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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.

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PREFACE

This report from the 15th World Congress of the Union Internationale de Phlébologie (UIP) which was held in Rio de Janeiro, Brazil, from October 2 to 7, 2005 has been prepared by our Medical Reporters' Academy (MRA) group. We are all medical doctors with hospital practices, and we come from different countries around the world (Belgium, France, Italy, Poland, Portugal, Spain, and Russia). This MRA group, whose members rotate by thirds every year, was created and sponsored by Servier 9 years ago. Since then, the group has been attending major international congresses in Phlebology and Angiology. This gives us the opportunity to share our experiences in the field and pass on to specialists all over the world selected information on recent developments and new techniques. The international participation at the last UIP congress with world experts in the fields of vascular medicine and biology, dermatology, phlebology, and angiology as well as interventional vascular, and endovascular surgery, was a major opportunity for many countries to be represented and to compare experiences. Daily lectures alternated with plenary sessions covering the many facets of venous and lymphatic diseases. In order to promote the work of a wide range of speakers and young scientists, the scientific committee of the congress selected abstracts on each topic for free communications or poster sessions. In addition, several prizes were granted for oral presentations (eg, the UIP/Servier Prize and the UIP/Bauerfeind Prize). Unfortunately, it was only possible for the participants to attend a small number of the presentations. Therefore, we have collected and selected the best information on the many presentations and have organized it in different chapters: epidemiology and socioeconomics, prevention of venous diseases and risk factors, fundamentals, investigations and hemodynamics, and invasive and noninvasive therapy. We hope this report will be useful, not only for those who were present at the Congress, but also for those who were unable to attend.

We wish you enjoyable reading.

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Chronic venous disease in developing countries

Chairpersons: M. Cazaubon (France), A. Scuderi (Brazil)

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M. CAZAUBON (France)

Epidemiology of venous disorders in Morocco

A. BENJELLOUN (Morocco)

The incidence of venous disease in Brazil based on the CEAP classification: an epidemiological study

A. SCUDERI, P. SCUDERI NETO, M. A. SCUDERI, C. G. BRUGINSKI, B. RASKIN, F. A. ASSAL (Brazil)

1. The incidence of the venous disease in developing countries is similar to that in Western countries.
2. The CEAP classification is an important method for standardizing the clinical manifestations of the venous pathology. It allows everybody, around the world, to speak the same language when referring to venous disease.
3. The varicose syndrome is much more common in women than men.
4. Age and pregnancy are important factors in the development of venous disease and its complications. This fact was clearly demonstrated in the female group over 48 years.
5. More than 50% of women in the groups ranging from 14 to 22 and from 23 to 48 years old presented a large number of incidences of visible veins without any symptoms.
6. Venous disease, besides being a physiological and public health problem, is also an important esthetic factor, especially for women.

Chronic venous disease in the obese male: an epidemiological survey

J. P. BENIGNI, M. CAZAUBON, M. MATHIEU, I. ACHHAMMER (France)

To assess the relationship between obesity and chronic venous disease (CVD) in adult male patients, a cross-sectional study, including clinical descriptions of the disease by phlebologists and angiologists, was performed. Four hundred and ninety-four male patients (obese and nonobese) were included in the study.

The authors stated that:

1. CVD severity increases with age.
2. Twenty-five percent of patients with venous ulcer are obese.
3. Disease duration is longer in obese than in nonobese patients.
4. Popliteal reflux is more frequent in obese than in nonobese patients.
5. Paresthesia and pruritus are more severe in obese patients.
6. Pain and heaviness are more severe in obese patients.
7. Obesity effect on CVD severity is a result of age.

Epidemiology and socioeconomics

Chairpersons: F. Pace (Argentina), D. Gama (Portugal)

Leg ulcer prevalence in a defined geographical population: a repeated cross-sectional study

O. NELZEN, A. JAKOBSSON, I. FRANSSON (Sweden)

The same postal cross-sectional study with health care providers was performed in 1988 and repeated in 2002 in a defined geographic population of Sweden. Between 1988 and 2002, a radical change in leg ulcer management had been introduced by the creation of an organized structured care of leg ulcer patients in this district. After correction for wrong inclusions and clinical examination of a random sample of patients, the leg ulcer prevalence, previously found to be 0.31% of the general population in 1988, had decreased to 0.24% in 2002. The 23% decrease in the number of leg ulcer patients was probably related to the radical change in leg ulcer management in the district. This result is interesting, as it is usually believed that the increasing number of elderly people may lead to an increasing number of leg ulcer patients. In this study, 82% of the leg ulcer patients were over 64 years old.

Venous ulcer prevention: socioeconomic issues

C. ALLEGRA (Italy)

Varicose disease is a chronic and evolving disease. The etiology of leg ulceration is venous disease in 70% to 80% of cases, and among them, 30% are the result of the post-thrombotic syndrome. The prevalence of leg ulcers is high, reaching 0.8% to 1% of the general population, but it increases with age. Indeed, among people over 65 years old, ulcer prevalence is 3.6% of the population. The duration of venous ulcer is more than 4 months in 50% of the cases, and more than 2 years in 20%. Chronic venous disease is supposed to consume 1% to 2% of the health care budget of European countries. The prognosis for healing is largely dependent on age, so the ageing of the population in developed countries is likely to increase the prevalence of venous leg ulcers in the next 10 years. The total CVI-related direct costs (CVI diagnosis and management: hospitalizations, consultations and drug costs; loss of working days not included) was evaluated in Italy before and after the Italian healthcare reform (drug dereimbursement) in 1993-94. The total CVI-related costs were 360.4 million Euro before the reform and 384 million Euro after the reform, but the distribution of the costs has changed. The 23.6 million Euro increase in CVI management costs was due to cost redistribution from prescriptions and consultations to hospitalizations. Fewer patients were treated overall, with consequent disease worsening and increase in complications. Primary prophylaxis of venous ulcers includes clinical examination and careful family and personal history assessment. Secondary prophylaxis, including compression therapy, pharmacotherapy and two consultations a year with duplex examination, is estimated at 1.08 Euros/patient/day. Both primary and secondary prophylaxis are cost-effective.

Prophylaxis and treatment of leg edema

Chairpersons: H. Partsch (Austria), A. Scuderi (Brazil)

Leg edema, a frequent sign in a European population

E. RABE (Germany)

Lymphedema is an important cause of chronic leg disease in the general population. Up to now, almost no epidemiological data concerning lymphedema of the legs has been available concerning prevalence and distribution in the general population. In the Bonn Vein Study, a population-based cross-sectional study in 3072 individuals randomly chosen from population registers in the city of Bonn and the surrounding rural townships, aged between 18 and 79 years, the prevalence and risk factors of chronic venous diseases were evaluated. In addition to the questionnaire and the phlebological investigations, a skin-fold test at the dorsum of the second toe was performed. The so-called Stemmer´s sign was slightly positive (Stemmer I) when the skin fold was between 0.5 and 1 cm wide. Stage II was reached when the skin fold measured more than 1 cm, and Stage III when the skin fold was extremely enlarged. In the history questionnaire 1.8% of all individuals claimed to have lymphedema; 1.1% of the male and 2.4% of the female population. In the clinical investigation 12.4% of the men and 15.2% of the women had a slightly positive Stemmer´s sign; 1.5% of the men and 2% of the women had a manifest lymphedema represented by Stemmer´s sign stages II and III. The prevalence of positive Stemmer´s sign II and III was markedly higher in the urban population, at 2.4%, compared with the rural population with 0.7%. The prevalence of the positive Stemmer´s sign increased significantly with age, and also with the clinical stages of chronic venous disease in the CEAP classification. These data show the prevalence of lympedema of the legs in the general population and the close connections between chronic venous disease and a positive Stemmer´s sign.

II

PREVENTION OF VENOUS DISEASE

RISK FACTORS

Obesity: an important risk factor for the development of chronic venous insufficiency

E. RABE (Germany)

Obesity: a risk factor for chronic venous disease?

J. P. BEGNINI (France)

In the framework of the Symposium of the German-speaking Phlebological Societies of Austria, Germany and Switzerland.

The Bonn study is an epidemiologic study which took place in Bonn between October 2000 and March 2002. This study in 3072 members of the general population evaluated the prevalence and the risk factors of chronic venous disease. This population was selected randomly from registries. All participants were examined by clinical means and by duplex ultrasound. Among this population, 87.5% had telangiectasia, 23.2% varicoses veins, and 17% chronic venous insufficiency (CVI, C3 to C6). The main risk factors for varicose veins, after adjustment for gender, age, and region of residence, were: age, female gender, and pregnancies but not obesity. One of the most important risk factors of CVI was obesity, and the relative risk increased with the body mass index (BMI = weight in kg/[height in cm]^2). In a multivariate analysis, the odds ratio reached 10.5 for men and 7.9 for women for a BMI >40 (respectively 6.5 and 3.1 for a BMI between 30 and 40).

In a French longitudinal survey, 241 obese patients (BMI between 32 and 59) were recruited before gastric surgery (gastroplasty or bypass) and examined by clinical means and duplex ulltrasound. No significant difference in BMI was found in this population for prevalence of varicose veins or the classification in CEAP. This study had an evident bias of recruitment. Because of this, the mean age in this study was only 36.6 years.

EDEMA

Prophylaxis and treatment of leg edema

Chairpersons: H. Partsch (Austria), A. Scuderi (Brazil)

Prevention of occupational leg swelling by compression stockings

H. PARTSCH, J. WINIGER, B. LUN (Austria)

Twelve patients - 8 females, 4 males, aged 21 to 60 years (mean 41.4 years) with sitting and/or standing professions - were investigated. Clinical and duplex examinations revealed large varicose veins (CEAP class C2) in 5 legs and venous edema (C3) in 1. Five patients reported heaviness and tiredness in the evening; three of these had varicose veins or venous edema. The volume of both lower legs up to a height of 43 cm was measured using water volumetry, once in the morning and then 7 hours later. The procedure was carried out for 4 days, during which the patients wore below-knee compression stockings of different compression levels, alternately on one leg only in a random order. The pressure of each individually fitted stocking at b-level was measured using the Hatra method. According to this compression pressure the tested stockings fitted into the following CEN classes: support stockings (pressure 5.9±2.4 mm Hg), class A (11.2±1.8 mm Hg), class I (18.1±2.8 mm Hg) and class II-stockings (21.8±1.8 mm Hg). As a result the average evening edema of the noncompressed legs over 4 days (n=48) was 76.7±45.9 mL. There is no correlation between the amount of leg swelling and subjective complaints. Support stockings with a mean pressure below 10 mm Hg achieved a reduction of evening edema of 27.3+60.6 mL ($P<0.05$). With the other stockings the mean values of the lower legs could be reduced to values, which on average were lower in the evening than in the morning (Class A: -34.1±56.7 mL, class I: -40. 4±45.2 mL and class II: -59.1±42.2 mL. All differences compared with the volume increase without stockings were statistically highly significant ($P<0.001$). Subjective symptoms were improved mainly by the stockings exerting a pressure above 10 mm Hg, but not by the support stocking. The author has concluded that swelling of the lower legs after sitting and/or standing work is a phenomenon which can be found in all individuals, and may be more pronounced in patients with varicose veins. Calf-length compression stockings with a pressure range between 11 and 21 mm Hg are able to reduce or even totally prevent this evening edema, and may therefore be recommended for people with a profession involving long periods sitting or standing.

