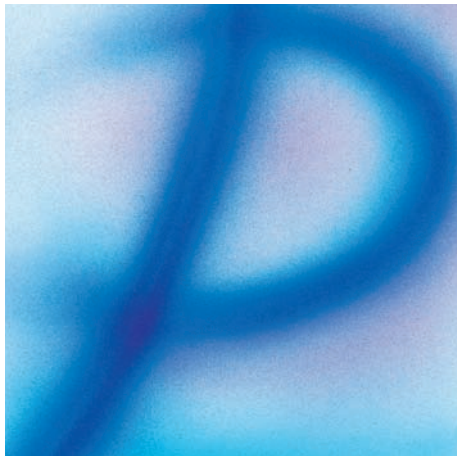
PHLEBOLYMPHOLOGY

ISSN 1286-0107

Special issue



Vol 20 • No.1 • 2012 • p1-56

AIMS AND SCOPE

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

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

Phlebolymphology is scientifically supported by a prestigious editorial board.

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

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

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Indexed in EMBASE , PASCAL, Index Copernicus and Scopus.

ISSN 1286-0107

Phlebolymphology

Preface

Angelo SCUDERI

The European Chapter Meeting of the Union Internationale de Phlébologie (UIP) which took place in Prague, Czech Republic, closed the 4-year Presidency of Eberhard Rabe. The presidency was handed over to me in Prague, and I will serve the UIP during the next four years as President. I will do my very best to advance the interests of the UIP with new ideas and activities and to continue what was started by the former presidents.

The aims of the UIP are:

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

In line with these aims, one major activity of recent years has been the inauguration of consensus groups, working towards a worldwide curriculum of phlebology. This is a step towards an UIP-based educational system which may result in an UIP Certificate in the future. A major step in this direction was the consensus on a Training Curriculum in Phlebology which was published in 2010. In addition, the following consensus documents that have been published so far were described during the Prague meeting:

- Curriculum in Phlebology (K. Parsi)
- Primary lymphedema as a lymphatic malformation (B.B. Lee)
- Venous malformation (B.B. Lee)
- Classification of duplex findings after treatment of saphenous varicose veins (M. de Maeseneer)
- Deep venous insufficiency (F. Lurie)

The reinforcement of the UIP Fellowships with supportive sponsors from industry is in line with the aim of the UIP to encourage studies and research on disorders of venous origin. Three new awards were given in Prague.

Because it is the aim of the UIP to improve the recognition of chronic venous disease for the benefit of phlebological patients, a big epidemiological project was started in 2009. This is an observational, multicenter, descriptive survey of chronic venous disease. It is the largest international screening program including up to now 20 countries worldwide and approximately 90.000 participants. It is endorsed by the

UIP and supported by an unrestricted grant from the Servier Research Group. The first results on 70 000 subjects were presented during the UIP Chapter Meeting in Prague.

Meetings like the European Chapter Meeting in Prague 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.

As the new president of the UIP, my main goal, following the worldwide trend, will be to use modern means of communication such as the website and newsletter to "spread the word" regarding phlebology. Clearly the Medical Reporters' Academy ties in well with this aim.

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 their work in updating venous disease specialists' skills.

Happy reading.

Angelo SCUDERI
President of the UIP

Medical Reporters' Academy (MRA)

The reports from the European chapter of the Union Internationale de Phlébologie were prepared by the following members of the MRA team:

- **Giuseppe CALANDRA** (Italy)
- **Sylvain CHASTANET** (France)
- **Fidel FERNANDEZ-QUESADA** (Spain)
- **Jana HIRMENOVA** (Czech Republic)
- **Armando MANSILHA** (Portugal)
- **José Benhur PARENTE** (Brazil)
- **Attila PUSKAS** (Romania)
- **Igor ZOLOTHUKIN** (Russia)

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- **Andrew NICOLAIDES :** Vascular Screening and Diagnostic Centre; 2 Kyriacou Matsi ; Ayios Dhometios ; 2368 Nicosia - CYPRUS

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UIP CONSENSUS, UIP FELLOWSHIPS

Prague, Czech Republic, September 15-17, 2011

UIP News

Chairpersons: E. Rabe, A. Scuderi

Training curriculum in phlebology

K. Parsi (Australia)

K. Parsi presented a brief resume of the structure of the consensus document from the International Union of Phlebology that was published in *International Angiology* last year (Int Angiolog 2010 December; 29(6): 533-59). The aims of this consensus about Training Curriculum in Phlebology were to be incorporated in a Training Program by member countries, to act as a guide and to be adopted and modified to suit local needs for a 4-year training program. The different chapters were related to Anatomy, Basic Sciences, Pharmacology, Clinical Sciences, Consultation, Diagnostic Evaluation, Treatment Modalities, Adjunctive Education and Literature Reading.

- He also referred to the example of the Australian College of Phlebology and what is now its training program.
- Parsi concluded his presentation with reference to future directions: the curriculum should be used in training programs, the committee must receive feedback from members societies about the implementation of the program so that the consensus document can be revised every 2-4 years.

Deep venous insufficiency

F. Lurie (USA)

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 activity, 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 are 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 that of 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 deep vein thrombosis 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- to 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.

UIP Awards

BAUERFEIND Fellowships.

Compression therapy in superficial thrombophlebitis (winner of 2009)

K. Böhler (Austria)

Preliminary results of the still ongoing randomized, unblinded, controlled trial were presented. Adult patients with superficial thrombophlebitis (ST) are included (ST at least 5 cm long, not closer than 2 cm to saphenofemoral or saphenopopliteal junction, with clinical symptoms of inflammation). Those with concomitant deep vein thrombosis (DVT), known thrombophilia, cancer, immobility, peripheral artery disease or with ST after sclerotherapy are excluded. All patients receive low-molecular-weight heparin in a prophylactic dose and nonsteroidal anti-inflammatory drugs (NSAIDs) on demand. Patients are randomized to Group I (compression stockings, tailored to fit to every patient with the help of special 3D video imaging system) or to Group II (no compression used).

The main outcome is the reduction of pain – spontaneous pain (visual analogue scale), induced pain (Löwenberg test), and the consumption of NSAIDs. Additional outcomes are: reduction of erythema, change of thrombus length, development of DVT, and impact on quality of life.

So far, 36 patients have been included. Spontaneous pain and induced pain as well as the consumption of NSAIDs decreased significantly over time, but there were no significant differences between the compression and noncompression groups, only a tendency to slightly faster relief of induced pain and less consumption of NSAIDs after day 7 in the compression group. So far, the effectiveness of compression therapy in pain reduction in ST has not been proven in this study. More patients are needed before any definitive conclusions can be drawn.

The influence of compression stockings in the prevention of venous disorders in pregnancy (winner of 2011)

D. Milic (Serbia)

This project is an open, prospective study with three parallel study groups. The primary objective is to determine if use of Class 2 (23-27 mm Hg) or Class 1 (18-20 mm Hg) compression stockings reduces the incidence of venous disorders during pregnancy: emergence of varicose veins of any kind, hemorrhoids, leg swelling, VTE (thrombophlebitis, deep vein thrombosis, pulmonary embolism), and symptoms of venous hypertension (pain, night cramps, numbness, tingling, ache, itching, and heaviness). The secondary objective is to determine if regular use of Class 1 or 2 compression stockings reduces dilatation of superficial veins (great saphenous and small saphenous) and deep veins (femoral and popliteal) or decreases the incidence and level of reflux in the superficial and deep vein systems.

For this purpose, there will be follow-up of 300 pregnant women assigned to three different groups:

- 100 Pregnant women who will wear compression stockings (23-27 mm Hg-Class 2) during pregnancy and 6 months after delivery
- 100 Pregnant women who will wear compression stockings (18-20 mm Hg-Class 1) during pregnancy and 6 months after delivery
- 100 Pregnant women who will be without compression hosiery during pregnancy and after delivery.

The participants will be evaluated using both clinical and quality of life parameters.

KREUSSLER Fellowships

Catheter-directed foam sclerotherapy of varicose veins under tumescent anesthesia (winner 2009)

N. Tetsch (Germany)

Sclerotherapy in the treatment of varicose veins is a minimally invasive procedure, economical, with no general anesthesia, good aesthetic results, and various treatment options.

In the literature, occlusion rates vary after 3 months from 69% to 96% and after 1 to 2 years from 53% to 80%. The aim of this prospective, blinded, randomized, controlled trial was to achieve higher occlusion rates than those reported in the literature by adding perivenous tumescent solution (TA) during catheter-directed foam sclerotherapy (CDFS) of the great saphenous vein. The author presented preliminary data of 50 patients enrolled from August 2010 to August 2011 and divided into two groups. Group 1: 25 p CDFS +TA, group 2 CDFS with follow-up at 1, 6, and 12 months. Primary end point: 100% occlusion rate at 12 months with CDFS+TA, secondary end point: comparison of occlusion rates of great saphenous veins after treatment with CDFS with and without TA, comparison of patient satisfaction and symptom severity. Inclusion criteria: men and women age 18-89, diameter of incompetent great saphenous vein 5-10 mm measured 3 cm distal to the saphenofemoral junction. Exclusion criteria: symptomatic foramen ovale, pregnancy, ABI <0.9, severe cardiovascular disease, acute thromboembolic diseases, high risk of DVT (>3 of the following criteria: oral contraceptive, obesity, smoking, thrombophilia, long phases of immobility). The procedure included direct puncture of the GSV below the knee using duplex ultrasound guidance with application of 8 mL of 2% polidocanol foam (Easyfoam®) and in group 1 infiltration of saline solution (TA) along the whole length of the GSV. Post-interventional class II compression stockings (4 weeks), 30-min walking, low-molecular-weight heparin for 10 days. Study closure in August 2012.

Evaluation of systemic inflammatory response after varicose vein ablation with foam sclerotherapy and thermal radiofrequency ablation (winner 2011)

T. Willenberg (UK)

The study focuses on the systemic side effects that may appear after endovenous procedures and on whether the systemic side effects that may appear after foam sclerotherapy (FS) or radiofrequency ablation (RF) are related to the inflammatory response of the endothelial wall.

For this purpose, consecutive patients admitted to a unit of vascular surgery for treatment of varicose veins will be screened, with 15 patients undergoing RF and 15 FS. The exclusion criteria are pregnancy or breastfeeding, age <18 or > 80 y, inflammatory, infectious, or thrombotic disease, anti-inflammatory treatment, or obesity.

Blood will be sampled from the arm and from the common femoral vein in the treated limb, before, at the end of treatment, and 24 hours after treatment. Data will be collected for assessment of side effects.

Primary outcomes are levels of endothelin 1, tumor necrosis factor a, interleukin 1-b, and interleukins 4 and 5 before and 24 hours after FS or RF ablation.

Secondary outcomes are leukocyte count, D-dimers, and any related adverse effect.

The results of this pilot study may provide key information for further investigation of venous endothelial damage and help understand the mechanism of FS.

SERVIER Fellowships

Reduced expression of fragment dii-diii of soluble urokinase receptor (supar) predicts venous ulcers that fail to heal (winner 2009)

A. Ahmad (UK)

Based on the hypothesis that the cleavage of uPAR into its fragments (D1 and D2-3) is an important mechanism in ulcer healing, the aim of the research was threefold:

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.

Preliminary studies have shown a positive effect of suPAR in keratinocyte migration towards the ulcer wound that might help in venous ulcer re-epithelialization

Our initial results have confirmed the presence of uPA and its receptor within the environment of a venous ulcer. There was no uPA activity detected in any of the chronic wound fluids. Urokinase was detected in most of the wound fluids but not in tissue lysates. In contrast, suPAR immunoreactivity was present in both wound fluids and tissue lysates. Wound fluids showed increased amounts of all forms of suPAR (ie, DI-III, DII-III and DI) as compared with tissue lysates.

