificial venous valves**

M. Dalsing

Artificial venous valves can be defined as any venous valve substitute. Two groups are distinguished – non-autologous and autologous valves. Many experimental and clinical studies have been done so far. Clinically, only autologous valves demonstrated any longevity. With non-autologous valves, the choice of material is the difficult task.

A percutaneous approach will likely be the most appropriate, using self-expanding metal designs (but with minimal metal exposed to the blood flow).

Other possibilities are still being studied: bioabsorbable organic biopolymers, corroded metals, decellularized allograft valves. Tissue engineering is promising in this field, with the possibility of creating a tube from various natural or synthetic materials seeded with fibroblasts.

Research on artificial valves is still in its early stages and many problems remain to be solved: mechanical and biological challenges to the valve, the risk of rejection, the risk of early thrombosis or delayed fibrosis.

## Venous malformation

### Venous Malformations and Lymphedema

Chairperson: B-B. Lee

Moderator: N. Piller

#### **Comparative prospective study between volume and low and high interface pressure under short-stretch compression bandages in the treatment of breast cancer lymphedema**

R. Damstra, H. Partsch

R. Damstra presented a prospective study in which the authors compared the efficacy of low-pressure versus high-pressure short-stretch compression bandages in patients with postmastectomy arm lymphedema, stage 2,3 (with pitting edema). 36 breast cancer patients with one-sided lymphedema of the arm were randomized into two groups: Group A (n=18) received short-stretch bandages applied with low pressure, between 20-30 mm Hg, and group B (n=18) the same type of bandages applied at a pressure of 44-58 mm Hg. The pressures under the bandages were measured at distal and proximal levels (wrist and elbow) using air-filled transducers (Kikuhime device). The bandages were renewed after 2 and 24 hours. Arm volume was measured by water displacement volumetry before bandage application, after removal of the bandages at 2 and 24 hours. The results show that the arm volume reduction was significantly greater in group A (low pressure) at 2 hours and there were no significant differences between the two groups at 24 hours. Assessed using a visual analogue scale, bandages in group A were better tolerated.

In conclusion, the speaker pointed out that in contrast to the leg, where a dose-response relationship between compression pressure and volume reduction could be demonstrated, in arm lymphedema light short-stretch bandages provoke fewer complaints and are as effective as tightly applied short-stretch bandages after 24 hours. Whether these different results are caused by the various pathophysiological conditions (eg, muscle pump differences, pathological lymphatic drainage characteristics of the arm, etc...) remains a question of debate.

## Miscellaneous

### Esthetic treatments and phlebology practice

M. Goldman

Venous abnormalities are often associated with other cosmetic problems and skin diseases such as pigmentation, solar lentigos, angiomas seborrheic keratosis, scars, etc. Elimination of the scar telangiectasia may reduce the swelling and bulkiness of the scar and normalize the surface texture. Phlebectomy, sclerotherapy, and different types of lasers are commonly used in these cases. Ambulatory phlebectomy or foam sclerotherapy is used to treat veins > 4 mm. Only then would one consider the laser or intense pulsed light for any remaining veins. Prominent veins on the breast, forehead, and eyelid are not uncommon and patients often seek their removal. Sclerotherapy is a procedure that has been successfully used to permanently remove them.

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1 - Ramelet AA, *Clin Hemorheol Microcir.* 2005;33:309-319. 2 - Nicolaidis A, *Int Ang.* 2008;27:1-60.



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