POST-THROMBOTIC SYNDROME

Prophylaxis and treatment of leg edema

Chairpersons: H. Partsch (Austria), A. Scuderi (Brazil)

Leg compression for the treatment of symptoms of deep vein thrombosis and the prevention of post-thrombotic syndrome

W. BLÄTTLER (Switzerland)

Compression started immediately upon diagnosis of proximal DVT leads to a more rapid and sustained relief of symptoms and regression of signs than bed rest, and allows a faster return to daily activities. The benefit is almost the same whether bandages or stockings are used. Observational studies showed that most patients with proximal (crurofemoral) DVT can be fitted with ready-made calf-size stockings exerting a pressure of 23 to 32 mm Hg (Sigvaris 503) and one third of patients with pelvic DVT are treated similarly. Comparison of two management studies showed that stockings are increasingly preferred over bandaging for outpatient management (in 71% versus 29%). Two randomized controlled trials compared compression treatment with stockings for the prevention of the post-thrombotic syndrome (PTS). Its incidence (around 50%) was reduced by half when started about 2 weeks after diagnosis, usually at discharge from the hospital. Ready-made round-knitted stockings exerting a pressure of 30 to 40 mm Hg at the ankle were as effective as custom made flat-knitted stockings exerting a pressure of 35 to 45 mm Hg. No reliable data are available on the rate of recurrence of DVT. In conclusion the author has underlined that leg compression is effective for both the treatment of the clinical symptoms of acute DVT and the prevention of the PTS. These findings suggest that leg compression should be started immediately upon diagnosis. Despite a clear trend towards the easier-use stockings, compression with bandages remains the optimal regime for handicapped patients and those with severe edema.

RECURRENCE 0F VARICOSE VEINS AFTER SURGERY (REVAS)

LECTURE

The profile of the "REVAS patient"

M. PERRIN (France)

Fourteen clinics in 8 countries enrolled 201 lower limbs (170 patients). The mean age was 55.6 (range 27 to 82). Female patients constituted 69%, and the number of previous surgical procedures was 1.2 (range 1 to 3). The period of time between last intervention and consultation was 136 months (range 1.8 to 692.1). The C of the CEAP was used in a descriptive way (elaborated CEAP). By definition all patients were quoted as C2; 24.6% were only C2 and 75.4% C2+ (14 combinations), C1 was present in 52%, C3 in 37%, C4 in 20%, C5 in 8%, and C6 in 2%; 77% were symptomatic and 23% asymptomatic. Concerning the etiology, 181 were quoted as P (91%), 10 secondary (5%), and 8 congenital (4%). Fifty-five patients (27%) had a deep venous abnormality and 110 (55%) an incompetent perforator. One hundred and eighty-eight (95%) patients had reflux only and seven (4%) a combination of reflux and obstruction. Topographical sites of recurrence were: groin 37%, thigh 68%, popliteal fossa 23%, lower leg 85%, and other 11%. Sources of recurrence were: pelvic or abdominal 17%, saphenofemoral 47%, thigh perforator 30%, saphenopopliteal junction 5%, popliteal perforator 5%, gastrocnemius vein 9%, lower-leg perforator 43%, and no source 10%. The numbers of sources were: 0 10%, 1 37%, 2 32%, 3 15%, and more than 3 7.5%. Clinical significance of reflux was: probable 82%, unlikely 10%, uncertain 8%. Then nature of sources for the same site were: technical failures 19%, tactical failure 10%, neovascularization 20%, uncertain 20%, mixed 17%, and information not given 14%. For a different site there were: persistent 12%, new 32%, uncertain/not known 21%, and information not given 35%. Possible contributory general factors were: family history 68%, obesity 24%, pregnancy 16% (percentage based on female population), oral contraception 9.9% (percentage based on female population aged less than 65 years old), and lifestyle factors 43%. Possible specific contributory factors were: primary deep vein reflux 13%, postthrombotic syndrome 5%, angiodysplasia 3%, and calf pump dysfunction 10%. The profile of patients with REVAS shows that the majority were symptomatic, with various combinations of patterns. Sources of reflux feeding the recurrence were predominantly of multiple origins, and its causes were variable. When recurrence occurred at the site previously operated on, revascularization was as frequent as technical failure.

Recurrence of varicose veins: can it be reduced?

J. FERNANDES E FERNANDES (Portugal)

Professor Fernandes e Fernandes presented his own results after varicose vein surgery (stripping the insufficient long saphenous vein and avulsion of collaterals) with a minor recurrence rate of 11% and a major recurrence rate of 4%. He pointed out the value of mapping the sites of incompetence in order to treat them and preserve normal venous segments.

III

FUNDAMENTALS OF VENOUS DISEASE

ANATOMY

Basic anatomy

Chairpersons: J. T. Hobbs (UK), L. K. Moura (Brazil)

Collagen fiber networks of the human proximal long saphenous vein valve: a scanning electron microscopic study

A. KOLESNIK, T. SKADORWA (Poland)

This study used scanning electron microscopy to determine the characteristics of collagen fibers of the four saphenous venous cadaveric veins in normal subjects without signs of clinical venous insufficiency. The images obtained showed intrinsic collagen bundles, arranged in layers of parallel fascicles, crossing at different angles. The findings confirmed that the collagen fibers are organized a the way that strengthens the valve wall, especially in the area of its attachment to the venous wall and in the venous pocket. Future work should compare normal collagen architecture with the changes found in patients with venous insufficiency.

Changes in purine receptor expression in varicose veins reflect the phenotype transition of the smooth muscle

M. J. METCALFE, G. BURNSTOCK, M. TURMAINE, D. M. BAKER (UK)

This is an interesting study about purine receptors in the smooth muscle cells of the great saphenous vein. This work has demonstrated, for the first time, the changes in purine receptors in longitudinal and circular smooth muscle in the long saphenous vein in venous insufficiency. This change in purine receptors is reflected in the contractile strength of smooth muscle. The electronic microscopy findings confirm the phenotype change observed, from contractile to synthetic of smooth muscle cells in the varicose veins. Interventions targeting purine mediator pathways may be a useful approach for treating chronic venous insufficiency in the future.

Anatomy of the short saphenous vein and companion nerves: the high-risk zones for the treatment of varicose veins

J. F. UHL, C. GILLOT, P. LEMASLE, V. DELMAS (France)

This study, performed with anatomic cadaver dissection, showed that the ankle, the apex of the calf, and the popliteal level are points where the small saphenous vein is very close to various important nerves. All surgical and endovenous laser procedures undertaken at these three points must be carried out carefully to avoid nerve injuries.

Is MRI a tool for the diagnosis of soleus syndrome? Preliminary report

I. STAELENS, P. PETROONS, L. LEBRUN, S. VAN SINT JAN, X. DEMONDION (Belgium)

This report describes the MRI characteristics of soleus architecture in seven subjects described in order to study the soleus syndrome, a rare case of calf pain produced by venous entrapment in the soleus arch. The MRI results must be compared with those of phlebography in a large group of patients and normal subjects with this very infrequent syndrome in order to reach conclusion.

Anatomic variations of the great saphenous vein studied by color Doppler ultrasound

S. AMARAL, M. MATHIAS, S. LEITE (Brazil)

This study analyses the anatomic variants of the great saphenous vein by ultrasound studies. The very frequent anatomic variants can be discovered by the use of routine ultrasound to prevent problems of inadequate surgery during venous treatment procedures.

Relationship between diameter and reflux time of the saphenous veins; implication for preoperative mapping for selective stripping surgery

M. MO, C. TANAKA, M. NAKAMURA, O. KANEKO (Japan)

Venous reflux is proportional to the venous diameter. The authors of this work concluded that reflux studies can be omitted when the great saphenous vein is larger than 9 mm or smaller than 2 mm. In any other case it is necessary to perform a Doppler reflux study to test the presence of venous insufficiency. In any case, great venous insufficiency cannot be studied only in terms of venous diameter, because of the variability in height and weight of patients is related to the venous diameter.

CHRONIC VENOUS DISEASE

SERVIER/UIP Fellowships

Chairperson: C. Allegra (Italy)

Results of the project by the previous winner (2003/2005) of the SERVIER/UIP Fellowships:

Elastin dysregulation in varicose veins

M. G. PASCUAL GONZALEZ (Spain)

The aim of this study was to examine the in vivo and in vitro expression of lysin oxidase, like proteins (LOXL) and tropoelastin and explore their association with tissue growth factor β1 (TGFβ1) as a marker of tissue remodeling. Also, the elastic components of the vein wall (BA4, fibrillin 1 and 2) and differentiation state of the muscle component of normal and varicose veins (vimentin, desmin, myosin, and α-actin) were evaluated and correlated with age of patients with varicose veins.

Results:

- The markers involved in the synthesis of vein elastic components (LOXL/tropoelastin) in the vein wall diminished with age. In varicose veins, they showed an inverse relationship (LOXL decreased, tropoelastin increased)
- The previously established reduction in the level of elastin in the varicose condition may be related, at least in part, to the observed reduction in lysin oxidase like-1 (LOXL-1) levels which decreased the spontaneous covalent cross-linking of elastin
- The varicose pathology induces dysregulation of the expression of TGFβ1
- Altered TGFβ1 could be a good marker of vein wall damage. The dysregulation of both its active and latent TGFβ1 forms detected in the varicose specimens could play an important role in the fibrous process, representing the end point of venous insufficiency.

Project by the last winner (2005/2007) of the SERVIER/UIP Fellowship:

Physiological and morphological characterization of a porcine model of superficial varicose veins

G. T. JONES (New Zealand)

In this project, the creation of an arteriovenular fistulae in the pig is an experimental model which produces superficial varicose veins (VV) with valve changes which appear to mimic that observed in human patients. Rather than produce acute distension of the overlying superficial veins, the veins dilate slowly after an initial lag period of 1 to 2 weeks. Interestingly, in the model, the superficial VV that develop are more pronounced when the animals are placed in an erect posture. Also of great interest in this model is the formation of similar changes within the superficial veins of the contralateral limb which may allow more extensive valve remodeling before becoming incompetent, a hypothesis which the author hopes to test by measuring levels of the tissue remodeling enzymes, the MMPs.

The main objectives of the study are the following:

- Determine the physiological basis of the superficial varicose veins that develop in this porcine model: intravenous blood pressure and velocities at baseline, 6, and 12 weeks; quantify postural reflux into the superficial veins
- Measure the venous tissue levels of matrix metalloproteinases: determine correlations between MMP levels and vein wall structure, diameter, and physiology.

Bauerfeind/UIP Fellowships

Chairperson: H. Partsch (Austria)

Results of the project by the previous winner (2003/2005) of the BAUERFEIND/UIP Fellowship:

Apoptosis-related proteins, extracellular matrix molecules (ECM) and microangiopathy of the skin: their role in chronic venous insufficiency

S. HEISING ET AL (Germany)

The epidermis is continuously renewed and, this process is ensured by cell-cycle-related proteins. During wound epithelization, cell-cycle regulatory proteins having a blocking (bcl-2)or promoting (bax, caspace 3) play a role in this process.

Main conclusions:
- Not only patches of skin in the perimalleolar area, but even perfusion of proximal calf is impaired
- Loss of bcl-2 may be a signal for upward migration of cells within the epidermis.

Project by the latest winner (2005/2007) of the BAUERFEIND/UIP Fellowship:

Gastrocnemius vein follow-up under compression and correlation to clinical symptoms

C. JEANNERET-GRIS, I. VON PLANTA (Switzerland)

Main study objectives:
- To study the influence of compression stockings on venous diameters of the gastrocnemius veins in patients with leg symptoms (VCS - score >2)
- To study the correlation between gastrocnemius vein diameters and quality of life measurements.

Is primary chronic venous disease an evolving disease?

In the framework of the SERVIER Symposium.