The role of innate inmunity in venous ulcer healing (winner 2011)

G. Szolnoky (Hungary)

A large number of putative genetic factors in the development of venous leg ulcer (VLU) have been described, most of them being involved in the mechanism of altered immune response in chronic wound healing. The role of humoral immunity remains to be elucidated. It is known that patients with VLU have a significantly weaker tuberculin skin test (TST) response than matched patients without VLU.

The aim of this study is to measure *Candida albicans* killing activity as a general and functional assessment of polymorphonuclear leukocyte (PMNL) function, to determine the expression of proinflammatory cytokines/chemokines along with the expression of TAM receptors.

40 patients with VLU and 40 controls (age- and sex-matched without VLU) will be compared in terms of isolation of PMNLs, total RNA isolation, and real-time quantitative PCR (QPCR) detection of the expression of TAM receptors (Tyro3, Axl, Mer), their ligands (Gas6 and proS), and pro- and anti-inflammatory cytokines/chemokines (TNFa, IL1, IL6, CXCL8, and IL10).

It is expected that in patients with VLU the baseline mean candida killing activity will be substantially lower than in subjects without VLU.

II
EPIDEMIOLOGY

Prague, Czech Republic, September 15-17, 2011

The Vein Consult Program, results from the first 70 000 screened subjects.

Chairpersons: E. Rabe, J-J. Guex
With the participation of F. Fernandez Quesada, J-J. Guex, A. Mansilha, A. Puskas, E. Rabe

VEIN CONSULT Program: an Update

E. Rabe (Germany)

The VEIN CONSULT Program, a joint initiative by the Union Internationale de Phlébologie and Servier, is the largest global effort to raise awareness of chronic venous disease among patients, health care professionals, and health authorities. It has been endorsed by the Union Internationale de Phlébologie (UIP) and supported by an unrestricted grant from Servier Research Group, and involves the collaboration of 4500 GPs and 500 venous disease specialists.

The aim of the program is to update information on the prevalence of primary chronic venous disease in different geographic areas, to compare the management of the disease between countries, and to improve our understanding of the relationship between general practitioners and venous specialists, in order to propose a straightforward approach to earlier diagnosis.

In this international, observational, prospective survey, the prevalence and impact of chronic venous disease were assessed in two steps. First, a screening program in primary care was used to describe the adult patient population with chronic venous disease. All consecutive adult outpatients over 18 years of age, male or female, who had signed an informed consent form and were not consulting for an emergency, were screened in a short period. Second, the follow-up program was carried out in secondary care to assess confirmation of diagnosis, patient description, venous risk factors, history of chronic venous disease, lower leg examination, investigations recommended, evaluation of costs, venous complications, and treatment. Patients were asked to fill in a self-administered quality-of-life questionnaire and to answer questions related to the cost of the disease.

The program ran throughout 2009 and 2010 in 20 countries worldwide. Thirteen countries have already completed the survey, in Eastern Europe (Georgia, Hungary, Romania, Russia, Serbia, and Slovakia), Western Europe (France, Spain), South America (Brazil, Mexico), and Asia-Africa (Pakistan, Singapore, UAE), totaling almost 70 000 patients. Meaningful data from these geographic areas will be presented during the special session devoted to the program in Prague. The findings clearly show that chronic venous disease is under-recognized and undertreated, and has a considerable impact on health care.

VEIN CONSULT Program is screening a very large number of patients from many countries using the same questionnaire and the same classification (CEAP), and

is the first to consider symptomatic patients, even at a very early stage (C0s), and to assess patients who consult spontaneously for chronic venous disease.

Clinical results from the first 13 countries

A. Puskas (Romania)

The VEIN CONSULT Program is the largest international epidemiological survey ever undertaken in the field of phlebology. The program ran throughout 2009-2011 in 20 countries worldwide. Thirteen countries have already completed the survey in Eastern Europe, Western Europe, Central and Latin America, and the Middle East/Far East, totaling almost 70000 patients. Subject screening was performed over a short period of time (1 week) in GPs' offices in a framework of nonemergency ordinary consultation for every person more than 18 years old. Primary care patients were mostly women (except in Pakistan) and were older in Europe than in other geographical areas. A majority (>60%) said they had a maternal history of primary chronic venous disease and around 9% had a personal history of venous thrombosis. For the first time symptomatic patients at the early stages (C0s) have been considered: 20% of screened patients complained of venous symptoms without any visible CVD. Reported symptoms in order of importance were: heaviness, pain, sensation of swelling and night cramps and were found to intensify mainly at the end of the day or after prolonged standing. Symptoms significantly increased with age and with severity of disease. Most screened subjects believed they had leg problems at the time of consultation (52.8%), while only about 20% presented spontaneously for venous care. This shows that patients underestimate chronic venous disease. Chronic venous disease is also underestimated by GPs, who often need the presence of one sign to diagnose the disease. After examination of legs by physicians, it appeared that 62% of subjects had visible signs at least on one leg. So in the global population 81% of patients suffer from chronic venous disease of stages C0s to C6s.

Quality of life and costs of chronic venous disease: first results from the Vein Consult Program

A. Mansilha (Portugal)

The author presented the results of the VEIN CONSULT Program concerning the evaluation of the impact of chronic venous disease on patients' professional activities and health, and its effects on their quality of life.

The subjects found to have chronic venous disease after examination by general practitioners were requested to fill in a self-administered questionnaire reporting features about their professional activities and quality of life. The CIVIQ-14 was used to assess quality of life (score 0 for bad to 100 for very good quality of life). Patient data were compared with the clinical outcomes reported by practitioners. Data from the countries that had completed the survey at the time of analysis were pooled.

A total of 25 819 questionnaires from 10 countries (Russia, Romania, Slovakia, Georgia, Serbia, Hungary, Mexico, Emirates, Singapore, France) were analyzed. Eighty one percent of questionnaires were completed. Six percent of patients had been hospitalized and 3.7% had changed their professional activities

because of venous leg problems. Loss of work days was reported in 15% of chronic venous disease patients. Number of lost work days did not exceed 1 week for most (45.2%), while 30% of them lost more (18% >1 week and 12% >1 month). Quality of life scores decreased with higher frequency of lost work days (from 68.40±19.50 for 1 time to 43.04±22.32 for >3 times) and with duration of the absence from work (from 77.25±18.84 for <1 week to 56.97±22.19 for >1 month). And so with increasing severity of chronic venous disease, ranging from 80.71±16.15 in patients with telangiectasias to 44.17±23.51 in those with an ulcer, and with the presence of a symptom (84.77±15.96 in patients without pain versus 66.86±19.80 in those with pain).

The author concluded that chronic venous disease worldwide is responsible for large productivity losses, as well as the physical and psychological suffering of patients which is reflected in worsened quality of life.

Results drawn from the venous specialists

F. Fernandez (Spain)

The second step of the VEIN CONSULT Program, carried out by venous specialists, aims to characterize the typical chronic venous disease patient, and studies the characteristic of those who are referred for further studies and treatment.

Patients previously diagnosed by general practitioners as suffering from chronic venous disease (Step 1) usually went to specialized centers for confirmation of diagnosis and more in-depth investigations (Step 2). In countries which performed both Steps 1 and 2, patient data from specialists were pooled and compared with the corresponding data recorded by general practitioners.

A total of 4502 subjects diagnosed with venous disease in Step 1 of the survey had a secondary diagnosis and investigation in specialized centers, of which 20% were from Mexico and 80% from Russia. This shows a different behavior between countries regarding the need to refer diseased patients to specialists.

Patients referred to a specialist were older (54.8 vs 50.3 years), more often women (78.8% vs 73.5%), had higher body mass index (28.3 vs 27.5 Kg/m^2), had more family history of chronic venous disease (52.8% vs 47.2%) and more personal history of thrombosis (18.6% vs 13.4%), and were at more advanced stages (51.6% vs 37.2% in C3-C6) than subjects screened in Step 1. The pathophysiology was reflux in 70.6% and obstruction in 15% of patients. When reflux was present, it was mostly in superficial veins (68.3%), then in perforators (17.2%) and the deep venous system (14.5%). Superficial reflux was mostly seen in patients with varicose veins, edema, and skin changes. Obstruction was found in deep (53.7%) and superficial veins (46.3%). Of the invasive treatments that were set up, open surgery ranked top (25.8%) ahead of liquid sclerotherapy (17.8%), foam sclerotherapy (9.1%), and endovenous ablation (4.7%).

There were no between-sex differences in the initial stages of the disease (CEAP C0-C2), but C3 was more frequently found in females (35.8 vs 28.6%, $P<0.01$) and skin changes (C4-C6) in males (15.6 vs 23.9%, $P<0.001$).

These results mainly mirror Russian and Mexico habits regarding patient referral, diagnosis, and treatment, but less than 40% of patients who were referred to a specialist were visited by the latter, and only 41% of those referred to a specialist underwent instrumental exploration. Further results involving more countries are desirable.

Conclusion

JJ. Guex (France)

The proportion of patients presenting with CVD signs (C1 to C6) fluctuates between 61% and 72%, except in the Middle and Far East where numbers are lower (38.4%), but the population there is younger. These figures show that CVD is present throughout the world. Early stages of CVD predominated (C0s-C2=58%), but patients only consulted spontaneously at more severe stages, pointing to the need for earlier diagnosis. In addition, GPs did not refer patients to a venous specialist before they present with varicose veins. This shows the crucial role GPs may have in the early detection of the disease. It was also noticed that CVD was underestimated by GPs and by patients themselves, with more than 5 in 10 subjects diagnosed as CVD patients thanks to the VCP, while 2 in 10, mostly at severe stages, consulted spontaneously. Public awareness campaigns are needed to encourage patients to contact their physicians for care. Educational programs are also needed so that primary care physicians recognize cases of early CVD. This is one of the main goals of the UIP.

III
PATHOPHYSIOLOGY

Prague, Czech Republic, September 15-17, 2011

Genetic basis of the chronic venous insufficiency and its implication in thromboembolic disease

JM. Romero-Carro (Spain)

Chronic venous insufficiency (CVI) is an extremely common disease with a multifactorial and complex basis, where the interaction between genetic and environmental factors creates a predisposition to disease development and progression. Despite the high prevalence of CVI, the hereditary component is still unknown. The purpose of this study was to quantify the genetic basis (heritability) of CVI and its relationship to other clinically important thromboembolic diseases.

895 individuals in 35 extended families were enrolled in the Genetic Analysis of Idiopathic Thrombophilia (GAIT). After history taking and clinical examination, blood samples were collected for phenotypic and genetic analysis of DNA & mRNA

52 individuals had CVI using the CEAP classification (CEAP C2-C6). Although 13 of them were classified as C0-C1, they were considered as patients with CVI because they had undergone surgery for varicose veins. 843 showed no CVI (CEAP C0-C1).

The heritability (h2: the relative proportion of the phenotypic variation that is attributable to additive genetic effects) of the trait studied (CVI) and correlation with other clinical parameters were estimated using maximum likelihood methods based on variant component analyses.

The study estimates that 97% of the variation in susceptibility to CVI is attributable to genetic factors (h2: 0.97, P=3.6x10^{-11}). The study shows that the risk of developing CVI has a significant genetic correlation (0.72, P=0.01) with venous thrombosis, indicating that genes that influence susceptibility to CVI also influence the risk of venous thrombosis.

This study formally documents the high-risk genetic component of CVI, based on analysis of data in methodically recruited extended families, and allows conclusions to be drawn regarding the general population. Therefore, the high heritability of the risk of CVI justifies the search for genetic factors predisposing to this disease and shows a common genetic basis between CVI and thromboembolic disease.