Chairpersons: C. Allegra (Italy), A. N. Nicolaides (Cyprus)

Venous hypertension and the inflammatory cascade: major manifestations and trigger mechanisms.
G.W. Schmid-Schönbein*; L. Pascarella(USA)

Chronic venous disease and the endothelium-leukocyte interaction: from early symptoms to open ulceration.
A. N. Nicolaides (Cyprus)

MPFF* and venous valve damage induced by venous hypertension.
G.W. Schmid-Schönbein (USA)

MPFF*, symptoms and edema: clinical update.
G. Jantet (France)

MPFF* and venous leg ulcer: new results from a meta-analysis.
P. D. Coleridge-Smith (UK)

Rapidly advancing understanding of the mechanisms involved in chronic venous disease (CVD) progression might allow the identification of targets for pharmacological intervention aimed at preventing future morbidity.

Recent histological and immunocytochemical evidence of venous leg ulcers supports the hypothesis that lesions observed at different stages of chronic venous disease may be associated and possibly caused by an inflammatory process. Primary venous insufficiency is associated with venous hypertension, largely as a result of reflux through failed venous valves. One of several theories put forward as a possible cause of CVD progression is that primary valvular dysfunction is acquired. This view is supported by findings such as activated leukocytes that have been shown to migrate into the endothelium of proximal surfaces of the vein valves and to promote remodeling of the valves with consequent valvular insufficiency. Schmid-Schönbein and his team have sought to weigh the responsibility of triggering mechanisms such as genetic risk factors, hormonal impregnation, prolonged hydrostatic load, and abnormal fluid shear stress in the process that leads to a cascade associated with such inflammation. They have also obtained evidence that venous valve deficiency may be associated with leukocyte infiltration into valve leaflets, and hypothesize that a key event in the inflammatory cascade is the enzymatic degradation of the valve leaflets and venous wall. Accordingly, they examined, in a rat femoral fistula model with venous hypertension, the metalloproteinases (MMP) in veins exposed to elevated pressures for up to 6 weeks. Zymography shows increased activity of Pro-MMP 2 at 3 and 6 weeks. MMP 2 and MMP 9 activity was predominantly observed at day 7 and 21 after creation of the fistula. The degree of extracellular matrix remodeling correlates with the morphologic finding of macroscopic lesions. They conclude that MMP 2 and MMP 9 activation is present in veins already days after exposure to elevated blood pressure, and coincides with periods of early alterations of the valve morphology and early forms of reflux.

In a pharmacological model set up by the same team, chronic elevation of venous pressure was associated with an inflammatory reaction in venous valves, a process that may lead to their dysfunction, reflux, and upstream elevation of venous pressure. These effects were mitigated by the anti-inflammatory action of MPFF* in a dose-dependent manner, as evidenced by J. J. Bergan et al.

As pointed out by A. N. Nicolaides, we are just beginning to understand the pathophysiology of venous disorders, and the optimum management of their various manifestations remains to be improved. It is generally agreed that primary chronic venous disease, with its diversity of symptoms and signs, is related to venous hypertension.[1,2] Not

only elevation of pressure, but also a cascade of biochemical events cause venous valve deterioration, and vein wall remodeling and restructuring with microcirculatory dysfunction which lead to reflux, varicose veins, and finally to skin changes and ulceration. These underlying processes prevail throughout the progression of chronic venous disease. Among the many proposed mechanisms linking venous hypertension to macroscopic and microcirculatory changes, "leukocyte-endothelium interaction" is currently the most credible. This mechanism involves valve and venous wall infiltration by monocytes and macrophages, leading to valve destruction and varicose remodeling. In the microcirculation, the accumulation of leukocytes in the lower extremity under conditions of high venous pressure is thought to be largely due to leukocyte adhesion to the endothelium and migration through small vessels, especially postcapillary venules.

It is now agreed that abnormalities in the microcirculation greatly contribute to the etiology of varicose veins as well as to the chronic skin changes of CVD. Work on animal and human models has shown that MPFF* modulates leukocyte adhesion, prevents endothelial damage, and activates the microlymphatic system. As concluded by G. Jantet, such treatment is useful first-line for edema as well as other symptoms of CVD. It continues to be effective in all subsequent stages of the disease, including leg ulceration.

The results of a recently published meta-analysis of a randomized prospective study using MPFF*, presented by P. Coleridge-Smith, confirm that venous leg ulcer healing is accelerated by adding MPFF* to conventional treatment. Medical literature databases and manufacturer's records were searched for relevant clinical trials to be included in the analysis. Five prospective, randomised, controlled studies, in which 723 patients with venous ulcers were treated between 1996 and 2001, were identified. Conventional treatment (compression and local care) in addition to MPFF* was compared with conventional treatment plus placebo in two studies (N=309), or with conventional treatment alone in three studies (N=414). The primary end point was complete ulcer healing at 6 months. The results were expressed as reduction of the relative risk (RRR) of healing with 95% confidence intervals (CI). At 6 months, the chance of healing ulcer was 32% better in patients treated with adjunctive MPFF* than in those managed by conventional therapy alone (RRR: 32%; CI, 3%-70%). This difference was present from month (RRR= 44%; CI, 7%-94%), and was associated with a shorter time to healing (16 weeks vs 21 weeks; *P*=0.0034).

The benefit of MPFF* was found in the subgroup of ulcers between 5 and 10 cm^2 in area (RRR: 40%; CI, 6%-87%), as it was in patients with ulcers of 6 to 12 months, duration (RRR: 44%; CI, 6%-97%). Larger ulcers and long-lasting ulcers were found to benefit most from such treatment. These ulcers tend to heal more slowly, and an adjunctive treatment may be of advantage in such circumstances.

In summary, it is now acknowledged that it may be possible to prevent worsening of CVD. This can be drawn from the experience in Italy, where preventative measures, including patient education and prophylactic treatment, have demonstrated both clinical effectiveness and cost-effectiveness. This symposium highlighted the fact that better understanding of the etiology of venous disorders and better prevention will lead to better care, allowing alleviation of the considerable suffering of patients in the long term.

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LYMPHATIC DISEASE

Lymphology

Chairpersons: P. Poredos (Slovenia), S. Nieto (Argentina)

Peripheral lymph low-molecular-weight proteins in normal subjects and patients with lymph stasis

B. INTEREWICZ (Poland), W. L. OLSZEWSKI (Poland), L. V. LEAK (USA), E. F. PETRICOIN (USA), S. ROSS (USA), L. A. LIOTTA (USA)

Lymph contains a great number of proteins that are similar to blood plasma, as it is generally referred to as an ultrafiltrate of plasma. The identification and validation of tissue fluid and lymph proteins under normal conditions and associated with particular diseases have so far been carried out only sporadically. In the absence of protein databases for efferent lymph in comparison with those well established for plasma there is a need for rapid multiparametric and reproducible method for identification and analysis of lymph proteins.

The aim of this study was to define lymph and plasma peptide profile collected from healthy subjects and patients obstructive lymphedema. Lymph and plasma samples (10 uL each) were directly applied to a weak cation exchange (WCX2) protein chip and analyzed using a PBS II Ciphergen SELDI-TOF -MS.

The protein profile patterns of normal lymph were similar in all samples. Only minor differences were seen between the plasma samples. Thirteen proteins were detected in plasma and seven in lymph. Five identical proteins, although of different relative intensities, were found in lymph and plasma. The protein profile patterns in inflamed lymph discriminate them from normal ones while the plasma profiles are similar. Seven proteins were found in all examined lymph samples of lymphedema patients.

Low-molecular-weight proteins produced in tissues are identified in lymph but not in serum due to their dilution. On the other hand, there are low-molecular-weight proteins in serum that are not filtered to tissue fluid probably due to binding to high-molecular-weight proteins. The function of the low-molecular-weight protein remains to be determined.

The obtained data will be correlated with clinical observations by the authors to establish their validity for understanding of the inflammatory process in tissues deprived of lymphatic circulation.

Proteases in human peripheral lymph in normal subjects and inflammatory conditions

B. INTEREWICZ, W. L. OLSZEWSKI, A. DOMINIA (Poland)

Long-lasting edema of the skin and subcutaneous tissue of limbs is caused by inflammation. Controlled degradation of the extracellular matrix (ECM) is required for the removal of damaged components and to allow cell migration and angiogenesis. A key step in the degradation of the ECM is the extracellular secretion of metalloproteinases (MMPs). The proteolytic MMPs profile of human normal and inflamed lymph has so far not been evaluated. The aim of this study was to determine proteolytic environment of lymph and plasma collected from healthy subjects and patients with obstructive lymphedema. Twelve subjects in each group had their leg lymphatic vessels cannulated, and lymph samples were collected. Proteolytic profiles were examined using gelatin and casein zymography. Samples of lymph and plasma-derived clarified serum were subjected to polyacrylamide SDS gel electrophoresis under nonreducing conditions. After electrophoresis enzymes separat- ed on gels were renaturated and activated.

The gelatin zymography of the normal lymph samples consistently showed 6 bands of 53, 55, 60, 72, and 88 kDa characteristic for activated MMP-9. In lymph of patients with rheumatoid arthritis the proteolytic profile was similar, but without one band of 70 kDa (MMP-2). In lymph from lymphedematous limbs there were detected: up to 11 bands 32, 35, 38, 48, 50, 53, 55, 57, 58, 72, and 88 kDa with maximal intensities for bands 38 and 48 kDa. There were no differences in the proteolytic profile of plasma samples. The casein zymograms showed a different pattern of hydrolysis, with band formation at 150, 100, 65, and 29 kDa, without any significant difference between the samples.

Ultrasound volumeter and limb meter 3D: a new future for phlebolymphology volumetry?

L. TESSARI (Italy)

Searching for a valid method of volume measurement of the limbs in lymphedema is indispensable to: i) highlight the clinical status of the disease, ii) to evaluate the improvements obtained with the adopted therapeutic procedures, and iii) to monitor the trend of the pathology over time. There is still not a validated and worldwide recognized method for the measurement of edema and for the volumetric study of lymphedema; the principal current reference methods are water displacement volumetry and measurement of the circumference of the limbs at several levels. The water volumeter has been considered the reference method, though it has some routine applicability limitations and cannot be used in open wounds and infected cases; furthermore it does not allow one to analyze the distribution of lymphedema along the limb. The measurement of the circumference of the limb at different levels is strictly operator-dependent with a high probability of intrainterobserver errors due to: a) the variable tension of the device which is used to take measurements on the skin of the limb; b) the reproducibility of the points of reference on the limb; c) the position of the measuring device in relation to the limb. Moreover, this technique does not take into account the volume of the limb. On the basis of the flaws mentioned above, the authors developed a project for a new volumeter and a new method of measurement of the limbs, based on the use of ultrasound. In fact, on one hand it is possible to measure the change of volume in an ultrasound field in the presence or absence of a limb within the same ultrasound irradiation. On the other hand it is possible to use the echo effect of ultrasound, which is emitted by a system with spiroidal movement for the measurement of the limbs.

FROM SKIN CHANGES TO ULCERATION

LECTURE

The eclipse effect in ulcer pathogenesis: the overlapping of primary CVD and the C282y gene mutation

P. ZAMBONI (Italy)

The author presents this study after the observation of a relationship between chronic venous leg ulceration and disturbances in iron metabolism. He studied a cohort of 238 selected cases rated as CEAP C4-6 looking for the HFE C282Y mutation, the most commonly recognized genetic defect in iron metabolism in Northern Europeans. Among patients affected by primary CVD, this mutation increased the risk of developing chronic venous ulcers more than three times when compared with healthy controls. This finding may lead to the development of new strategies in the prevention and treatment of severe CVD.

Chairpersons: S. Hoshino (Japan), J. A. Puentes (Uruguay)

Microcirculatory flow abnormalities in patients with healed and active leg ulcer

A. JAWIEN, P. BRAZIS, A. MIGDALSKI, T. GRZELA, M. SZEWCZYK, R. PIOTROWICZ, M. CIECIERSKI (Poland)

Chronic venous insufficiency (CVI) is associated with a great number of microcirculatory abnormalities, but there are a limited number of studies demonstrating correlation of microcirculatory flow failure with different stages of CVI severity. The aim of the present study was to compare microcirculatory flow characteristics in patients with healed and active venous ulcerations (stages C5, C6 of CEAP classification) against a control group. Thirty-nine patients were enrolled in the study (45 legs): 14 patients (15 legs) with healed ulcer (C5 group); 14 patients (15 legs) with active ulcer (C6 group) and, as a control group, 11 patients (15 legs) without any symptoms and signs of CVI. All patients underwent duplex scan investigation, and the microcirculation was assessed by laser Doppler flowmeter. The following parameters were investigated in the study (supine and standing position): skin blood flux (SBF), concentration and velocity of moving blood cells (CVMBC); venoarteriolar response (VAR) values; and thermal stimulation test values. The statistical analysis was performed by the Mann-Whitney test. The significant difference in calf SBF values (supine and standing position) between all tested groups ($P<0.01$) was observed. The calf SBF reached the highest level in the C6 group and the lowest level in the control group. The values for CVMBC in supine position at the calf level were higher in the C5 and C6 group vs the control group ($P<0.001$). Statistically significant decreased intensity of the VAR on the toe in C5 and C6 group vs the control group was also observed ($P<0.05$). Impairment of thermal stimulation test values was found in the C5 and C6 group in comparison with the control group ($P<0.001$). It seems that advanced stages of CVI (C5,C6) are associated with significant microcirculatory flow abnormalities at the calf level, which are expressed mainly by: increased skin blood flux, increased concentration and velocity of moving blood cells, and impairment of thermal stimulation test values.

Cell cycle-related proteins and apoptosis in epidermis of human chronic leg ulcers

H. GALKOWSKA, W. L. OLSZEWSKI, U. WOJEWODZKA (Poland)

The epidermis is continuously being renewed, and this process is ensured by antigen p63+ CD29+ epidermal stem cells in the basal layer. Terminally differentiated keratinocytes expressing cytokeratine 10 undergo cellular renewal or apoptosis. Both mechanisms are controlled by similar molecular regulators. During wound epithelialization, keratinocytes (KC) undergo many changes, including cell migration, proliferation, and differentiation. Cells become activated and express PCNA and p53, the cell cycle regulatory proteins. KC apoptosis and terminal differentiation are regulated by proteins having a blocking (bcl2) or promoting (bax, caspase3) effect on DNA fragmentation. In order to evaluate the role of regulatory proteins in the pathogenesis of protracted epithelialization of leg ulcers we characterized immunohistochemically the expression of these proteins in the epidermis.

The aim of this study was to evaluate the role of epidermal apoptosis and cell cycle-related proteins in the pathogenesis of protracted reepithelialization of calf venous and diabetic foot ulcers.

Studies were carried out in 12 patients with diabetic foot and 10 patients with varicose ulcers of the calf. Skin biopsies were obtained under local anesthesia from the border area of ulcers and from corresponding sites of normal subjects (orthopedic patients).

KC at the edge of both types of ulcer and in the distal areas expressed cytokeratin 16 and 17, but not cytokeratin 10. KC were p63+, CD29+, PCNA+, p53-. The intensity of bcl2 staining was higher at the edge of foot ulcers compared to calf ulcers, whereas the intensity of bax staining was the same. The intensity of caspase 3 staining was higher in foot than in calf ulcers. The intensity of DNA break staining (TUNEL) was lower at the edges of both types of ulcers compared with controls. This means that impaired epithelialization of chronic ulcers is not caused by impaired epidermal stem cell proliferation, differentiation, and apoptosis. This may reflect a distorted organization of the ulcer bed, hampering keratynocyte migration from the ulcer edge.

Chronic leg ulcers: innate antimicrobial peptide β defensin-2 expression and Langerhans cell density in epidermis

H. GALKOWSKA, U. WOJEWODZKA, J. MIJAL, W. L. OLSZEWSKI (Poland)

Normal human skin is resistant to penetration by micro-organisms that routinely colonize its surface. Skin epidermal antimicrobial peptides and Langerhans cells are the most prominent factors in the defensive responses. Two major classes of dermal peptides, cathelicidins and β-defensins expressing antibacterial activity, are produced by keratinocytes. Epidermal expression of β-defensin-1 is systemic, whereas expression of β-defensin-2 is upregulated by the inflammatory process in human skin. β-defensin-2 has also chemotactic and - in vivo - activating effect on dendritic cells. In vivo recruitment of epidermal dendritic cell precursor from blood into skin and Langerhans cell mutation can also be influenced by other keratinocyte-derived factors.

The aim of this study was to investigate immunohistochemically whether chronic skin ulceration can influence hBD-2 expression, Langerhans cell (LC) density, and activation of epidermis in diabetic foot and venous leg ulcers. Studies were carried out in 10 patients with diabetic foot ulcer and 10 patients with varicous ulcers of the calf, without clinical signs of infection of adjacent tissues. Control biopsies were taken from corresponding sites of 10 normal subjects (orthopedic patients).

There was significantly higher hBD-2 staining in sole skin epidermis, both in normal and diabetic foot ulcers ($P<0.05$) compared with normal calf skin. There was no difference in defensin staining between ulcerative and normal epidermis. Studies of CD1a+ LC densityrevealed lack of these cells in neoepidermis at the edge of calf ulcers compared with normal epidermis ($P<0.05$). In contrast, there was increased density of CD1a+ LC and DR+ LC in epidermis from diabetic foot ulcers compared with normal, nondiabetic foot sole skin ($P<0.05$). Moreover, there was significant reduction of CD1a+ LC in normal foot sole epidermis compared with calf skin ($P<0.05$). Significantly higher expression of GM-CSF was observed in diabetic foot epidermis compared with normal sole skin and calf epidermis ($P<0.05$). Overexpression of CD1a+ LC and GM-CSF in epidermis from diabetic foot ulcers suggests in vivo GM-CSF contribution to the observed LC upregulation in diabetes.

Topical treatment of phlebostatic ulcers with recombinant human growth factor with Sulfadiazina de plata (Ag Sulfadiazin)

M. QUIÑONES CASTRO, M. BORRÁS MIGUES, L. RODRIGUEZ VILLALONGA, L. CHIRINO DÍAZ, S. GARCÍA PELEGRÍ (Cuba)

Chronic venous insufficiency is the main cause of the appearance of the leg ulcer, giving rise to a medical-social problem that can be extended to lifelong incapacity for the patient. Many topical treatments have been used and reported in the worldwide medical literature aimed at achieving faster healing of the ulcerous lesions. The proposal of the topical use of growth factor cream with Sulfadiazina de plata (Ag Sulfadiazin) in patients with phlebostatic ulcers was performed. Ninety patients with 6- to 10-cm diameter ulcerous lesions not healed over 1 year of the treatment were included in this research work. They were divided into three groups: Group A (control group): Antiseptic warming; Group B: Ag sulfadiazin, cream 1%; Group C: Recombinant human growth factor cream with Ag Sulfadiazin. The general treatment was the same for all groups. Two parameters were used to measure the treatment success: healing time given by hospitalization period and percentage of healed ulcers.

In group A, the medium hospitalization period was 93.8 days and a good result - total ulcer healing - was observed in 23.3% of treated patients. Nonhealing ulcer was observed in 40% of patients from this group. In group B, the medium hospitalization period was 54.4 days, and total healing was observed in 76.7% of treated patients. In group C, the medium hospitalization period was 38.8 days, with 90% of cases having good results. The results suggest that recombinant human growth factor together with other antiseptic vehicles can lead to total wound healing in ulcer resistant to previous treatment.

Chairpersons: L. Norgren (Sweden), P. Mendonça (Brazil)

Changes in P2X and P2Y receptor expression reflect keratinocyte function on skin epidermis during chronic venous insufficiency

M. J. METCALFE, G. BURNSTOCK, D. M. BAKER (UK)

Purines are extracellular nucleotides that have long-term effects on keratinocyte proliferation (via P2Y 1 and P2Y 2 receptors), differentiation (via P2X 5 receptors), and death (via P2X 7 receptors). The authors studied the changes in expression of these P2 receptors on epidermal keratinocytes in chronic venous insufficiency (CVI), a condition leading to skin changes including lipodermatosclerosis and ulceration. The study was performed in a small group - 5 patients with venous leg ulcer. Significant increase of P2Y 1 and P2Y 2 receptor expression (representing increased keratinocite proliferation) in basal and spinosal layers of the epidermis in all CVI patients was observed. P2X 5 receptor expression in CVI was increased too, largely in the spinosal layer.

Basic Science

Chairpersons: J. Strejcek (Czech Republic), C. Canedo (Brazil)

With the participation of:
M. J. METCALFE, G. BURNSTOCK, D. M. BAKER (UK), Y. HEROUY, E. SCHOEPF, L. BRUCKNER-TUDERMAN (Germany), S. BRAUN, M. JUENGER, A. OSTROWITZKY, F. RIEDEL, E. MANSFELD, H. HAASE, E. KAUTSCHKE; J. FANGHANEL, J. GIEBEL (Germany), J. NORGAUER (Germany), B. ARAVIND, T. NAVIN, B. SHARP, C. MONACO, E. PALEOLOG, A. H. DAVIES (UK), S. R. REWERK, C. D. DUCZEK, A. G. GRUBER, M. W. WINKLER, H. N. NULLEN, G. W. H. HALLER, S. FREUDENBURG (USA/Germany)

This session consisted of a selection of presentations which addressed the pathophysiology of leg ulceration. The underlying mechanism by which venous and capillary hypertension leads to trophic skin damage is inflammation. Inflammation results in a migration of neutrophils, macrophages, and lymphocytes followed by a proliferation of endothelial cells and fibroblasts. Secreted proteins influence different enzymatic functions at the cellular and extracellular levels.

Proteolysis of cell surface-and extracellular matrix molecules is intrinsically linked to cell function. Apoptosis of dermal and epidermal cells results in venous leg ulcers.

Alteration of concentration of several proteins such as Fas, Fas-L, bcl-2, collagen, elastin, tenascin, fibronectin, and changes in the proteolytic activity of enzymes (metalloproteinases and its inhibitors) were compared in healthy skin and lesional skin. Besides clinical investigation, methods used by the presenters included epiluminescence microscopy, laser Doppler fluxmetry, transcutaneous oxygen measurements, protein expression in skin biopsies determined by immunohistochemistry, zymography, Western-Blot assay, and TUNEL assay (DNA fragmentation).

Extracellular matrix remodeling by metalloproteinases and its inhibitors in the vein wall can result in structural weakness with varicose vein formation. High levels of MMPI have been formed in atrophic areas of varicose veins, and VEGF expression was higher in recurrent varicose veins.

The data from studies on the skin microcirculation provide evidence that venous leg ulcers could be the result of an apoptotic pathway. The entry of keratinocytes into the apoptopic pathway may be regulated by bcl-2 in congested areas and at the ulcer edge.

Tenascin and fibronectin deposition is rising in the damaged skin region. Soluble and membrane-bound metalloproteinases may favor enhanced turnover of the extracellular matrix in the lesional skin.

These results suggest that controlling programmed cell death may have therapeutic potential in preventing venous leg ulceration. For example, Factor XIII is an effective antifibrinolytic drug for the topical treatment of ulcers because it regulates the activity of matrixmetalloproteinases by influencing their conversion into the enzymatically active form.