Servier Symposium

Making sense of venous pain

Chairpersons: A. Scuderi, J. Strejcek

Venous symptoms: a signal of things to come

E. Rabe (Germany)

There has been little focus on the prevalence of symptoms in most epidemiological studies of primary chronic venous disease (PCVD). We must wait for more recent investigations, most of which have used the CEAP classification, to have some idea

of the prevalence of symptomatic patients. However, these data remain elusive. Only the VEIN CONSULT Program, carried out under the auspices of the UIP, details the prevalence of symptoms and their association with the signs of PCVD. The prevalence of C0s, En, An, Pn patients, that is to say patients presenting with symptoms without any visible clinical signs and without reflux, is not well known, for the simple reason that this patient group is not considered as having PCVD. The VEIN CONSULT Program, set up by the UIP in 20 countries from 4 continents, shows that the prevalence of the C0s group was 20%. However, it would be interesting to know if these purely symptomatic patients progress to more severe stages of disease, and if their presenting symptoms are predictive of PCVD. The proportion of C0s patients can sometimes be found or calculated indirectly from existing studies: it varies from 4% to 20%,(1-4) a prevalence that should not be neglected.

In the VEIN CONSULT Program, the prevalence of symptoms, and in particular of heaviness and pain, increased with CVD severity. In summary, all patients, whatever the stage of their PCVD can be symptomatic. This observation is in agreement with previous findings in the literature (5).

In the literature, venous symptoms were found to be not always present (6), to be independent of trunk varices (6) or telangiectasias,(7) and to have little association with inflammatory mediators (8). In particular, venous pain varies according to sex (1,9), and according to geographical area. In the VEIN CONSULT Program, pain is more often reported in the Far and Middle East than in the other continents, even though the proportion of men there is higher than elsewhere. Latin America was in second position for the frequency of pain, and then Europe. Venous pain is difficult to define, which explains the variations in the wording used. Quality of life is greatly impaired by PCVD, more particularly when patients are symptomatic. In patients in relatively early stages of CVD (C0s to C4), an increase in pain intensity of 1 cm on a VAS was correlated with a loss of quality of life of 2.4 cm on CIVIQ (10). In patients with venous leg ulcers, pain was nearly always present and its effect on quality of life was felt as strongly as impairment in the case of heart failure (11). Although pain appears very early in CVD progression, there are few data on its predictive value for complications of the disease. In the Bonn Vein Study II, the symptom 'sensation of swelling' was found to be predictive of the development of venous insufficiency (C3-C6).

Why venous pain is so specific.

N. Danziger (France)

Pain is the chief complaint that leads to the diagnosis of venous disease and has a significant impact on patients' quality of life. But for the clinician as well as the researcher, pain in venous disease is difficult to assess, both because of its multifaceted nature and due to the absence of a close relationship between pain as a symptom and the severity of venous disease.(12) Current hypotheses on the mechanisms of pain in venous disease emphasize a local inflammatory origin. However, although indicators suggesting an inflammatory reaction in varicose veins have accumulated dramatically over the last five years, 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 difficult to explain, both clinically and experimentally.(13)

Data obtained by electron microscopy show that veins are innervated by sensory nerve fibers whose cell body is located in the dorsal root ganglia of the spinal cord. These sensory fibers are located along the venous wall and are subdivided into collaterals, which have two possible destinations. Some collaterals cross the tunica adventitia and end in the venous wall between endothelial cells and smooth muscle cells of the tunica media. Other collaterals reach the connective tissue of the perivenous space where they branch into unmyelinated free nerve endings, in close contact with

the microcirculation. These subendothelial and perivascular nerve endings are nociceptors: they are the sole source for transmission of nociceptive afferent signals generated both in the venous wall itself and also in the perivenous connective tissue. The properties of venous and perivenous nociceptors account for the type of stimuli that can generate a painful sensation of venous origin. It is most likely that venous nociceptors are activated by inflammatory mediators in both the micro- and macrocirculation. The nociceptive response in venous disease is the same as in any visceral disease: venous pain is diffuse, difficult to describe, is felt by patients as unpleasant, and has a negative impact on quality of life. In addition, venous pain is not always associated with signs. For these reasons, such pain is underestimated and even denied by health care providers.

Is microcirculation implicated in venous pain?

E. Bouskela (Brazil)

In the experiment on the effect of Daflon 500 mg on microcirculatory and inflammatory parameters, women were investigated using the orthogonal polarization spectral technique (noninvasive method), and measurements of functional capillary density (FCD, number of capillaries with flowing red blood cells/mm^2), capillary morphology (CM, % of abnormal capillaries/mm^2), and diameters (μm) of dermal papilla (DDP), capillary bulk (DCB) and capillary limb (CD) were determined in the medial perimalleolar region and later analyzed using CapImage software. Included were women with regular menstrual cycles, and suffering from PCVD class C2 to C4. The double-blind, placebo-controlled trial included 100 patients in each group: a treatment group with Daflon 500 mg, 2 tablets a day for 4 consecutive cycles, and a placebo group. The female patients were young, 34 to 39 years old on average. This is explained by the recruitment of nonmenopausal women, undertaken to avoid any effects of hormonal cycles on the microcirculation. The young age of the patients can also explain the relatively low BMI, as well as the mild symptoms (low VAS and VCSS scores). The majority had complained of pain and other symptoms for at least 13 years and had reported signs of venous disorders for at least 9 years.

In the control group, the mean diameter of capillary bulk (DCB) and diameter of dermal papilla (DDP) increased with CEAP class in the study population, reflecting the morphological changes and increased capillary leaks that lead to edema. The capillary diameter (CD) remained, but the number of functional capillaries (FCD)

decreased uniformly with increasing CEAP class, indicating a loss in terms of capillary number and function.

In the Daflon 500 mg group, a tendency to reduce DCB and DDP compared with placebo was shown, mainly in patients over 40 years of age or in overweight C2 and C3 patients, indicating a possible protective effect of Daflon 500 mg against the morphologic changes occurring in the capillaries and an ability to prevent capillary leaks. In C3 patients with a BMI <26, there was a tendency for a reduction in capillary diameter (CD), and in C1 patients for a maintenance in the number of functioning capillaries (FCD), indicating an effect of Daflon 500 mg on capillary number and function.

In terms of the biochemical parameters, Daflon 500 mg significantly reduced PAI-1 in C2 to C4 patients, suggesting it has a fibrinolytic effect, which would avoid the fibrin deposits characteristic of the complications of CVD. The tendency for a reduction in some selectins (in particular sP- and sL-selectins), which are proteins implicated in venous inflammation, was noted with Daflon 500 mg in patients with trophic skin changes (C4). The same was observed for MMP-9 in C3 patients, implying that Daflon 500 mg limits venous remodeling and morphologic changes in the capillaries. As for the angiopoietins, the level of Ang-2 slightly decreased with Daflon 500 mg while that of Ang-1 was increased, suggesting a protective effect of Daflon 500 mg on the endothelial capillary wall.

It can be assumed that the protective effect of Daflon 500 mg against the morphologic changes occurring in the capillaries will maintain their functioning and avoid plasma leaks, throughout the progression of CVD. Less plasma leakage means less subcutaneous edema and, indirectly, less pain. The reduction of some biomarkers with Daflon 500 mg suggests it may have a protective effect on endothelial structures and the microcirculation, both of which are subject to inflammation during disease progression. With fewer inflammatory mediators circulating during Daflon 500 mg treatment, there will be fewer nociceptive messages and perhaps less pain.

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Effect of Daflon 500 mg on the quality of results of sclerotherapy in the dorsal rabbit ear vein model.

E. Bouskela (Brazil)

The authors tested the effect of Daflon 500 mg on perivascular inflammation after sclerotherapy in an experimental model of rabbit ear vein. 48 rabbits were given Daflon 500 mg (in an adequate dose) or placebo (lactose solution). The therapy started 7 days before sclerotherapy and lasted 30 days. Several parameters were measured with the help of intravital microscopy: arterial and venous diameter, functional capillary density (ie, the number of capillaries with flowing red blood cells per cm^2; this parameter is a good indicator of skin nourishment), leukocyte adhesion (leukocyte considered adherent if it sticks to the endothelium for more than 20 seconds), macromolecular permeability. Histology was also evaluated. In the Daflon group, the authors observed a significant decrease in macromolecular permeability and leukocyte adhesion as well as better preserved functional capillary density in comparison with controls. The efficacy in the reduction of inflammation and endothelial permeability by Daflon 500 mg in an animal experimental model and may therefore improve the results of sclerotherapy by limiting its side effects. The results should be confirmed in humans.

IV
INVESTIGATIONS

Prague, Czech Republic, September 15-17, 2011

Systematic review of sonographic chronic cerebrospinal venous insufficiency findings in multiple sclerosis.

T. Lane (UK)

The relationship and prevalence of the chronic cerebrospinal venous insufficiency (CCVSI) and multiple sclerosis (MS) are still controversial. A systematic review of literature to identify the diagnostic accuracy and reproducibility for the Zamboni ultrasound (US) criteria for CCSVI has been performed. The inclusion criteria were cross-sectional methodology using the five Zamboni US criteria, MS diagnosed using McDonald criteria, age- and gender-matched healthy controls, and sonographer blinding.

Of 115 articles screened, 4 were included in the systematic review (Zamboni, 2009; Zivadinov, 2011, Centonze, 2011 and Baracchini, 2011). The diagnosis OR varies from 1.80 (0.9-3,6) to 26.499,0 (519,2-1.352,3), sensitivity from 0.07 (0.2-0.16) to 1.00 (0.97-1.00), and specificity from 0.64 (0.94-1.00) to 1.0 (0.94-1.00), with a Cohen s kappa statistic of 0.75-0.93 (intra-sonographer) and 0.80 (inter-sonographer).

Studies disagree markedly on the prevalence and strength of the association between CCSVI and MS. No one has repeated the initially perfect diagnostic accuracy and each group appears to find different prevalence rates and odds ratios for CCSVI and MS. The results indicate that the sonographic findings are more variable than can be explained through biology alone and reflect subjectivity in the examination. There is no consistent evidence that sonographic CCSVI is ubiquitous in MS, or that it constitutes a useful clinical test for MS. Guidelines on the methodology of screening with ultrasound are urgently needed.

Classification of Duplex Scan findings after treatment of saphenous varicose veins

M. de Maseeneer (The Netherlands)

Treatment follow-up consists of four phases: immediate: 1-4 weeks, short-term: 1 year, mid-term: 3 years, and very long-term: 10 years. Medical reports had to include the following: vein diameter, absence or presence of reflux > 0.5 s, and localization of superficial epigastric vein (endovenous procedures). It is important to avoid terminology as: full success, partial success, no success.

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V
TREATMENT

Prague, Czech Republic, September 15-17, 2011

Acute venous disease

Superficial venous thrombosis

Symposium in cooperation with Central European Vascular Forum

Chairperson: C Allegra

Superficial thrombophlebitis: thromboembolic risk.

C. Allegra (Italy)

The term superficial thrombophlebitis (ST) refers to an inflammatory and thrombotic process in a superficial vein. Its incidence has never been properly investigated, but is probably higher than that of deep vein thrombosis (DVT). ST may extend to the deep vein system through the saphenofemoral or saphenopopliteal junction or by perforators. The risk of thrombus extension is especially high if it is close to the saphenofemoral junction (£ 2 cm). The reported prevalence of complicating DVT or pulmonary embolism (PE) varies widely. According to a Cochrane systematic review (published in 2008), it was 6-44% for DVT (concomitant or subsequent), 20-33% for asymptomatic PE, and 2-13% for symptomatic PE. These discrepancies are probably caused by the differences in methodology used in respective studies. However, the evidence of optimal ST therapy is scarce. So far only one randomized controlled trial (RCT) has been performed – CALISTO which proved the efficacy and safety of fondaparinux at prophylactic dose in ST. The management of ST patients may present a problem from a medicolegal point of view.