IV

INVESTIGATIONS AND HEMODYNAMICS

VENOUS DISORDERS

Venous and lymphatic disorders: noninvasive investigations

Chairperson: Z. Rybak (Poland)

Knee perforating veins as a source of varicosities: prevalence and clinical relevance

M. V. L. BARROS (Brazil)

The authors studied the incidence of anterior knee perforating veins (PV) in 752 patients using Duplex scanning.
They found out that almost 5% of patients with varicose veins had such incompetent perforators that provoked reflux in the leg in anteromedial and anterolateral collateral veins or a great saphenous vein local insufficiency in the calf.
These perforating veins were usually small in diameter and not associated with severe disease.

Duplex investigation of the lesser saphenous vein

R. MORETTI (Italy)

The author described his experience studying the small saphenous vein with Duplex Scanner, and reported high incidence of asymmetric origin.
Most veins originated from the popliteal vein or the lower third of the thigh, and one out of five patients had multiple connections.

Noninvasive venous pressure measurement by controlled compression sonography

C. THALHAMMER (Switzerland)

Information about increased venous pressure is useful in many clinical situations, but is rarely used because it is invasive, requiring venous puncture.
Using a manometer that is transparent to ultrasound, the compression is exerted by the probe on the tissue and the underlying veins until they collapse could be measured. Applying such a manometer to the probe of their duplex scanner, the authors were able to accurately measure, noninvasively, venous pressure in the arm, where for experimental purposes, the pressure was artificially increased.

Venous and lymphatic disorders - conventional and nonconventional ultrasound

Chairpersons: G. Botta (Italy), A. Lechter (Colombia)

Hyperflow conditions new concept in venous diseases

N. A. NAZARE CASTRO, S. SALLES CUNHA, T. PINHO NAVARRO (Brazil)

This observational study describes the presence of a spontaneous cephalad flow (hyperflow or overflow) without compressing the calf in the Giacomini vein due to an insufficiency in the saphenopopliteal junction. In these cases, the incompetence of deep venous system is transmitted to the superficial system throughout the Giacomini vein, causing some cases of recurrent varicose veins.

Ultrasonography diagnosis of recent venous thrombus: experimental study in dogs

M. G. GIANNINI, H. A. R. ROLLO, F. H. A. M. MAFFEI (Brazil)

In the authors' opinion the ultrasound study by power Doppler, B flow, and harmonic tissue imaging of a recent thrombus created surgically in the inferior vena cava of dogs in this experimental study offers greater sensitivity, specificity, and accuracy than phlebography studies. Currently in the medical literature, the majority of comparative studies between ultrasound and phlebograpy for the diagnosis of acute deep venous thrombosis suggests that phlebography is the more accurate.

3D CT venography to investigate the venous system: value and results for assessment of congenital malformations and varicose veins

J. F. UHL, C. GILLOT, V. DELMAS, O. PLAISANT, O. AMI (France)

The authors presented a most impressive reconstruction of three-dimensional CT venous studies of patients with complex venous disorders. The possibility of rotating the images and suppressing muscles and other structures offers a very clear and understandable image of the venous system. These anatomic studies should be combined with hemodynamic information for a better understanding of venous disease.

On-table varicography is still a useful investigation in the treatment of varicose veins

J. T. HOBBS (UK)

The ultrasonic study is the gold standard in the study of varicose veins disorders, but the equipment is expensive and not universally available. In inexpert hands ultrasonic studies cannot recognize significant reflux. In complex venous disorders (vulvar veins, recurrences, and a complex pattern of veins of the poplitea fossa) on-table varicography is a very helpful. On-table varicography investigation demonstrates correctly complex venous anatomy disorders with the injection of a nonionic contrast directly and taking a simple X ray with basic equipment, which is available everywhere.

Hemodynamics of the saphenofemoral junction, patterns of reflux, and their clinical implications
Relationship between the caliber of the greater saphenous vein and the competence or absence/incompetence of the femoral valve in subjects with incompetence of the saphenofemoral junction

M. CAPPELLI, R. MOLINO LOVA, S. ERMINI, P. ZAMBONI (Italy)

The disconnection of the saphenofemoral junction in cases of femoral vein insufficiency has a high percentage of recurrences. To correctly study venous reflux in the saphenofemoral junction it is necessary to record venous flow on the side of the femoral vein using power Doppler. The study of venous flow at this level can offer prognostic information regarding crossectomy.

In the second presentation the author demonstrated the relationship between great saphenous vein diameters and femoral vein competence/incompetence studied by ultrasound in patients with saphenofemoral junction insufficiency. In cases of femoral vein incompetence the great saphenous vein will increase its diameter.

The sub diaphragmatic IAP: physiologic classification and instrumental test

Chairpersons: E. Brizzo, (Argentina), C. Belczak (Brazil)

Propellent-suction pumps phlebographic assessment: plantar, gemelar, gluteal and pelvic

S. ZUBICOA EZPELETA (Spain)

One hundred and twenty-one patients were studied in order to evaluate the plantar and gemellar pumps by means of dynamic ascending phlebography. The examinations of the gluteal and pelvic pumps were performed with selective phlebography with catheterization from a vein at the elbow, canalizing the gluteal veins and other pelvic tributary branches. The authors also registered measurements of ambulatory venous pressure. They concluded:

Plantar and gastrocnemial pump

1. In the case of the plantar pump activation (loaded foot) the emptying of the plantar arch which drains by the posterior tibial veins, is almost complete.
2. In patients with malformation (flat feet) the emptying in the plantar arch is scarcely noticeable.
3. The hallux flexo-extension movement also shows the unloading of the internal plantar vein, although slower and less complete than with the heel step.

Gluteal pumps

1. Although the interconnected abdomino-pelvic venous system makes up a functional unit, gluteal pumps actively participate in the return circulation, experiencing with the gluteal muscle contraction a slight increase in the emptying velocity and reduction in the vein caliber.

Functional unit

J. LEAL MONEDERO (Spain)

1. The veins of the abdomen, pelvis, and lower limbs make up the subdiaphragmatic functional unit.
2. The pelvic venous system works in a way related to that of the lower limbs, but they present a different pumping hemodynamic and valvulating system.
3. The impulse-aspirative pumps need to perform their role in the valvular system which acts as a compartment.
4. These valvular systems can be internal and external.
5. For the diagnosis and treatment of the venous pathology in the pelvis , the knowledge of the type of the pathology which has created this alteration in the centripetal-centrifugal flow is vital.
6. The infra-diaphragmatic vascular rehabilitation should not only be performed in the lower limbs (plantar, sural, popliteal-gastrocnemial), but also in the pelvic floor, as well for as the abdominal wall and breathing.

Compression and its efficacy on the venous pump

H. PARTSCH (Austria)

In the presented paper measurements of interface pressure and stiffness of compression stockings and bandages, using mainly the MST tester and the Kikuhime transducer, were performed. The authors described the effects of stockings and bandages on venous diameter (n=26), venous reflux (n=21), expelled volume and on ambulatory venous hypertension by means of duplex, air plethysmography, foot volumetry, and phlebodynamometry. Although the interface pressure on the distal lower leg in the supine position may go as high as 40 mm Hg with a class III-stocking and also with a short-stretch bandage, so during standing and walking a material with high stiffness (stretch bandages, zinc-plaster) will produce pressure peaks of 70 mm Hg or more. This allows the occlusion of the veins intermittently during walking. The authors concluded that, although the use of compression stockings is the method of choice in patients with chronic venous disease, multilayer compression bandages have a superior effect on the disturbed venous hemodynamics to stockings, because the latter compress the leg veins in the upright position only to a minor extent.

Duplex color ultrasound venous assessment in pelvic chronic venous insufficiency

A. SÁNCHEZ GUERRERO (Spain)

To prove the usefulness of pelvic venous ultrasound (transparietal and transvaginal) in subdiaphragmatic chronic venous insufficiency the authors compared angiographic findings (iliocavography with pressure measurements) with the data obtained with the echographic assessment with color duplex. The authors studied patients with ultrasound investigations suggesting a picture of pelvic venous insufficiency during the last 3 years. The authors emphasized the ability of duplex ultrasound to differentiate normal subjects from pathological ones, and among these to distinguish centripetal hemodynamic pictures (venous obstruction, May Thurner, nutcracker) from centrifugal (gonadal and/or hypogastric insufficiency).

Development of reflux in the perforator veins

N. LABROPOULOS, A. BHATTI, L. LEON, A. K. TASSIOPOULOS (USA)

The aim was to describe the mechanisms by which perforator vein (PV) reflux develops in patients with primary chronic venous disease (CVD), patients with CVD who had had at least two duplex ultrasound (DU) examinations prior to any treatment were included in the study. All affected limbs were classified by the CEAP system. Reflux was induced by distal limb compression followed by sudden release using rapid-inflation pneumatic cuffs, and by dorsiplantar flexion. The perforator vein reflux was divided into ascending and des-cending types (re-entry flow) and those developed in new locations, which did not have reflux in any system.

There were 29 limbs in 26 patients with reflux development in the PV. In total 38 new incompetent PVs were identified. The median time of the examination was 25 months (range 9 to 52).

Reflux in a previously normal PV at a re-entry site	15
In ascending manner from extension of superficial vein reflux	8
New previously intact location	5

Anatomic location of the new incompetent perforators:

Location	Segment	Number
Thigh (6)	Medial	3
	Lateral	3
Calf (31)	Medial	22
	Lateral	2
	Posterior	6
	Anterior	1
Knee (1)	Posterior	1
Total		**38**

Worsening of clinical class was observed in 11 limbs:

- 7 from Class 2 to 3 or 4
- 2 from Class 3 to 4
- 2 from Class 4 to 6

The authors concluded:

1. Reflux in perforating veins develops in ascending manner through the superficial veins
2. Worsening of CVD is observed with new PV reflux but many other factors play a major role. A causative association is difficult to prove.

LYMPHATIC DISORDERS

Venous and lymphatic disorders: noninvasive investigations

Chairperson: Z. Rybak (Poland)

Accuracy of continuous wave Doppler in lower limb venous examination

J. FARRAH (UK)

Continuous-wave Doppler (CWD) is still used in many practices to assess patients with varicose veins.

To assess its validity, the authors studied 101 varicose patients with CWD and with Duplex Scanning, on the same day with different "blind" operators. They showed that CWD is reliable in studying the saphenofemoral junction, but it is of little value in studying recurrent varices and other parts of the venous system, so a Duplex Scanner examination is recommended before surgery.

EDEMA

The swollen leg

In the framework of the JOBST symposium.

Chairpersons: H. Partsch (Austria), M. Goldman (USA)

Clinical differential diagnosis of the swollen leg

H. PARTSCH (Austria)

Edema is the main symptom of various diseases. It is the symptom of underlying pathology but not of a particular diagnosis. Edema is a visible and palpable swelling caused by an increased fluid content of the interstitium. Depending on the underlying pathology it can be unilateral or bilateral (*Table I*).

It is very important to exclude malignant lymphedema of the limbs. For example, unilateral lower-limb edema may be a sequel of compression of the iliac vein by a tumor. Edema of the left leg can be provoked by the pelvic spur due to compression of the left iliac vein by the right iliac artery. There are some rare causes of leg edema. For example, edema due to depression immobility or pretibial myxedema (EMO syndrome: exophtnalmus, myxedema, osteoarthropathy). Arm edema is often due to mastectomy with lymph node resection.

Unilateral edema	Bilateral edema
• Deep venous thrombosis	• Lipedema
• Posthromphlebitic syndrome	• Idiopatic cyclic edema
• Chronic venous insufficiency	• Cardiac edema
• Angiodysplasisas	• Renal edema
• Cellulitis	• Hepatic edema
• Arthritis	• Dysproteinemia
• Baker's cyst	• Drug-induced edema (cortisone, Ca antagonists, diuretics, etc)
• Lymphedema	

Table I. Differential diagnoses of swollen limbs.