Superficial thrombophlebitis – CEVF consensus proposal for diagnosis and treatment

V. Stvrtinova (Slovakia)

Superficial thrombophlebitis (ST) is not as benign as has long been thought and is included by some authors as a part of venous thromboembolism (VTE). It may quite often be complicated by deep vein thrombosis (DVT), sometimes even in the contralateral leg, or pulmonary embolism (PE). The real incidence of ST is not exactly known. The extent of ST may be underestimated by clinical examination and should be assessed by ultrasound.

New data of ST epidemiology were provided by POST, the French observational multicenter study. Of 844 patients with ST, 24.9% had DVT at the time of ST presentation. In the rest of the group, 10% of thromboembolic complications occurred during follow-up, in spite of anticoagulation therapy, which was given to the vast majority of them.

Moreover, the CALISTO trial has recently shown significant reduction of thromboembolic complications in ST patients treated with fondaparinux at prophylactic dose for 45 days (compared with placebo). In the light of the new data, the CEVF has reached a consensus on how to manage ST patients:

- to look properly for risk factors in all cases of ST on nonvaricose veins and in recurrent ST on varicose veins (potential cancer, thrombophilia, systemic disease)
- to examine the superficial and deep vein system in both legs by duplex ultrasound immediately after ST clinical diagnosis if ST is close (£10 cm) to the saphenofemoral or saphenopopliteal junction
- to use compression in all patients
- immediate mobilization in all patients
- to use fondaparinux 2.5 mg daily subcutaneously for 45 days for ST that is at least 5 cm long on ultrasound

Superficial thrombophlebitis, anticoagulation and CALISTO trial – finally a piece of evidence?

J. Hirmerova (Czech Republic)

CALISTO is the first and the only randomized, placebo-controlled trial of anticoagulation in superficial thrombophlebitis (ST). Patients (n = 3002) with isolated ST (length at least 5 cm on ultrasound) were included; those with ST close to saphenofemoral junction (£ 3 cm) or with recent cancer or venous thromboembolism (VTE) were excluded. The trial has proven the efficacy and safety of fondaparinux (2.5 mg daily for 45 days), namely85% reduction of the relative risk of thromboembolic complications (deep vein thrombosis, pulmonary embolism, ST extension or ST recurrence). This is a great contribution to the hitherto poor evidence for optimal ST treatment, but many questions and doubts remain. Some authors suggest changing the guidelines for ST treatment with recommendation of fondaparinux. Others do not consider this approach cost-effective, arguing that the rate of VTE in the placebo group in CALISTO is also relatively low and that ST has however an extremely low mortality. Further studies are needed to document the cost of the suggested therapy and the impact on quality of life. Defining the high-risk group of ST patients will probably be a crucial issue.

Deep venous thrombosis

Thrombosis: deep venous thrombosis – what is evidence based?

PH. Carpentier (France)

The first evidence about the life-saving effect of anticoagulation in patients with venous thromboembolism (VTE) was provided by the historic trial by Barritt and Jordan (published in 1960 in *The Lancet*). The other milestone in the history of VTE treatment came in the last decade of the last century with the introduction of low-molecular-weight heparin (LMWH) and the published evidence about its noninferiority in comparison with unfractionated heparin (UFH) as well as about the efficacy and safety of outpatient treatment of VTE. The last ACCP guidelines (published in 2008) recommend LMWH subcutaneously (sc), UFH intravenously (iv) or sc or fondaparinux sc for the initial VTE treatment, followed by warfarin.

Recently published evidence about new anticoagulants may cause revolutionary changes in the treatment (dabigatran and rivaroxaban as effective and safe as warfarin). Moreover, unprovoked VTE is associated with increased risk of recurrence and ACCP guidelines recommend treatment duration of at least 3 months with possible therapy prolongation according to the benefit/risk evaluation. Quite recently, long-term rivaroxaban has been proven to have beneficial effects in the patients with unprovoked VTE.

Another promising new anticoagulant, idraparinux (applied sc only once weekly), was noninferior to standard care in the patients with deep vein thrombosis (DVT) but worse in those with pulmonary embolism (PE). It is highly probably that the first days of VTE treatment are crucial and PE is probably a sign of a more active thrombotic process. This fact is reflected in ACCP recommendation to start anticoagulation even in the presence of suspected VTE pending the results of diagnostic studies as well as in the recommendation to start warfarin with adequate overlap with LMWH or UFH.

There is also slowly growing evidence about the benefit of the strategy of thrombus removal (catheter-directed thrombolysis) in the sense of achieving better venous patency and less postthrombotic syndrome than standard treatment. ACCP guidelines suggest this method in selected patients with ileofemoral thrombosis.

Finally, elastic compression stockings have proved effective in preventing postthrombotic syndrome in proximal thrombosis and their use is recommended by ACCP guidelines in symptomatic DVT as soon as possible. The problem may be the known poor compliance of the patients.

Venous thrombosis of lower extremities in young patients

R. Kreidy (Lebanon)

The incidence of venous thromboembolism (VTE) increases exponentially with age. Therefore, in younger VTE patients a proper examination of the cause seems prudent. The study presented was a retrospective evaluation of 75 under-50s (mean age 40.7 years) with deep vein thrombosis (DVT), compared with a control group of older VTE patients (283 patients, mean age 64 years).

In the younger group, DVT in the left leg prevailed (60%; right leg 30.7%, both legs 9.3%). The risk factors for DVT in the younger group were: inherited thrombophilia, pregnancy, estrogen therapy, family history of VTE, long-haul air travel, and inferior vena cava congenital malformations.

The effect of ONPULSETM in improving lower limb blood flow in healthy volunteers

H. Jawad (UK)

ONPULSE™ is a new device, constructed for mechanical thromboprophylaxis. It is based on the activation of the foot and calf venous muscle pump. Transcutaneous electrical stimulation of the peroneal nerve provokes controlled isometric

contraction of the muscle. The effects of this technique were studied in 10 healthy volunteers. Several parameters were measured in the stimulated and nonstimulated leg and the control study without stimulation was performed later. Duplex ultrasound, laser Doppler and pulse oxymetry were used to assess the following parameters: blood flow volume, velocity, oxygen saturation. Safety and acceptability of the technique were evaluated as well.

ONPULSE™ had a positive effect on the microcirculation and increased mean venous velocity without having any significant effects on vital signs. The results seem promising and research with this new technique is still going on.

Venous thrombosis prevention in acutely ill medical patients

J. Spáčil (Czech Republic)

Thromboprophylaxis in medical patients was incorporated in practice two decades later than in surgical patients and is still quite underused in many facilities. Two large studies have proven the efficacy of pharmacological thromboprophylaxis in medical patients – MEDENOX (with enoxaparine), PREVENT (with dalteparine) and ARTEMIS (with fondaparinux). The author analyzed the use of thromboprophylaxis in his own medical department. The first analysis was performed between 2004 and 2005 and the second in 2009-2010. The situation has improved – in the first period thromboprophylaxis was given to 51% of patients and in the second period it was given to 64% of patients at risk of venous thromboembolism (VTE). The results were compared with those of international studies – in the ENDORSE cross-sectional study only 39.5% of medical patients at risk received thromboprophylaxis (the Czech Republic also participated in the study and 44% of patients received prophylaxis). The last ACCP guidelines recommend using thromboprophylaxis with anticoagulation for all acutely ill medical patients with congestive heart failure, severe respiratory disease, confined to bed, and having one of the additional risk factors: cancer, previous VTE, sepsis, acute neurologic disease, inflammatory bowel disease. Several issues need to be resolved in the future – thromboprophylaxis for outpatients, thromboprophylaxis of extended duration, and the use of emerging new anticoagulants in prophylaxis in medical patients.

Chronic venous disease

Generalities

The integration and better utilization of modern varicose vein treatments and technologies will improve outcomes

M. Malouf (Australia)

M. Malouf provided an overview about how to choose the best treatment for varicose veins worldwide with the integration of modern technologies. He considered good quality duplex ultrasound to be the key to improving outcomes. This essential investigation of venous incompetence by ultrasonography must be performed preferably by the treating physician with the aim of revealing the exact hemodynamic pathophysiology in superficial, deep, and perforating veins. One important issue is that good quality venous duplex sonography in not available in many areas of the world, thus limiting diagnosis and excluding certain treatment options. Again, it was emphasized that there is a need for a new UIP consensus on this, to standardize the technique around the world.

The speaker reminded the audience of the importance of venoactive drugs and compression stockings in this overall strategy, and of the interventional treatments, including chemical ablation (liquid, foam), thermal ablation (laser, radiofrequency and steam) and varicose vein surgery, that need to be duplex ultrasound-guided. He pointed out that different geographic regions contain bias in which treatments are reimbursed and by whom and to whom. Patients are biased by perceptions and advertising, and by the availability of treatments. He concluded that it is essential to integrate the above techniques if we wish to arrive at the same end point of absence of symptoms, improved clinical appearance and quality of life, no further duplex ultrasound evidence of venous reflux, with little or no recurrence over time. The speaker considered that the treatment options are all effective if employed appropriately on the basis of accurate duplex mapping. On the other hand we must avoid over-treatment based on just duplex results. One should treat patients and their symptoms rather than incompetent veins.

Conservative treatments

VENOACTIVE DRUGS

AA. Ramelet (Switzerland)

A. Ramelet reminded the audience that venoactive drugs (VADs) form a heterogeneous group of plant-derived (flavonoids, saponins, among others) or synthetic (mainly calcium dobesilate) medicinal products that have effects on certain signs (edema) and symptoms associated with chronic venous disease (CVD). Their principal mode of action includes an anti-edema effect (reduction of capillary permeability, improvement of lymphatic drainage, reduction of orthostatic edema), increase of venous tone, inhibition of leukocyte adhesion to the venous and valvular wall, inhibition of the release of inflammation mediators,

of leukocyte adhesion molecules, and of prostaglandin synthesis, and reduction of the inflammatory reaction in venous valves.

He emphasized the role of inflammation as a key point in the pathogenesis of CVD and the specific effect of VADs in reducing venous pain, which is not achieved by nonsteroidal anti-inflammatory drugs. This specific painkilling mechanism effect needs further elucidation.

Besides some concerns in the past, it is now possible to differentiate the efficacy of several VADs that have been evaluated through basic research, randomized controlled trials, meta-analyses, and consensus conferences. They are useful if their indications are respected, if they increase the effect of compression, and if their side effects are rare.

He concluded his lecture with a SWOT analysis of these VADs: **S**trengths (painkilling effect, effectiveness from C0s to C6, low toxicity and long experience, increasing research, new drugs), **W**eaknesses (bad reputation in the past, old studies of low quality whence difficulty of establishing effectiveness, unproven awareness of toxicity), **O**pportunities (increase of prevalence of CVD, new interest in CVD, research about polyphenols, interest for nutraceuticals) and **T**hreats (academics' ignorance, social insurance, new low-level studies)

Are all venoactive drugs equivalent? A meta-analysis of randomized controlled trials of the main venoactive drugs on the reduction of venous ankle edema

FA. Allaert (France)

Venoactive drugs are recommended and widely used in patients with venous edema. However, very few studies have documented their effect on ankle edema of venous origin. The author searched Medline for the articles published from 1975 to 2009. Only double-blind studies comparing venoactive drugs against placebo or against other comparators and providing A, B or C levels of evidence were included in the meta-analysis. Finally, 10 studies with 1010 patients were identified, documenting the effect of micronized purified flavonoid fraction (MPFF), hydroxyethylrutoside, ruscus extract, and diosmin. All the drugs were associated with a significant reduction of ankle edema compared with placebo, except for diosmin. MPFF was significantly more effective than ruscus extract and hydroxyethylrutoside. The meta-analysis confirms the validity of the grade A recommendation for use of MPFF in venous edema in recent international guidelines. The author himself pointed out the heterogeneity among the studies as a possible limitation of the meta-analysis.

COMPRESSION THERAPY

Chairpersons: M. Malouf, JC. Ragg

A wrong dogma in compression therapy: low pressure for superficial vein, strong pressure for deep veins

J. Uhl (France)

The author presented a study designed to shed light on the mechanism of action of external compression on superficial and deep veins. MRI of the calf was performed before and after compression by different stockings and bandages in 13 patients (5 with varicose veins, 8 healthy subjects). The results were really exciting. Low compression (20 mm Hg) believed to be indicated in superficial venous insufficiency did not lead to significant changes in extrafascial veins but it led to 60-80% reduction of volume of the deep veins. Only if a pressure of at least 60 mm Hg was applied was there flattening of the superficial veins. This can explain, of course, the effectiveness of 20 mm Hg compression stockings alone in prevention of venous thromboembolism. This study clearly demonstrated that compression needs to be investigated further, because our perceptions may be mistaken.

Pressure and compression – different concepts

F. Vega (Mexico)

F. Vega pointed out some discrepancies in using Laplace's law that mislead investigators and practitioners when they are dealing with compression. In his opinion Laplace's law talks about blood pressure which is transmitted from the inside, whereas compression acts from the outside. So, this law applies to pressure exerted from the inside and it is wrong to talk about compression forces exerted in the opposite direction. Because of this we can't say that we get real measurements of pressure of stockings, since they depend on the structure under the measuring chamber.

Edema reduction by elastic stockings, a technique used since 1985

A. Cornu-Thenard (France)

The author presented his method of reducing edema by means of compression stockings prescribed initially, instead of the usual way of using bandages first and then compression stockings. If a reduction of edema is judged sufficient after three to four days of day-and-night wearing of a stocking, the same one is used daily. If not, a second or even third stocking is superimposed. This is an interesting approach because it is believed that to achieve good results in venous or lymphatic edema we need to use the bandages because they have a high stiffness index. As for stockings, there are not many studies published about their stiffness. So it is generally accepted that they have low stiffness not quite suitable for initial treatment of edema. The next presentation was just devoted to this point.

Increased stiffness compression stockings

JP. Benigni (France)

JP. Benigni pointed out that increasing of the stocking's stiffness can be achieved by superimposition of them. A good example of such an effective superimposing could be sets of two stockings for patients with venous ulcers. These are actively used now by many specialists.

Some papers were rather far from fundamental problems. J. Ragg (First experience with a new compression modality (Phlebopress) and J.P. Benigni (Efficiency on pain reduction of a thigh pad under elastic compression after stripping of the great saphenous vein: results of a case control study) conducted studies of compression devices which were applied under the bandage after stripping or foam sclerotherapy for eccentric compression. In a group of 64 patients undergoing microfoam treatment, J Ragg showed that a new pad with a lentiform cross-section reduced vein diameter by 68.8% (95% CI 32.2-82.1%) compared with 48.2% (95% CI 24.1-62.7%) in the control group (no pads). There were no adverse events. Minor skin irritation not limiting the patient's comfort or application time occurred in 9.4% of cases. JP Benigni (France) and colleagues included 53 patients in a study to evaluate pain reduction if a pad was added at thigh level under the elastic stockings. 36 patients were included in the pad group and 17 in the control group. The level of pain was measured on a visual analogue scale from day 1 to day 7. On day 1 pain was 40.8$\pm$ 20.8 in the control group and 27.4 $\pm$ 24.2 in the pad group (P=0.05). On Day 7, pain was 15.3 $\pm$ 13 in the control group and 3.7 $\pm$ 5.5 in the pad group (P<0.0001).

J. Uhl (Evaluation of symptoms in CVD patients with foot static disorders: a prospective study) described the role of orthopedic soles in addition to medical compression stockings (MCSs) in patients with foot static disorders. 30 symptomatic CVD patients were divided into four groups (control: no treatment; compression: MCS alone; sole: sole alone; MCS + sole) and evaluated over four consecutive weeks. The efficacy of stockings in relieving the venous symptoms was confirmed and also, in cases of associated foot static disease, the quality of life of the patients was further improved by adding an orthopedic sole.

VENOUS LEG ULCERS

Chairpersons: JP. Benigni, A. Pospisilova

Non-healing venous ulcers: use and efficiency of Varolast bandaging without wound dressings

JP. Benigni (France)

He presented the results of a prospective study in 19 patients (mean age 76) with C6 and without diabetes or peripheral artery disease. Oxide zinc bandages were applied directly on the ulcer without dressings and were changed every 5 days. After 45 days, 5 ulcers had healed and 14 had improved. The author concluded that this kind of bandage, which is similar to Unna's boot, achieved good healing rates at low cost. He also stated that randomized controlled studies comparing the above method with a multi-layer bandage need to be performed before drawing a definite conclusion.

The same author conducted a study (Compression stockings for treating venous leg ulcers) comparing the in vitro pressures given by the manufacturers of three anti-ulcer kits with the in vivo interface pressures measured in 18 healthy subjects. Two stiffness indices were calculated (static stiffness index – SSI and dorsiflexion stiffness index - DFSI). Two anti-ulcer kits (Hartmann's Saphenamed UCV and Medi Mediven Ulcer kit) provided the recommended compression, but one of them (Jobst's Ulcer care) did not. All three kits were rigid enough only when strong muscular compression occurs (SSI less than 10, DFSI more than 10).

The influence of different sub-bandage pressure values on venous leg ulcer healing when treated with compression therapy
D. Peric (Serbia)

A study by the Serbian team showed better healing results with two- or multi-layer compression systems than with single-component compression systems. They performed the open randomized prospective study in 131 patients with an ulcer surface area of more than 3 cm^2 and ulcer duration more than 3 months. In a single-layer group (tubular-form compression device Tubulcus, III class) healing rate during 26 weeks of treatment was 25% (13/42 patients), in a two-layer group (Tubulcus plus one 15 cm wide elastic bandage with 200% stretch) – 67.4% (31/46) and in a multi-layer group (Tubulcus plus two elastic bandages) – 74.4% (32/43).

V. Stojiljkovic from the same team presented a study entitled "Risk factors related to the failure of venous leg ulcers to heal with compression treatment". 189 patients were treated within 52 weeks by the multi-layer bandaging system mentioned above. 24 (12.7%) of ulcers failed to heal. A small ulcer surface area (<20 cm^2), duration of venous ulcer <12 months, a decrease in calf circumference of more than 2 cm during the first 50 days of treatment, and emergence of new skin islets on the wound surface were favorable prognostic indicators of ulcer healing. BMI >35 kg/m^2, short walking distance during the day (<200 m), history of wound debridement, and deep ulcers (>2 cm) were indicators of slow healing. Calf-ankle circumference ratio <1.3, fixed ankle joint, and reduced ankle range of motion (<20 degrees) were the only independent parameters associated with non-healing ($P< 0.01$). The results suggest that non-healing ulcers are related to impairment of the calf muscle pump.

Two papers pointed out a role of sclerotherapy in accelerating venous ulcer healing and preventing recurrence. L. Hnatek, Czech Rep, (Foam sclerotherapy – a safe and fast intervention for acceleration of venous ulcer healing) included in his study 85 patients with C6 who were treated previously by compression alone (22 of them for more than a year). After foam sclerotherapy with polidocanol (0.5-2%), the ulcer did not close in only 9 patients. F. Zernovicki, Slovakia (Recurrent leg ulcers) presented his experience of using compression and compression plus chemical obliteration of perforating veins in 270 patients. The recurrence rate after closure of perforators was much lower (0.7% vs 5.2% with compression only).

Skin climate and Tencel C: innovations in fibre technology – the Tencel C fibre

M. Jünger (Germany)

A new type of compression stocking, enriched with chitosan (a derivative of chitin, with reported antibacterial, antifungal, anti-inflammatory effects) has been studied. Stockings with chitosan in low or high concentrations were compared with cotton stockings. The study was performed in 10 healthy volunteers. Healthy volunteers were compared with patients with chronic venous insufficiency. A study was done in healthy volunteers after a standardized exercise (treadmill test). Several parameters were monitored: skin humidity, transepidermal water loss, skin roughness, microbial burden of the skin, skin temperature, patient comfort. Cutaneous moisture and barrier function were slightly better after stockings with chitosan and smoothing of the skin was observed in comparison with cotton stockings. This new type of compression may have positive effect on skin microclimate.

Update in compression treatment

MH. Meissner (USA)

Compression therapy is supposed to have beneficial effects on hemodynamics as well as on the microcirculation. However, research in healthy volunteers and in patients with leg ulcers has proven only some of these putative effects – in the light of available studies the effect of compression on venous flow velocity is doubtful, vein diameter is reduced only in the supine position, improvement in muscle pump function is probable, and there is a positive effect on the microcirculation (maintaining of the anti-inflammatory and anticoagulant properties of the endothelium).

In clinical practice, compression is used to prevent deep vein thrombosis (DVT). In surgical patients, the meta-analysis of randomized controlled trials (RCTs) provides evidence about significant reduction of DVT risk. However, in medical patients the benefit is only marginal or even nonexistent (in stroke patients). This paradox may be explained by the role of intra-operative venodilation, endothelial tears with exposure of subendothelial collagen followed by initiation of thrombosis.

Compression has a beneficial effect on healing of venous ulcers – this is also proven in the meta-analysis of RCTs.

According to the ACCP (American College of Chest Physicians) guidelines, compression stockings should be used in high-risk surgical patients as an adjunct to pharmacologic thromboprophylaxis and should also be applied in patients with acute DVT. Randomized controlled studies have demonstrated their efficacy, when worn for 2 years, in preventing postthrombotic syndrome.

Nonconservative treatments

VARICOSE VEIN SURGERY

Chairpersons: AA. Ramelet, L. Veverkova

Methods that failed in the treatment of varicose veins

L. Veverkova (Czech Republic)

This Czech team reported a retrospective study comparing two different endovenous treatments for varicose veins: 62 patients underwent RF on the GSV and 68 underwent endovenous laser on the GSV and SSV. There were no statistical differences between the 2 groups in the occlusion rate (more than 90%) at 36-46 months. Failures in both groups were due to technical faults or unsuitable GSV diameter. RF has the advantages of shorter operating time, shorter time of work disability, and lower postoperative pain.

Unfortunately, the lack of precise statistical analyses and precise data related to the tools used to evaluate quality of life and disability prevent any conclusion regarding the best method to choose.

Anesthetic management of endovenous laser treatment

R. Vellettaz (Argentina)

The author wanted to establish and evaluate a perioperative anesthetic protocol in order to decrease complications and patient discomfort when using local anesthesia during endovenous laser treatment (EVLT). In this retrospective nonrandomized study, 699 great saphenous veins (GSVs) were treated with a diode 980 laser with intravenous sedation associated with local tumescent anesthesia according to the Klein protocol. All the procedures were well tolerated. Postoperative pain was mild in 67.55% of patients and recovery was fast.

Tumescent local anesthesia is widely used with endovenous techniques (1): it reduces peri- and post- operative pain to a very low level, reduces or even eliminates ecchymosis, and preserves postoperative quality of life, as reported in several studies. The high dilution of local anesthetic allows injection of a large volume without adverse effects (2). The combination of intravenous sedation with local tumescent anesthesia improved surgical conditions by decreasing perioperative pain due to local anesthetic injection, with no incidence on the discharge criteria. This anesthetic management should be used for almost all kinds of varicose vein ambulatory treatment.

References

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Vanst- a different approach in aesthetic phlebology

V. Ciubotaru (Romania)

VANST (ambulatory nonstripping surgical therapy of varicose veins) consists in disconnecting the varicose veins from the venous circuit by ligation without removing them. It is done under local anesthesia and in an ambulatory setting. No ecchymosis or hematomas have been reported. No compression was needed. The rate of recurrence at 5 years was 4.3% with good aesthetic results. The author considers that all kinds of varicose veins can be treated by this noninvasive technique.

Only one center and one surgeon tried this new method. We need much more data concerning the design of this study as well as for the evaluation criteria used and the analysis of the results.