Dermatologic manifestations of the swollen leg

M. GOLDMAN (USA)

The main dermatological manifestations of the swollen leg are:

1. Edema
2. Hair loss
3. Stasis dermatitis
4. Hyperpigmentation
5. Lymphostasis verrucosa cutis
6. Lipodermatosclerosis
7. Ulceration.

The leg edema is characterized by pitting and erythema, and is susceptible to infection. The basic treatment of this condition must include:

1. Treatment of the underlying cause
2. Exercise/physical therapy
3. Lymphatic massage and endermology
4. Intermittent pneumatic compression
5. Graduated compression stockings
6. Diuretics (special indications).

Localized alopecia is due to decreased oxygenation of the tissue, venous hypertension, and dermatosclerosis.

Stasis dermatitis is often associated with swollen legs and is remarkable due to pruritus and lichenification. The basic treatment of stasis dermatitis must include correction of the venous hypertension, compression, bland ointment, and low-potency topical corticosteroids.

Pigmentation is caused by extravasation of the RBC, perivenulitis and inflammation. Hyperpigmentation can be treated with graduated compression, retinoic acid, deferoxamine, and laser.

Characteristic features of lipodermatosclerosis are:

- Chronic inflammation
- Calcium deposits
- Fibrous, indurated skin.

Lymphostasis verrucosa cutis is one of the more severe complications of the swollen leg. This syndrome is caused by chronic edema, chronic stasis changes, and recurrent infection. The treatment of the lymphostasis verrucosa cutis must include:

1. Exercise/physical therapy
2. Lymphatic massage
3. Intermittent pneumatic compression
4. Graduated compression stocking
5. Whirlpool debridment
6. Prevention of infection.

Ulceration is the final stage of CVI and swollen limb. Adequate and prompt treatment is necessary. Sometimes it can progress to malignancy.

Classification and investigation of the swollen limb

K. G. BURNAND (UK)

Lymphedema is edematous swelling of a region of the body as a result of defective lymphatic drainage. There are two forms of lymphedema:

Primary (75% female, 25% male)

- Congenital (11%)
- Praecox (precocious) (75%)
- Tarda (late) (14%).

Secondary

The main causes of secondary lymphedema are trauma, iatrogenic (block dissection), infection (filiariasis, cellulitis), inflammation (rheumatoid, eczema), malignancy, and irradiation. Investigation of patients with lymphedema usually includes clinical examination, venous tests (duplex), isotope lymphography, contrast lymphography, ECG, echocardiography, genetic analysis and some laboratory tests (albumin, urea, creatinine). Isotope lymphography is a gold standard for outpatient investigation of lymphedema. Differential diagnoses of lymphedema are necessary for dealing with cardiac, renal, and hepatic failure, hypoproteinemia, fluid retention syndromes, venous edema, hysterical edema, factitious edema, eythrocyanosis frigida, lipoidosis or lipodystrophy, postarterial reconstruction, gigantism, and arteriovenous fistulas. In conclusion, the author has underlined the necessity of a new classification of the lymphedema.

THROMBOSIS

Thromboembolic pathology

Chairpersons: R. Gesto (Spain), J. Chunga-Chunga (Peru)

Nutcracker syndrome: echographic diagnosis with color duplex ultrasound

A. SÁNCHEZ GUERRERO (Spain)

Significant left renal vein compression in the aorto-mesenteric entrapment, or Nutcracker syndrome (NS), is less well-known than other compressive syndromes as the subclavian steal syndrome or May-Thurner syndrome, also related to anatomical narrowing. More frequently it is described in the literature by its urological manifestations secondary to renal venous hypertension, which is a common cause of pelvic and scrotal varicocele and even of lower-limbs varicose veins, although not usually diagnosed. It is also a cause of failure and recurrence of the previously treated varicocele.

Sixteen patients (15 female and 1 male) diagnosed with NS by color duplex ultrasound and confirmed by hemodynamic studies were compared with a control group of four patients (all female). In all patients - from both groups - the pressure gradient was estimated after additional phlebography. The results obtained were surprising. The average velocity ratio between the aorto-mesenteric entrapment area and the pre-entrapment area was 11.20 (13.89-5.6) in the group with NS compared with 2.25 (1.29-3.24) of the control group.

The diameter ratio between the renal vein in the aorto-mesenteric entrapment area and the pre-entrapment area was 6.45 (4.46-8.13) in the NS group compared with 1.96 (1.33-2.67) in the control group. In the 62% with NS, continuous flow inversion in the left gonadal vein was observed, opposed to none in the control group. The patients with NS presented pelvic varicocele with average diameter of venous lakes of 7.6 mm (14-5) with velocity of high spontaneous flow average 9.6 cm/seg opposed to none in the control group (diameter of the venous lakes 4 mm) with spontaneous average velocity of 0.75 cm/seg. About 94% of patients (n=15) with NS presented a hypogastric vein with centripetal flow, except one patient, due to the presence of an associated May-Thurner syndrome. The left average cavo-renal pressure gradient was 4.37 mm Hg in the NS group as opposed to 0.75 in the control group.

It seems that CDU could be an excellent method of choice in the diagnosis of NS. The diagnostic criteria are simple:

- the presence of a ratio of velocity or diameter >5
- continuous flow inversion in the left gonadal vein or pelvic varicocele (venous lakes >5 mm) with high velocity of spontaneous flow (>4 cm/seg) with a hypogastric vein with flow in a centripetal direction.

PELVIC SYNDROME

Venous pathology in the female pelvis

Chairpersons: J. Leal Monedero (Spain), C. L. S. Figueiroa (Brazil)

Pelvic venous insufficiency pathophysiology: centrifugal and centripetal syndromes

J. L. MONEDERO (Spain)

One cannot diagnose a disease if one does not know that it exists, and Dr Monedero suggests that for pelvic chronic venous insufficiency (PCVI), this is often the case.

At the pelvic level, venous syndromes can be due to two causes: one is an increase in centripetal pressure, when there is an obstruction to blood flowing toward the heart, like in nutcracker syndrome (left renal vein entrapment by aorta and mesenteric artery), May-Thurner syndrome (left iliac vein compression by right iliac artery), malformations such as double cava vein, or compression due to tumors or other causes. The other is an increase in centripetal pressure, for general causes like heart failure, or local venous insufficiency, mainly in gonadal, hypogastric, and gluteal veins.

Knowing that PCVI exists can help clinicians to correctly diagnose many atypical varices.

PCVI etiological and triggering factors

C. L. S. FIGUEIROA (Brazil)

The author suggests that pain in PCVI can be caused by a neurological insult due to venulo-capillary hypertension.

Treatment by embolization of the pelvic vein insufficiency in women presenting with nonsaphenous perineal veins - anatomic and clinical correlation: 2-year follow-up

D. CRETON (France)

Pelvic vein syndrome includes pelvic heaviness, bladder irritability and urgency, constipation, vulvar varices, and haemorrhoids. It provokes three precise clinical signs: pelvic and varicose pain just before or during the menstrual period, and dyspareunia just after intercourse. Associated varicose veins are often perineal veins, perforators on the buttock, and more rarely the sciatic vein.

Using an analog visual scale for the three signs, with a cumulative maximum score of 30, the

author found that in women of reproductive age suffering from PCVI the mean score was almost 14, and that after treatment with embolization, 67% of the patients improved more than 80%, with results stable for up to 2 years, but to obtain these results it was necessary to perform wide embolizations, that involved both ovarian and hypogastric veins. Such good results are not confirmed in menopausal women, whose symptoms usually do not improve with treatment.

The main message of this section is that if you are confronted with atypical varices, especially in patients with pelvic pain and dyspareunia, you must look for pelvic venous insufficiency and that if such a situation is detected, it can be corrected with effective and non-aggressive treatments.

V

THERAPY

VARICOSE VEINS

Surgery

Chronic venous insufficiency – surgery

Chairpersons: H. A. Maffei (Brazil), J. P. Albino (Portugal)

Transilluminated miniphlebectomy

A. J. C. FLOR (Austria)

Reduction in:
- unnecessary manipulation
- bleeding
- lesion of lymphatic vessels
- sensitive skin nerves
- operation time

can be achieved by means of transilluminated miniphlebectomy.
The veins were visualized by insertion of the light rod into the subcutaneous tissue, and removed by means of Varady's hook. The light rod, with an oblique tip, was equipped with an exit for light fibers and a canular opening for the saline flow solution. Miniphlebectomy following hydrodissection was performed by incision at the marked perforating veins and crossing. The author emphasized the importance of quicker recovery time and better cosmetic results.

Segmentary ambulatory saphenectomy

G. CHAVEZ REYES, S. J. CHIRINOS CARAZA (Peru)

New surgical approach to varicose veins: color duplex evidence base

C. PEREIRA ALVES, J. NEVES, L. MONIZ (Portugal)

Color duplex ultrasonography is the "gold standard" in varicose vein diagnostics. According to this method, modern surgery should remove the incompetent vein segment and junctions, preserving the competent ones. C. Pereira presented early results of the surgical approach of the great saphenous vein (GSV) primary varicose veins. He suggested classic surgery only in saphenofemoral junction (SFJ) reflux plus truncal GSV reflux. In the segmental trunk, GSV reflux without SFJ reflux suggested no ligation of SFJ and tributaries. Segmental varicose branch avulsion in vein reflexive branches were performed. The authors presented promising results, but they emphasized the need for longer follow-up.

Alternative treatment of reflux of the long saphenous vein by crossectomy and microfoam injection through a multipurpose catheter

M. D. ANDRÉS, W. VERBERCK (Argentina)

Crossectomy with a 3-cm extirpation of the great saphenous vein (to reduce the possibility of neoangiogenesis) and introduction of a hydrophilic catheter with a Terumo quide into the distal trunk were performed. According to the Tessari method, microfoam was injected through the catheter so that the microfoam was distributed regularly. In the ultrasound control performed between 30 and 90 days, a total obliteration was observed in 90% of patients. In the clinical follow-up and Doppler ultrasound of 23 patients, no recurrences were seen for a year. The most dangerous complications were: varicophlebitis in two cases and hematoma in one case. The authors emphasized the possibility of controlling a frequent and progressing disease with this method, which is easy and economical.

Outcome of internal valvuloplasty with additional procedures for chronic venous insufficiency

N. HAYASHIDA, N. YAJIMA, H. MURAYAMA, K. MATSUO, H. KITO, S. ASANO, M. YANAI, M. YAMAMOTO (Japan)

The purpose of this study was the evaluation of the outcome of internal valvuloplasty with additional procedures for chronic venous disease. Valvuloplasty with additional procedures (high ligation and stripping of large saphenous vein, etc) were performed in 30 limbs of 28 patients with CVI. The indication for the valvuloplasty was reflux of the femoral vein valve above grade III assessed by means of descending venography. Deep vein thrombosis occurred in two limbs on the 14th day after the operation. All patients received oral warfarin preventatively for one month.
Internal valvuloplasty with additional procedures is an effective treatment option for primary chronic venous insufficiency. However, postoperative deep vein thrombosis should be prevented by antithrombotic therapy.

The crochet needle: three decades as a surgical instrument in varicose vein surgery

T. TAKAYANAGI (Brazil)

Although the crochet needle has been used as a surgical instrument in varicose vein surgery for three decades, it still provides excellent benefits for vascular surgeons in terms of surgical dynamics, as well as aesthetics, obtained in the surgical treatment of varicose veins. The crochet needle is such a valuable tool that it has not been replaced by any other instrument.

Curettage of subcutaneous tissue in the treatment of spider-web telangiectasias

T. TAKAYANAGI (Brazil)

The etiologies of spider-web telangiectasias are: vascular dilatation secondary to estrogen and progesterone hormonal alterations, cellulites, phlebitis, trauma, and pregnancy, as well as shunt opening of micro arteriolar-venous fistulae. The author suggested removal of the feeding vein located by Doppler ultrasound or by decompression of the point where the feeding vein is located and rapid recanalization of the telangiectatic network. Through the same incision, the crochet needle was inserted to perform the curettage of the adjacent subcutaneous tissue or breaking any eventual residual branches. The author concluded that this procedure is incomparably more efficient that any other method.

Endoluminal treatment

LECTURE

1320 nm endoluminal laser treatment of the great saphenous vein: 2-year follow-up

M. GOLDMAN (USA)

The author described his experience with 810 nm endovenous laser closure devices, observing that there was a high incidence of pain and perforation of the vein walls, which caused ecchymosis. For this reason he experimented with the new 1320 nm endoluminal laser which is not absorbed by blood and permits little perivascular heat transmission, preventing perforation of the vein. He presented his experience with 95% venous closure after 1-year follow-up, and good cosmetic results.

Endovascular techniques for treatment of varicose veins

In the framework of the Joint Symposium UIP/Italian College of Phlebology (ICP).

Chairpersons: G. Genovese (Italy), S. Mancini (Italy)

This session consisted of a number of presentations from several countries, dealing with the value of endovascular techniques in the treatment of varicose veins. The experience and results from the last 5 years suggest that these minimally invasive procedures have the same efficacy as conventional surgery with less complications. At the end of the session there was general agreement that randomized controlled studies are needed.

G. Magi from Italy presented data from a personal experience of 120 procedures (111 great saphenous vein, 6 anterior saphenous veins, and 3 short saphenous veins) of venous obliterations using laser; 90% of veins remained occluded at 24 months.

G. Botta presented the data from the Italian endovenous laser register that was created in 2004 with 1076 procedures (77% female and 23% male; mean age 55 years; CEAP class 2-59%, class 3-19%, class 4-17%, class 5-1% and class 6-4%; GSV diameter <10 mm 67% by duplex assessment; surgical (61%) and percutaneous (39%) access to GSV) using laser 980 nm (power 12 watts, pulse 1 sec and interval 1 sec). The most frequent adverse effect was ecchymosis (40%) with no reports of DVT or hematoma. The conclusion was that this new technique has the same benefits of the surgery, with a lower rate of complications.

Based on the experience of using different levels of energy with ELVeS 980 nm, J. L. Gerard from France was able to give the following advice: a high rate of recanalization can be caused by inadequate energy, and so we must use a minimum energy of 40 joules/cm, calculate the energy before beginning, increase time rather than power, and use continuous mode instead of pulse mode. However, if more than 75 joules/cm are used there is an increased risk of paresthesias or pain. He also concluded that anticoagulation treatment is not a contraindication and does not affect the results, and duplex scan examination must be done before and during all the procedure.

E. Rabe from Germany presented the preliminary data (89 patients; 62 female; 67 GSV and 22 SSV; mean age 55.5 years) from the Bonn study (to evaluate endovenous laser in the treatment of the saphenous veins) and a review of the literature. He concluded that the advantages of this technique are: puncture of the vein with no groin incision, short recovery time, good short-term results, few side effects, minimally invasive with local anesthesia, improvement of QoL, high patient satisfaction, less time-consuming, and done on an outpatient basis. The disadvantages can be: cannulation not always possible in pretreated or tortuous veins, local pain in the first week, ecchymosis in the majority of patients, DVT rate 1%, additional treatment of branches is necessary, costs (comparable with surgery, cheaper than RF, but more expensive than foam schlerotherapy), poor standardization with results of occlusion rate depending on the energy applied (J/cm), sufficient publications only on GSV, no multicenter prospective randomized and comparative studies available.

The purpose of the presentation by L. S. Kabnick from the USA was to look at data using minimally invasive devices which were approved as early as 1999 for the ablation of the saphenous vein.

Analysis of 4-year radiofrequency (RF) data revealed a cohort of 916 patients (1120 limbs) treated. Clinical results revealed reflux free GSV at 1 year 89%, 2 years 88%, 3 years 86%, and 4 years 86%. Complications from RF treatment were: pulmonary embolism 0.1%, deep vein thrombosis 1%, skin burns 0.8%, infection 0.2%, paresthesia at 1 week 12.3%, and 2 years 4.9%.

Single center reports regarding laser reveal GSV closure rates from 93% to 99% with cumulative spawning 1 to 4 years. In the personal experience (275 cases) of the author there was no pulmonary embolism, skin burns, or infections and in most patients bruising disappeared within 2 weeks.

The author concluded that, presently, although not widely used, laser appears to be more efficacious in

controlling venous reflux. RF causes less discomfort and bruising than laser. Laser, when used in the continuous mode, causes less bruising and discomfort than previously reported by pulse mode. In contrast, RF is more complex to use in terms of setup, catheter-char accumulation, catheter cost, catheter pullback time, and total procedural time.

Finally J. FERREIRA from Brazil presented the results of a multicenter, open, retrospective, non-randomized review, using two wavelength lasers for procedures (810/980 nm) in continuous and pulsed mode. These data, from Argentina, Brazil, Chile, Ecuador, and Peru, are based on a total of 4755 GSV treated in 3169 patients, with no reports of serious complications, and a high index of functional and cosmetic success, minimal discomfort and high satisfaction scores. There were no differences when using 980 or 810 nm lasers, and there was no consensus on whether to do a concomitant crossectomy or not.

Prospective randomized study of endovenous radiofrequency obliteration (Closure®) versus ligation and vein stripping (EVOLVeS study): 2-year follow-up

In the framework of the Symposium of the German speaking phlebological societies of Austria, Germany, and Switzerland.

S. SCHULLER-PETROVIC (Austria)

This prospective multicenter study included 85 patients (86 limbs) with great saphenous vein (GVS) incompetency. They were randomily allocated to undergo radiofrequency obliteration of the GSV without adjunctive high ligation or stripping and high ligation, of the GSV. Sixty patients were re-examined at 2 years. At 2 years, the number of patients without any reflux in the GSV was not significantly different between the 2 groups (91.2% in the radiofrequency group versus 91.7 % in the surgery group). In two patients, recanalization of the GSV occured after initial occlusion. Prevalence of neovascularization was 2.9% in the radiofrequency group and 16.7% in the surgery group (NS). No significant difference was noted for presence of varicose veins between the two groups (14% in the radiofrequency group versus 21% in the surgery group). Analysis of the quality of life surveys showed statistically significant differences in favor of radiofrequency (global score and pain score) at 1 week and 4 months that persisted at 2 years.

References:

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State of the art on endo- laser vein treatment: "the light and the end of the tunnel"

Chairpersons: J. Ferreira (Brazil), L. Kabnick (USA)
Moderators: A. Scuderi (Brazil), E. Rabe (Germany)

With the participation of:
G. SPREAFICO (Italy), D. KONTOTHANASSIS (Greece), D. GREENSTEIN (UK), J. GERARD (France), F. PANNIER-FISCHER; E. RABE (Germany), M. DURAN (Ecuador), W. LAHL (Germany), S. GOCKERITZ (Germany), L. KABNICK (USA)

Laser light is absorbed by two chromophores, hemoglobin in the blood and water in the venous wall. The spectrum of water absorption is not the same for all laser lights. Using 980 nm laser light, 99.4% of water is absorbed in a volume of 1 mL of blood. Laser light absorbed by blood is transformed into heat. High temperature at the optic fiber tip carbonizes the blood, and water changes into steam and absorbs the heat that keeps the temperature at the tip stable around 100°. This is called "steam-bubble formation."

Laser light results in contact damage (coagulation and vaporization of the vein wall, perforations) and no-contact damage caused by the diffusion of heat throughout the vein. Different wavelengths from 810 nm to 1320 nm create this effect, and are used in endolaser treatment.

This session presents the ELVeS procedure which uses a 980 nm laser light (Biolitec).

The ELVeS kit consists of a 600 micron optic fiber, a 5 Fr introducer sheath, 0.035" J guide wire and a 18-19 Gauge needle. The step-by-step instructions were as follows:

- Preoperative duplex echography study
- Percutaneous entry into the vein
- Introduction of the J guide wire
- Withdrawal of the entry needle and insertion of the dilatator and introducer sheet
- Removal of dilatator and guide wire introduction of the laser fiber
- Positioning of the end of the fiber 1 cm below the inferior epigastric vein
- Perivenous anesthesia inside the "Egyptian Eye"
- Laser energy delivery in a pulsed withdrawal of 2 to 3 mm or continuous withdrawal of the fiber (the importance of fine tuning in real time with Computer-Assisted Control of the pullback speed was demonstrated by S. Gockeritz (Germany). Energy delivery of 60 to 80 Joule/cm is necessary to have a persistent occlusion of the treated venous segment. Vein occlusion by bandage or local compression is not necessary, because vein occlusion is preferentially caused by hemoglobin-mediated absorption and to a lesser degree by vein wall shrinkage.

Perivenous anesthesia or tumescence was believed to prevent skin burns and paresthesiae from nerve lesions, W. Lahl (Germany) demonstrated, in his study, no difference in thermic skin damage between patients treated with or without tumescence by placing a temperature probe at the outer venous wall.

The endovascular laser can be successfully used in the treatment of insufficient greater and smaller saphenous veins, Giacomini veins, recurrent varicose veins, and perforating veins. Positioning of the fiber tip in the insufficient vein at the level of venous ulcers stimulates wound healing. ELVeS treatment gives the best results in combination with completion phlebectomies. The success rate for the vein ablation ranges from 90% to 95%.

We have to accentuate the importance of a good knowledge of Duplex echography as a preoperative tool (hemodynamic diagnosis, vein diameter, defining where the reflux begins and where it disappears), operative tool (positioning of the fiber-tip below the epigastric vein) and postoperative tool (follow-up).

A large number of complications can be avoided by a good technique (venous puncture, duplex knowledge). Most frequent complications are ecchymosis (75%), paresthesia (3%), superficial phlebitis

(1.87%), burns (0.46%), inflammatory pain during the first week, and induration of the treated vein. Rather rare complications are deep venous thrombosis, pulmonary embolism, infection, major bleeding, and arteriovenous fistula formation.

The endolaser technique has been found to be easy, efficacious, and safe. The outpatient setting and the very short period of convalescence open new prospects in terms of health care and social costs. The further organization of International Endovascular Working Groups is important to obtaint answers to many phlebological questions (long-term results, final standardization of the endolaser procedure, antiocoagulation strategy) and for the results to be collected in a homogeneous and comparable manner.

LECTURE

Foam sclerotherapy in the treatment of varicose veins: state of the art

S. SADOUN (France)

The use of sclerosing foams (SF) for the treatment of varicose veins has become widespread and is becoming more popular, since more and more colleagues are becoming familiar with this treatment. Most of the recent publications and personal experiences indicate that foam sclerotherapy (FS) gives better results in comparison with classical liquid sclerotherapy (CLS) in larger veins. Some literature tends to indicate an increased rate of undesired side effects if foam is used, such as phlebitis, visual disturbances, and others. Some of these side effects are likely to have been caused by high volumes of foam, whereas for other side effects, the reasons are not known. Interestingly, very little attention is paid to the foam used itself. One hypothesis for the development of side effects is that eventually some of them are caused by the type of foam, which implies a closer look at the foam with regard to its standardization. A useful characterization of SF is provided by the European Consensus Conference on Foam Sclero-Therapy (ECCFS), where SF has been defined by (at least):

1. type and concentration of the sclerosing agent
2. type of gas
3. ratio of liquid to gas
4. the method of preparation
5. the time between processing and use
6. bubble sizes.