A czech invention for phlebology: the saw knife. our modifications and results

I. Bihari (Hungary)

The saw knife invented by a Czech surgeon many years ago is used to destroy and remove big varicose veins, perforators, or veins within lipodermatosclerotic tissues. The knife is anchored into the vein wall and twisted to remove the vein.

We have no data concerning post-op bruising or hematomas, but dysesthesia occurred after the procedure in 7% of cases, and disappeared within 6 months.

This method is of little interest because this knife is much more damaging than the hook and we don't have any data on post-procedure cosmetic results or quality of life.

Patients have a poor understanding of the risks and benefits of varicose vein treatment

K. Sritharan (UK)

The aim of this study was to evaluate the perceived risks and benefits of varicose vein surgery. Patients have to complete a questionnaire. The results showed that most of the patients relied on information from their doctor alone and that 44% thought treating their varicose vein would yield other health benefits, as preventing diabetes or aiding weight loss. Developing deep venous thrombosis was the main risk after the surgery for 52% of the patients even if 67% thought that varicose vein surgery is a low-risk procedure.

This very well designed study by A Davies's group showed that despite the many available sources of scientific information, patients are still unaware of the benefit-

risk ratio of varicose vein surgery, and that doctors should be much more involved in spreading medical information.

Esthetic procedures in the surgical treatment of the inferior limb varices

D. Radu (Romania)

The Babcock technique was used to remove the GSV, and the tributaries were treated with the phlebotome and Wolmark rings to improve the aesthetic results. Unfortunately, no details concerning the cosmetic results were provided. These two old methods were abandoned some years ago in many countries because of their poor cosmetic results: ecchymosis, hematomas, bruising, and scars. Many improvements have been made in stripping, by using, for example, a pin stripper, which is much less traumatic. Moreover, using a small hook through skin puncture avoids skin damage and nerve injuries.

Methods of our simplified subfacial endoscopic perforators surgery with the use of endotip® cannula. 6 differences from the original gloviczki's method

R. Haruta (Japan)

Subfascial endoscopic perforator surgery (SEPS) can be difficult to learn and some technical difficulties and complications have been reported. To simplify the technique, this team changed the access port using a two-port system to avoid inflation at the thigh, a dissecting balloon catheter, and CO_2 gas injection at high pressure. No complications have been reported and the operating time was short. This simplified method would probably help many surgeons who are uncomfortable with the original technique, even if the routine treatment of incompetent perforators is still under discussion. Multicenter studies are required to confirm the reproducibility of the technique.

The ambulatory surgical treatment of the varicose veins thrombophlebitis

V. Ciubotaru (Romania)

The author considers that thrombophlebitis is an emergency and should be operated on at the same time as varicose vein disease. The surgical method used was VANST combined with thrombectomy. The only restriction is that the time between the onset of the thrombosis and surgery should not exceed 14 days. No complications have been reported in 574 procedures. No DVT or PE mentioned and the postoperative course was uneventful.

No firm conclusion can be drawn because of the lack of data and the use of this specific surgical method. Nevertheless, removing the clot as soon as possible would probably decrease pigmentation and skin damage. Cosmetic results are still expected.

Diagnosis and treatment difficulties in the association of the saphenopopliteal valve insufficiency of the oblique communicating vein of the calf

V. Ciubotaru (Romania)

The author noted a frequent association between saphenopopliteal valve insufficiency and GVS dilatation. This saphenopopliteal reflux transmitted through an oblique communicating vein of the calf could influence the surgical strategy. This anatomical situation was observed in 10.8% patients and led to treatment of both saphenous trunks at the same time in order to limit recurrences. No varicose vein recurrence has been reported.

We don't have any data concerning the duration of follow-up or the type of the surgical procedure performed on the saphenous trunks. We can only suggest that a precise duplex scan as well as a good mapping prior to the intervention could avoid any misunderstanding and prevent any surgical failure.

SCLEROTHERAPY I

Chairpersons: Breu F.X.-Cavezzi A.

This was a session about the mechanisms, efficacy, side effects, and possible innovations in foam sclerotherapy.

K. Parsi (Australia) shared with us his experimental findings regarding in vitro effects of two detergent sclerosants, namely sodium tetradecyl sulfate (STS) and polidocanol (POL), on coagulation, platelet activation, aggregation, antithrombotic pathways, and fibrinolysis. Since POL is a nonionic and STS is an ionic detergent they have different effects on proteins, which are denatured by SDS. It was found that at higher concentration (>0.3%) STS prolongs all clotting times, and has anticoagulant properties, significantly destroying FV and FVII, enhancing the effect of activated protein C, and mimicking the effect of antithrombin. STS at high concentration has both an anticoagulant and a pro-thrombotic activity. It destroys protein C, protein S and antithrombin, but this effect is neutralized by its complex anti-thrombotic activity and the final net effect will be anti-thrombotic. At high concentration STS destroys plasminogen, but at the same time destroys inhibitors of fibrinolysis also and the effect will be antifibrinolytic and non-prothrombotic. At lower concentration both detergents have procoagulant properties, POL stronger than STS. Both STS and POL at low concentration stimulate platelet lysis, the release of platelet microparticles, and the release of intracellular calcium from platelets, but inhibit platelet aggregation. At low concentration clots are formed, coagulation time is reduced, clot formation rate is increased, and antifibrinolytic effect is present. Although in vivo confirmation of these effects is lacking, the data presented might have some clinical implications. Since high concentration sclerosants have anticoagulant activity it would be desirable to apply high concentration and low volume and to prevent the dilution and neutralization of sclerosant due to excessive mixing with blood. We should keep in mind that sclerotherapy acts not only on the vein wall but also on circulating blood. Further investigations are needed.

P. Coleridge Smith (UK) posed several questions regarding the efficacy of foam sclerotherapy. How well does it work? How safe is? What do we do to optimize the treatment? He concluded that current trials and meta-analyses do not entirely reflect the clinical outcomes that are achieved in practice. Clinical series published by experts show 80-85% efficacy in curing varicose veins at 5 years, which is a very good result compared with surgery. Foam sclerotherapy has excellent efficacy in treating recurrent varicose veins after surgery. But good technique in skilled hands is everything, emphasized the speaker at the end of his presentation. Unfortunately, we do not have a single standardized and validated technique at the present time.

A. Cavezzi (Italy) started his talk about possible innovations in foam sclerotherapy with two very important physical principles: the smaller the bubbles the higher the active area of foam, the smaller the residual empty space among bubbles and the longer the half-life of bubbles the longer the time of contact with the venous wall. His team did experimental studies to assess the influence of a few variables in the formation and injection of the sclerosant foam and to assess possible innovative procedures in foam sclerotherapy. He concluded that smaller syringes (2.5 mL) generally produce smaller bubbles when using air, not when using CO_2/O_2. Smaller syringes (2.5 mL) generally produce longer-lasting foam. Low silicon or no-silicon BD Discardit syringes (5 mL) produce smaller bubbles and longer-lasting foam. Conventional syringes (eg, BD, ICO, Braun, etc) produce larger bubbles and much shorter half-life foam. 21G or 23G needles do not denature foam. CO_2 produces the smallest bubbles and most homogenous foam, albeit short-lasting. CO_2/O_2 prolongs half-life compared with CO_2. Counter resistance and three-way valve 30 rotation significantly reduce bubble size and increase foam duration. Further studies will investigate how these experimental findings can be implemented in daily practice.

N. Morrison (USA) demonstrated ultrasonographically that foam was present in the peripheral veins, perforators, deep venous system, and right heart within 10-30 seconds after every injection, no matter the size of the vein injected, how peripheral it was, or the volume of injected foam. If transcranial Doppler is additionally employed, in the presence of the right-to-left shunt, emboli can then be identified in the cerebral circulation. Since 25-30% of the population has a right-to-left shunt, it is not just of theoretical importance that emboli or endothelial breakdown products can be transmitted to the systemic circulation. Methods such as leg elevation, patient immobility, limitation of volume of injected foam, avoidance of movement involving the Valsalva maneuver, all of which are intended to prevent the migration and distribution of these emboli, have been shown to be largely ineffective. Neurosensory side effects have been reported to be rare to uncommon (0-2.6%) in different clinical series and may include visual disturbances, headache, dizziness, hemiparesis, and syncope, all of which are nearly always transient. The question remains open whether the symptoms are related to cardiac and cerebral emboli or not. More recently it has been suggested that circulating emboli following foam sclerotherapy may not be related to neurosensory symptoms, but rather may be a result of endothelial damage releasing a powerful vasoconstrictor such as endothelin. "Biocompatible" gas (CO_2/O_2) may produce fewer untoward effects than air. The fact is that foam sclerotherapy is generally

a very safe and effective method of venous ablation, associated with few side effects and rare to uncommon adverse effects, but caution and training is advised and more information on the physiologic effects of foam is needed.

JL. Gillet (France) reported the results of a prospective, multicenter, controlled study regarding the side effects of foam sclerotherapy of incompetent great (n=818) and small saphenous (n=207) trunks in 1025 patients in 20 phlebology clinics. Duplex ultrasound examination was used to assess all patients between the 8th and 30th days and in addition 20% of patients were called by an external auditor. The saphenous trunk was occluded in 90.3% of patients. There was a low rate of adverse reactions, involving 27 patients (2.6%), including migraine with or without visual disturbance (8), visual disturbance alone (7), chest pressure alone (7), chest pressure associated with visual disturbances (5), infectious complication (1), deep vein thrombosis (10), and pulmonary embolism (1). Most side effects and complications are benign, but the eventuality of exceptional but more serious complications has to be taken into consideration in the managements of patients. A multicenter study like this one takes into account different practices and reports all possible complications, thus demonstrating the need for a common validated foam sclerotherapy protocol.

FX. Breu (Germany) presented the first experience in Germany with CO_2/O_2 gases in foam sclerotherapy. Based on a post-treatment observational German study on sclerotherapy he concluded that there is no advantage of CO_2/O_2 versus room air in the case of small volumes of foam. There is, however, a trend towards fewer side effects with CO_2/O_2 (especially visual disturbances and hyperpigmentation) in the case of high volumes. That's why CO_2/O_2 foam may be more effective because larger volumes can be administered and it is probably particularly suitable for large-caliber vessels. However, in a very recent publication (Sarvananthan T, et al, J Vasc Surg 2011, in press) in which a total of 10 819 patients were reviewed (1023 articles searched) no association between the volumes of foam used and the reporting of neurological side effects was identified and no association between the gas used or the ratio of gas and sclerosant and the number or type of neurological side effects was observed. In conclusion, the question of which gas is the best remains open.

SCLEROTHERAPY II

Chairpersons: Raymond-Martimbeau P, Frullini A.

This session consisted of a number of presentations dealing with sclerotherapy in the treatment of varicose veins.

F. Vega (Mexico) presented his personal experience using oxygen + polidocanol to make the foam in sclerotherapy in order to prevent serious neurological effects and improving microbubble quality and solubility in blood.

53 legs were sclerosed in 40 patients, foam prepared with 1 mL polidocanol (concentration from 0.5% to 3%) and 4 mL of O_2 with a maximum volume injected of 60 mL (average 26.6 mL). No patient had minor or major adverse

effects, three required a retreatment, all patients had thrombectomy after 7 days. Sclerosis with foam prepared with O_2 and polidocanol is a good option to prevent or reduce neurological effects; foam sclerotherapy performed with O_2 allows safer high volume injection.

A. Sommer (The Netherlands) presented a prospective, randomized, controlled study to establish the effectiveness and reduction in health care costs of ultrasound-guided foam sclerotherapy (UGFS) versus surgery. 227 patients underwent high ligation/stripping, 233 UGFS. Follow-up was at 3 months, 1 year, 2 year. Primary outcome: recurrence with a reflux > 0.5 s, 1 or more venous complaints. Secondary outcome: direct hospital costs. At clinical presentation,patients (83% CEAP class C2) were randomized and treated either by UGFS or by high ligation/stripping. GSV diameter in the upper thigh ranged 6.1 mm to 6.8 mm. At 3 months, foam sclerotherapy was performed again in 18 patients and surgery in 3, and at 1 year UGFS was done in 18 patients, and surgery in 7. At 2 years, 35% of the UGFS group showed reflux > 0.5 s, compared with 21% in the surgery group. Tired feeling and cramps improved by more than 50% and pain or restless legs by 50% in both groups. The treatment cost per patient was 1812 euros in the surgery group, and 731 euros in the UGFS group. Complications included thrombophlebitis (7.50%) and hyperpigmentation (12.3%) in the foam group. In conclusion, UGFS is as effective as surgery and costs less.

P. Raymond-Martimbeau (USA) reviewed 11 case studies related to neurological events and disturbance after liquid or foam sclerotherapy and established potential risks and prevention methods. Neurological effects were seen in 61% of women and 38.5% of men (mean age 45 years), 72.7% in large veins and 9% in small veins. The sclerosing agents used were mainly polidocanol and STS. Most patients developed symptoms within 5-20 min after the first treatment. 141 cases of migraine and visual disturbance have been described and among these 15 reported the presence of patent foramen ovale, but its presence was not checked in all cases. TIA and stroke cases typically resulted from paradoxical arterial embolism of the median cerebral artery or vertebral artery, but the underlying mechanism is poorly explained. Air embolism was reported in 6 case studies. Risk factors involved: volume of sclerosant and rate and number of injections, gas used, patient position (no sitting or head elevated), cytokines such as endothelin a strong vasoconstrictor released from the vessel during foam sclerotherapy, microbubbles can precipitate platelet aggregation. Finally the author suggested using the smallest bubbles possible, hydration to avoid constipation, and the Valsalva maneuver during the procedure and prescreening in patients with a history of cryptogenic stroke, severe migraines with aura, sleep apnea, platypnea orthodoxia, stroke with chronic obstructive pulmonary disease, severe co-morbidities.

A. Frullini (Italy) summarized the role of endothelin in visual and neurological disturbances during foam sclerotherapy. The vasoconstrictor endothelin is ten times more most powerful than angiotensin, and induces vasoconstriction and platelet aggregation. The production of endothelin was tested in two groups of rats, Group 1 at 0,1, and 5 min after injection of liquid POL or STS, and Group 2 at 0,1, and 5 min after foam POL or STS. After 5 min the highest production of

endothelin was observed in Group 2 with POL (22 pg/mL). Significant endothelin release is present after sclerotherapy and this could be the clue to a new pathogenesis of visual and neurological complications.

A. Cavezzi (Italy) presented his experimental data on the influence of a few variables in the formation and injection/dynamics of the sclerosant foam and to indicate a few possible procedures in foam sclerotherapy. Through an optical microscope an independent blinded observer examined videos and pictures at different time intervals. Several syringes, catheters, needles, gases, and techniques were tested as to bubble size and duration of the foam. 3% sodium tetradecylsulfate (STS) + air or other gases to form foam with a counter-resistance applied at one of the two syringes and 30° rotation in the three-way valve.

BD Discardit 5 mL and Terumo 2.5 mL syringes resulted in the smallest bubble diameter; higher silicone content syringes produced larger bubbles. 23G and 25G needles produced smaller bubbles, 27G and cannula 18 needles larger bubbles.

Gases: CO_2 alone produced smaller bubbles than CO_2 + O_2, and the smallest bubbles and consistent bubbles were produced with CO_2+O_2 and STS in a 3:1 ratio. An 4-F catheter resulted in 54 micron and 64 micron diameter bubbles at 10″ and 30″. When no resistance or no narrowing of the three-way valves was applied, the resulting bubbles showed a 10-20 micron larger diameter, mainly at 10″. Half liquid time (HLT) figures were 190″ for 5 mL + 10 mL BD Discardit combination, 163″ for 5 mL BD Discardit + 2.5/5 mL Terumo combination, 148″ for 2.5 mL Terumo + 5 mL Terumo combination. A 63% decrease in HLT was evident when using conventional, higher silicone content syringes. When no resistance or no three-way valve rotation was included , HLT was 30″ shorter. Using CO_2 instead of air gave 51″ shorter HLT, CO_2 + O_2 25% shorter HLT. SF with a 4F catheter showed 14″ HLT than needle based HLT.

Conclusions: smaller syringes (2.5 mL) produce longer-lasting foam. The BD Discardit syringe (5 mL) produces smaller bubbles and long-lasting foam. Conventional syringes produce larger bubbles and much shorter half-life foam.

BD Discardit 5 mL + Terumo 2.5 mL (or 5 mL) is the best combination in daily practice.

23G or 25G needles do not denature foam. CO_2 produces the smallest bubbles and more homogeneous foam, but short-lasting foam; CO_2 + O_2 prolongs half-life compared with CO_2 alone. Resistance and three-way valve 30° rotation reduces bubble size and increases foam duration.

RADIOFREQUENCY IN THE TREATMENT OF VARICOSE VEINS

Chairpersons: T. Proebstle, J. Marusiak

Endovenous radiofrequency ablation. a four year experience with the closurefast® catheter

C. Stuckey (USA)

The author related his experience of radiofrequency (RF) in private practice over 4 years. He treated a total of 1403 vessels using 1062 catheters through 1361 accesses. The originality of this report is that the author was able to treat more than one vessel from a given access site.

Application of higher energy during radiofrequency (rfitt) using a slower pull-back speeds is not associated with a higher complication rate

MS. Delbridge (UK)

The recommended energy setting used for the Olympus Celon system is 1.5-2 sec/cm at 18 W and led to a 73% occlusion rate. To increase the occlusion rate without increasing the degree of injury and complications, the author decreased the pull-back speeds to 3-4 s/cm in order to deliver higher energy levels. In this nonrandomized single-center retrospective study, when using lower pull-back speeds the occlusion rate at 6 weeks significantly increased to 97% with an average applied energy of 68 J/cm compared with 36 J/cm with faster pull-back speeds. There were no significant differences between the two groups concerning complications, even if a DVT occurred in the slower pull-back speeds group.

Since the present study is retrospective and single-center, further studies with longer follow-up are required to confirm these interesting results.

Ablation of saphenous trunks with the closurefast® catheter. immediate results and follow-up

S. Belentsov (Russia)

This prospective randomized study investigated the early results after RF ablation of the saphenous trunks. 146 patients with GSV diameters of 4-26 mm and SSV diameters 3-14 mm were treated. Only one minor complication occurred and the occlusion rate was 100% after 6 months.

Good results of RF ablation at 4-year follow-up have been already reported by Pichot and Proebstle. But it is interesting to note that even great saphenous trunks (diameter 26 mm) can be treated by RF with an excellent occlusion rate.

Radiofrequency ablation of gsv as a part of the therapy of chronic venous insufficiency

J. Marusiak (Czech Republic)

The author reported the results of a retrospective study of stripping and RF ablation in 180 varicose vein patients. Both groups were treated under general or spinal anesthesia associated with local tumescent anesthesia only for the RF group.

Hematoma, paresthesia, infection, cosmetic results, and recurrence were analyzed. There were no statistical differences between the two groups concerning the number of complications and the rate of clinical or hemodynamic recurrence, but the authors concluded that RF is less painful and results in a better quality of life.

It would have been interesting to compare cosmetic and quality of life results of two different surgical techniques, but because of the use of tumescent local anesthesia in RF group no conclusion can be drawn from this study.

Cyanoacrylate super-glue great saphenous vein ablation: preliminary results of a first-in-man feasibility study of a no-compression no-local anesthesia technique

TM. Proebstle (Germany)

The author described a new GSV ablative technique using N-butyl cyanoacrylate glue injected through a catheter. The author considers that the main interest of this technique is that no anesthesia is required and no compression needed. This preliminary study was designed to demonstrate the safety and early efficacy of the method. Eight patients from the Dominican Republic, with a mean GSV diameter of 6.2 mm, were treated using a mean volume of 1.6 mL. No pain was reported during or after the procedure and the complete occlusion rate was 97% at 180-month follow-up. No complications were observed.

Many techniques are used to ablate the GSV and glue is a new one. It seems to be a nonaggressive technique and does not require anesthetic drugs like sclerotherapy. But one would prefer local anesthesia before the puncture of the catheter.

No compression was applied in this study, but some teams have used one-day compression after stripping using a pin-stripper or an endovenous procedure under local tumescent anesthesia in an outpatient setting.

Cyanoacrylate has already been used in surgery to close the skin, to seal and reinforce suture lines, to treat digestive fistula, to control bleeding, and to anchor mesh for hernia repair. But strong inflammation has been reported in some cases leading to deterioration of the tissues, pain, or skin damage, but this was not the case in this study. The author considers cyanoacrylate glue to be quite different from others in that it causes chronic "cold" inflammation rather than acute inflammation. If there is no acute inflammation, there is a lower risk of neurologic side effects as observed with foam sclerotherapy and the immediate occlusion of the vein is probably due to the obliteration of the lumen by the glue itself. So, there could be a risk of embolism as described in one study (1). No embolism was reported in this study thanks to the high viscosity of the glue reported by the author.

These preliminary results have demonstrated the feasibility of the procedure even if the number of patients is very low. No immediate side effects were reported, there was no pain, and the early occlusion rate is excellent, but longer follow-up

is required. This could be an interesting technique when ablation of the saphenous vein is required, but should not be used routinely. If the procedure is cost effective and very easy to do, it could be very useful, particularly in poor countries.

Reference

Kirti Gupta: Embolization of Cyanoacrylate glue in systemic circulation in a case of hepatocellular carcinoma: an autopsy report *Diagnostic Pathology* 4:45 , 2009

Celon: a new radiofrequency technique for thermical ablation of the great saphenous vein: multicenter prospective study about 100 cases: 2 year results

JF. Uhl (France)

The aim of this study was to evaluate the effectiveness of Celon RF by assessing occlusion rate and clinical results. 100 GSVs were treated using recommended settings for the Celon Catheter (power 19W; pull back 0.6 cm/s, energy 40 J/cm). Few complications and little pain were noted at one week, but 11% of GSVs were recanalized at 2 years. Moreover, the author pointed out that a technical problem occurred during the procedure: the charcoalization of the electrode related to delivery of higher power. To avoid charcoalization and to improve the occlusion rate, the author suggested decreasing the power to 5 W and increasing the application time (pull back 0.1 cm/s). The results of a new study using these new parameters will be given soon.

Some studies have already reported a poor occlusion rate when using recommended settings. We agree with the author that decreasing the power will reduce side effects and that increasing the application time will increase the energy delivered, so a better rate of occlusion is expected. Meanwhile, a strict protocol should be established in a randomized controlled trial.

ENDOVENOUS ABLATION OF SAPHENOUS VEINS

Chairpersons: T Proebstle, J Strejcek

The role of different laser wavelengths and fiber tips

S. Kaspar (Czech Republic)

The aim of this study was to compare 980 diode (hemoglobin-specific) / 1320 nm Nd Yag (water-specific) / 1470 nm diode (water-specific) lasers and to analyze sides effects and occlusion rate on day 5 using a VAS, quality of life questionnaire, CIVIQ2, and duplex scan. Continuous fiber pull-back and local tumescent anesthesia were used in all cases. Results showed better results in terms of pain, return to daily activity, bruising, and induration with water lasers and better results in terms of bruising and induration with the 1470 nm diode compared with the 1320 nm Nd Yag diode. The occlusion rates were similar. Patients preferred the 1470 nm diode to the 1320 nm and 980 nm diodes.

This prospective study confirms what we know: radial fiber and higher wavelengths give better results in terms of side effects. A radial fiber tip was used with the 1470 nm diode only, but the author considers that this had no impact on the global results because the same quantity of energy was delivered with all 3 lasers.

Steam vein ablation

R. Van den Bos (The Netherlands)

The author described a new GSV ablation technique using steam, produced by a generator and delivered at 120°C into the vein through a catheter. The experimental study was done on sheep and showed good reduction of the vein lumen due to thrombotic occlusion. The human study was done on 24 patients to assess quality of life and GSV occlusion rate at 1 year. One pulse/cm of steam was delivered. Occlusion of the GVS was complete in 13/20 GSVs and partial in 11. No important side effects were noted and post-op quality of life was good. In order to increase the occlusion rate by increasing the heat on the vein wall, the author now uses 2-3 pulses/cm, and the new results will be reported soon.

This new technique seems to be effective in GSV ablation. It is safe and uses a natural product—water. We hope this will decrease the cost of the endovenous treatment of the GSV. With future development of very small and flexible catheters, we could probably use this technique to treat collateral veins. We are also waiting for randomized controlled trials comparing RF, laser, and steam.

Clarivein mechano-chemical ablation

S. Elias (USA)

The author described another new technique for ablation of the saphenous trunk. A wire was introduced through a catheter into the vein and guide by Doppler ultrasound. Rotation of the wire at the top of the catheter damages the vein intima. Starting 1 cm from the saphenofemoral junction, the catheter was pulled back at 1-1.5 mm/s and a 1.5% STS solution was injected slowly during the pull-back. No anesthesia was required and compression was applied for 2 weeks. The author reported a study where 30 GSVs were treated using 8-10 cc of STS for the GSV. No deep venous thrombosis and no complications were reported, and the occlusion rate was 100% at 6 months of follow-up. This is an interesting albeit single-center study with very short follow-up.

Non ablative concepts of endovenous laser

A. Frullini (Italy)

The author described a combination of laser and foam therapy in order to treat large veins (> 1.5 cm). An endovenous water-laser (Holmium 3100) was used to reduce vein diameter to facilitate the action of the foam. In a pilot study, a 50% reduction in vein diameter was obtained at 3 months, which is uncommon with foam alone. No anesthesia was required and no pain or complications were noticed.

Keynote lecture: 10 Years of Endothermal vein ablation – latest achievements and future perspectives

T. Proebstle (Germany)

Until 2004 the endovenous failure rate was 5-15% due the low energy doses delivered. After 2004 new concepts were discovered: the energy applied has to be proportional to the vein diameter.

Some details could improve the results: vein compression with the ultrasound probe during the laser procedure making more vein contact with the laser fiber and the slow pull-back of the fiber delivering enough energy (80 to 100 Joules).

Nowadays literature reports indicate 95% to 100% occlusion after five years of follow-up. The focus in recent years has been on reducing side effects by means of new laser wavelengths and new fibers (ceramic, radial). It seems that wavelength matters: the 1470 nm diode is better than the 810 nm diode. Comparative trials during the last 3 years show no relevant difference between endothermal treatments and surgery.

References:

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KEYNOTE LECTURE: Crossectomy during endovenous therapy of varicose veins – yes or no

S. Kaspar (Czech Rep.)

Crossectomy was first performed by Trendelenburg in 1890 and is still considered as an option in endovenous ablation. Papers analyzing the distribution of GSV reflux demonstrated: 54% in the terminal valve, 16% in the preterminal valve, 11% in the terminal vein, 6% in mid-thigh perforators, 8% in association with lymphatic and venous reflux, and 5% of other causes.

Observing these results we note that crossectomy is not necessary in 50% of cases.

The important endovenous laser treatment (EVLT) recommendations are: correct positioning (ultrasound-guided) of the catheter or fiber just below the superficial epigastric vein, during the procedure. Advantages of EVLT technique are esthetic results (no incisions), absence or very low incidence of neovascularization, less hematoma compared with surgery, and earlier recovery.

The main goals of EVLT are obliteration of the vessel and maintenance of venous drainage.

Marsh et al 2010 reported 0.15% DVT in 2195 cases of EVLT.

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ENDOVENOUS LASER TREATMENT

Chairpersons: S. Kaspar, H. Partsch

Complications of endovenous laser ablation of varicose veins

R. Vellettaz (Argentina)

The author did a retrospective analysis of complications of laser ablation. He did 1008 procedures with a 980 nm device. No EVLT turned into conventional surgery. Postoperatively there was pain in 67.55% of cases, ecchymosis in 100%, hematoma in 7.04%, superficial thrombophlebitis in 6.25%, paresthesia in 3.67%, and pigmentation in 3.27%. There were no serious complications either intra- or postoperatively.

Endovenous laser: 8-year recurrence is rare and benign compared to surgery

J. Ragg (Germany)

The author presented the long-term results of laser ablation. Of 11 900 endovenous laser procedures on great, small, or accessory anterior saphenous veins performed from 2002 till 2010, 614 cases were available for 8-year follow-up. 34 of them (5.5%) had recurrent reflux. Neovascularization in the junction area or residual stumps were not observed. This paper led to some debate about what should be assessed as an outcome of any kind of ablation procedure – technical or clinical parameters.

Endovenous simulated laser experiments at 940 nm and 1470 nm suggest wavelength independent temperature profiles

R. Van den Bos (The Netherlands)

This Dutch team compared in vitro the impact of wavelength, pull-back speed, and power level on the endovenous temperature profile. They measured temperature in an experimental setting using thermocouples. Different laser parameters and 2 different pull-back speeds (2 and 5 cm/s) with 2 lasers – 940 nm and 1470 nm – were used. The experiments showed that low pull-back speed and increasing of power (up to 14 W) both cause higher maximal temperatures. The use of different wavelengths did not influence the temperature profile so the heat induction is independent of laser wavelength. This study is interesting in view of current opinion regarding the clinical advantages of lasers of higher wavelength.

Endovenous procedures: evidence based endovenous treatment of varicose veins

R. Van den Bos (The Netherlands)

In spite of the large number of studies concerning varicose veins published in recent years, the literature providing evidence of the efficacy of endovenous treatment is relatively scarce. One reason may be the lack of interest shown by manufacturers of medical devices in research (unlike drug companies). In fact, endovenous techniques were implemented in clinical practice before good randomized controlled trials were published.

As to the comparison of endovenous techniques, some randomized controlled trials came to the conclusion that the efficacy is similar: in one trial EVLA was better than RFA and in the other trial EVLA, RFA, or stripping was better than foam sclerotherapy. Secondary outcomes were not routinely monitored. The problem is the lack of methodological consensus (defining what to monitor, how and at when). The parameters suggested to be worth evaluating may be pain, bruising, number of days before to return to normal activities, and patient satisfaction.

Lymphatic diseases

Lymphology

Chairperson: S. Michelini.

S. Michelini (Italy) shared with us his clinical experience on lipedema/lymphedema. Lipedema affects only women and consists of symmetrical, sticky edema of different sizes, pain, tenderness, and with poor response to diet and physical exercise. At the advanced stages it causes marked impairment of individual functions, with serious psychological repercussions, and can be associated with lymphedema. It is important to distinguish lipedema/lymphedema from pure lymphedema. 49 patients were studied at three clinical stages. The authors found an impairment of the ability of patients proportional to clinical disease stage and in the third stage higher-than-average values were noted in the qualifiers of the four domains related to lower limbs (structure, function, performance, and need for facilitators). The patients were treated with complex physical decongestive treatment and in 16 cases with liposuction. At the end of treatment the final garment with elastic compression of 25-40 mm Hg was prescribed depending on the tolerance shown by the patient during the intensive treatment. This disease is little known to the medical community and its effect on quality of life is underestimated as it is considered mainly a cosmetic and dietary problem. That's why more awareness and knowledge is needed in this issue.

A. Materankova (Czech Rep.) presented her team's experience with hyaluronidase enzyme injection in the treatment of secondary lymphedema, recurrent erysipelas, and lymphorrhea. The enzyme hyaluronidase degrades hyaluronic acid of subcutaneous proteoglycans, removes scarred tissue, and efficiently helps reconstruct lymphatic drainage of the affected area. Particular steps of the method were mentioned, especially the main rule of performing injections deliberately from the central collecting lymph nodes gradually towards peripheral parts of the body affected by secondary lymphedema, recurring erysipelas, or lymphorrhea. Through two case presentations the authors demonstrated how effective the method is. However, this has yet to be proved in larger studies.

F. Passariello (Italy) described the usefulness in the assessment of lymphedema of the ultrasound volumetry he has developed. The well-known indirect tape volumetry is an easy procedure, which isn't however able to evaluate the involvement of tissue layers in lymphedema. Ultrasound volumetry measures the volumes of the cutaneous, subcutaneous, and musculoskeletal compartments. Standard anatomical limb reference points are used to achieve more stable measurements. The computation uses the cone trunk formula, modified and extended to the computation of internal volumes. In addition, lengths can be related to the height and standardized according to the weight and to the body mass index or the standard length of limb segments. Measured data are managed by special software, which provide computation and data storage facilities. The method, though still in the observational phase and requiring validation, allows the clinician to detect even localized and subclinical dysfunction in upper and

lower limb lymphedema. It is rather time-consuming but is a low-cost lymphedema monitoring method and should be used by experts after validation.

Finally, **S. Michelini**, shared with us the results of a very impressive study of the genetics and clinical characteristics of Italian families with primary lymphedema. Primary lymphedema usually arises at puberty and may be associated with distichiae (double row of eyelashes). Transmission is autosomal dominant with variable penetrance. The genes involved are mainly those coding for the transcription factor FOXC2 and for receptor 3 of vascular endothelial growth factor VEGFR3. The authors conducted a clinical study in 47 patients from selected Italian families in order to analyze the genotype-phenotype correlation and shed light on prevalence of hereditary lymphedema associated with FOXC2 and VEGFR3 mutations. Patients were selected by a network of medical specialists in lymphology located in 11 Italian regions. The inclusion criteria was the assessment of lymphedema by lymphoscintigraphy, exclusion of secondary causes, enrollment of patients whose family had at least 2 cases of lymphedema and disease onset less than 25 years. Genetic tests involved the extraction of DNA by salting-out from 100 blood samples (1 mL each), which was followed by PCR amplification of the entire coding region and thus sequencing. The work is ongoing, but five new mutations, a mutation already described in literature and several as yet unpublished changes in intronic sequences, were detected. This is the first Italian study in which FOX2 and VEGFR3 mutations were sought among a wide range of clinically selected patients with primary lymphedema. Compared with American series this study shows a significantly lower rate of mutation, suggesting the existence of a new gene playing a major role in the etiology of primary lymphedema in Italian patients.

Chronic cerebrospinal venous insufficiency

Diagnostic and endovascular treatment of chronic cerebrospinal venous insufficiency (ccsvi)

L. Grozdinski (Bulgaria)

Multiple sclerosis is an inflammatory and neurodegenerative disease of the central nervous system, but its etiology and pathogenic mechanism are unclear. This study compares the ultrasound findings in 50 control patients with 500 patients with multiple sclerosis (from 20 different countries). In the control group the presence of CCSVI was 8% (4 patients) in contrast to 92.25% (461 patients) in those with multiple sclerosis. In all of them, venography confirmed the presence of stenosis, not only in the jugular (100%) but also in the azygos veins (73%). Ultrasound sensitivity was 98%, specificity 66%, and concurrence 91%.

Balloon angioplasty was performed in 1114 (91%) stenosed veins and stent implantation in 98 (9%). Stent thrombosis was high (20 of them, 20%) and low in angioplasty (1, 0.8%). There weren t any major events.

The clinical improvement after treatment was 81% in early follow-up and 60% at 12 months. 21% of patients returned to the previous situation without relapse and the score on the Expanded Disability Status Scale changed from 6.1 pretreatment to 5.2.

The authors concluded that in patients with multiple sclerosis a high frequency of CCSVI is present, and after dilatation of venous stenoses multiple sclerosis symptoms improve. Randomized controlled studies are needed.