With the choice of using one of two major sclerosing agents, one of 6 possible concentrations (0.25%, 0.5%, 1%, 2%, 3%, 4%), and one of 3 commonly used ratios of liquid and gas (1 plus 3, 1 plus 4, or 1 plus 5), already as many as 36 different foams may be generated. The choice of materials and the technique used for foam preparation increases this number to approximately 6000. In addition, the time between processing and use, the method of foam administration (cannula/ needle/ catheter), and injection speed rises the number of different possibilities to the enormous number of >100 000, not to mention differences in puncture sites and foam volumes administered to individual patients. It is the author's opinion that standardization of foam preparation and administration would greatly help to make clinical results (more) comparable, and may eventually help to increase efficacy, while eventually lowering the rate of side effects at the same time. Different parameters were systematically checked, and the parameters for obtaining the "best" foam (eg, the best stability) were identified, leading to a proposal for a standardization of sclerosing foam and for its use, which will be presented.

Sclerotherapy

In the framework of the joint round table UIP/Panamerican Society of Phlebology and Lymphology.

Chairpersons: N. Rosli (Argentina), S. Gomez (Brazil), D. Otrante (Cuba), M. Musich (Argentina)

This session consisted of a number of presentations, mainly from Argentina, dealing with the value of different techniques of sclerotherapy (ST) in the treatment of varicose veins (VV).

U. P. Tropper, from Fundación Flebológica Argentina, reported the experience from nine centers with over 300 000 patients treated with ST and combined approaches (high ligature, post-sclerotherapy phlebo-exeresis, safety angle of 45º, physical sclerosis by a foreign body) over the last 5 years. He mentioned that the action of a sclerosing substance depends on the type and concentration of the agent, the exposure time, and the vessel size. He also gave his personal point of view on the treatment of large VV with minimum doses of sclerosant by means of the microfoam technique. More than 300 cases were treated using hydroxypolietoxi-dodecane 0.5%, injected via catheter at the safety angle, and the results were satisfactory in 59% with one application. It was necessary to perform two applications in 32% of the cases, 3 in 6% and 4 in 3%. He concluded that the optimal results obtained with the microfoam technique, coupled with the fact that the usual complications of liquid sclerosing agents are minimized, suggest this technique may be more advantageous than surgical approaches in the future.

E. Tkach related his personal experience with the use of ST with turbulence (injection of 15 to 20 cm^3 of foam and immediate suction, procedure repeated 4-5X with echo-color Doppler visualization).

J. Sas focused his presentation on the more frequent sclerotherapy complications and possible forms of their treatment: pigmentation, cutaneous necrosis, temporary edema, pain, thrombophlebitis, allergic rections.

A. Avramovic reported the results of a retrospective study in 1032 patients between 68 and 90 years. The used solutions for ST were: hydroxypoliethoxi-dodecane from 0.5% to 3%, tetradecyl sodium sulphate from 0.5% to 3%, and glucose solution at 25%. It was practised in both GSV and SSV, isolated VV, reticulate and telangiectasias, with 80% of cases treated with a positive evolution. He concluded that ST is a very important weapon in the therapeutical arsenal for elderly people.

Finally, J. Chunga-Chunga, from Peru, gave his personal point of view about the importance of immediate elastic compression after ST.

Chronic venous insufficiency
Conventional sclerotherapy

Chairpersons: J. Strejcek (Czech Republic),
M. E. R. Castro (Brazil), H. Guedes (Brazil)

Antithrombotic potential of sclerosants: in vitro effects on coagulation, red cells, and platelets

K. PARSI, T. EXNER, D. D. F. MA, E. JOSEPH (Australia)

In this excellent presentation the authors tried to answer the question of whether the most commonly used detergent sclerosants: sodium tetradecyl sulphate (STS) and polidocanol (POL) cause haemolysis, platelet lysis, or prolonged clotting time when added to whole blood, platelet-rich plasma, and platelet-poor plasmas.

They stated that low concentrations of sclerosants have procoagulant activity because:

- they shorten phospholipid-dependent clotting tests such as NAPTT (non-activated clothing time), XACT (factor Xa- activated clotting time)
- they damage platelet membrane expressing procoagulant phospholipids
- they release procoagulant platelet-derived microparticles.

Very low concentrations of sclerosants achieve procoagulant activity with increased exposure time, and this may justify immediate walking after sclerotherapy to minimize exposure of deep veins to low concentrations of sclerosants.

High concentrations of STS dissolve and inactivate the procoagulant phospholipids and additional lysis of microparticles. STS has potent anticoagulant activity when compared with POL, and this may justify modification of the technique to use multiple injections of low volume and high concentration of sclerosants, rather than infusion of large volumes which, via dilution and neutralization may achieve procoagulant acivity.

Is there a need to standardize the preparation and the use of sclerosing foam?

J. C. WOLLMANN (Germany)

The use of sclerosing foam was standardized in 2003 by Breu and Guggenbichler. The type and concentration of the sclerosing agent, type of gas, ratio of liquid to gas, and the method of preparation were described. Nevertheless, sclerosing foam preparation is still subject to multiple choices. The author suggested defining very accurately:

1. The syringe sizes
2. Needle sizes
3. Sterile gas volume
4. Number of movements
5. Power of movements
6. Speed and duration of movements.

Risks and complications of sclerotherapy

M. VANDENDRIESSCHE (Belgium)

Leg vein polidocanol foam sclerotherapy in patients over 75 years

G. BROCHNER, M. HERRERA (Argentina)

Sclerotherapy is an effective and safe method of treating veins. Complications are rare, but can be severe. There can be the following most dangerous complications: allergic (urticaria, bronchospasm, anaphylactic shock) and thromboembolic (intravenous clot, superficial thrombophlebitis, deep vein thrombosis, pulmonary embolism).

Even persons over 75 years with chronic venous insufficiency can benefit from foam sclerotherapy. Brochner obtained good results with high selection criteria without patient immobilization. He considered this method especially useful in patients with bleeding varicose veins.

Evidence of arterial venous malformation theory on telangiectases development

I. BIHARI, E. MAGYAR, A. MURANY (Hungary)

The aim of the study was to characterize the differences between the circulation of the spider veins and the surrounding skin, as well as to assess what has a greater influence on their circulation, perforator vein insufficiency or arterial venous (AV) fistula. Biopsy and histological examination was performed from Doppler pulse-positive sites in 19 cases. Laser Doppler flowmetry was used to detect the flow in normal skin and spider veins in 22 limbs of 19 patients. At places where Doppler instrument could detect arterial pulse, AV malformations were found in 16 out of 19 cases. The flow in spider veins was 1.8 times faster on average than in the surrounding skin. The authors concluded that:

1. Higher flow in some spider veins suggests anopen AV shunt
2. Histologically found shunts were open
3. Not every spider vein is connected to an open AV shunt
4. Higher flow is more frequent than congestion
5. It is supposed that these are normal skin AV shunts, which are diseased because of trauma, estrogen therapy, hereditary disposition, or high venous blood pressure.

Advances in sclerotherapy and postsclerotherapy compression: "my way and my practice"

Chairperson: M. Goldman (USA)

Echosclerotherapy using Tessari foam: the Australian Experience

P. THIBAULT (Australia)

The author demonstrated an Australian method of echosclerotherapy of the incompetent trunk of the greater saphenous vein, using Tessari foam. A total of 1019 patients treated with foam echosclerotherapy over a 4-year period from 2000 to 2004 were analyzed for occurrence of adverse effects. The results were compared with those of 820 patients treated with liquid echosclerotherapy. The author concluded that foam sclerotherapy is safe and effective method for the treatment of incompetence of the greater saphenous vein with a low rate of complications compared with liquid sclerotherapy.

Efficacy of lauromacrogol foam vs liquid in sclerotherapy of the greater saphenous vein: a 2-year follow-up

P. OUVRY (France)

Patients with great saphenous vein (GSV) reflux with a diameter ranging from 4 to 8 mm were randomized to 3% aetoxisclerol solution (n=48) and the same volume of foam containing one fifth 3% aetoxisclerol and four-fifths air (n=47). Patient characteristics and vein diameter were similar in both groups. At 3 weeks foam sclerotherapy was superior to liquid in the complete elimination of reflux: 40/47 vs 17/48, $P<0.001$. There was no difference in the incidence of complications. At 6, 12, 18, and 24 months foam was superior to liquid. It was concluded that foam was twice as effective as the liquid.

Advances in sclerotherapy and postsclerotherapy compression: “my way and my practice”

P. COLERIDGE-SMITH (UK)

The author presented his technique of foam sclerothrapy. Tessari foam was used. The greater saphenous veins were cannulated under local anaesthesia with the patient in a supine position. The spread of the foam were controlled with ultrasound imaging. It is very important to prevent wicking of the sclerosant into the deep venous system by elevation of the limb and intensive exercises of the ankle joint. Just after sclerotherapy, a strong compression bandage was applied.

Post-foam sclerotherapy and post-varicose vein surgery compression

A. CAVEZZI (Italy)

Eighty patients were included in this study. Medical compression stockings (Struva 23 or Struva 35) were applied just after surgical operation or foam sclerotherapy. A good result was achieved in all cases. Compression stockings have demonstrated a high resting pressure in comparison with bandages, which had a higher working pressure. The author concluded that compression stockings (Struva 23 or Struva 35) after operation or sclerotherapy can be widely used, but with some limitations, such as obese patients or very large varicose veins.

The use of a microbubble contrast agent in the early assessment of foam sclerotherapy

P. RAYMOND-MARTIMBEAU (USA)

Three weeks post-treatment, 172 patients with 202 apparently sclerosed greater saphenous veins treated with intravenous injection of foam (ratio 4:1) sodium tetradecyl sulfate (1%, 4 mL) were evaluated with contrast-enhanced imaging after intravenous injection of microspheres of human albumin perflutren microbubble contrast agent. The lumen was evaluated 30 seconds after initiation of contrast agent injection. To evaluate the perfusion of the lumen, intermittent compression of the vein with the probe was performed. The results of contrast-enhanced imaging were compared with those of non-contrast imaging in terms of the presence or absence of visible residual flow within the lumen. Images were assessed qualitatively by two independent observers to determine the contrast enhancement effect. As a result, in 124 (61.4%) of the 202 treated incompetent greater saphenous veins, contrast-enhanced imaging showed multiple enhancing channel within the sclerosed zones. In conclusion the author underlined that contrast-enhanced venous imaging is a new reliable and useful tool in the early assessment of the therapeutic response to foam sclerotherapy for greater saphenous vein incompetence.

Sclerotherapy treatment of varicose and telangiectatic leg veins: “my way and my practice”

M. GOLDMAN (USA)

While it appears simple to inject a solution into a vein with a needle and syringe, proper technique can increase efficacy and minimize complications. Over the last 20 years, my technique of performing sclerotherapy concentrated on four important concepts:

1.The logical progression of sclerotherapy treatment;
   a. Treat refluxing points first
   b. Treat largest veins first
   c. Treat proximal to distal.

2. Use the minimum effective sclerosing concentration appropriate for the specific vein treated;
   a. Endolumnal 1320 nm laser closure of the GSV or SSV
   b. Ambulatory phlebectomy for vessels >6 mm in diameter.
   c. STS Foam for vessels >1mm in diameter:
      i. 0.25% for 1-3 mm diameter
      ii. 0.5% for 3-5 mm diameter
      iii. 1% for 5-7 mm diameter
      iv. 3% for >7 mm diameter.
   d. 72% glycerin for vessels < 1 mm in diameter
   e. 1064 nm long pulsed Nd:YAG laser for res tant vessels.

3. Treat the entire venous network of a single leg in a single session.

Post-treatment compression 24 hours a day for 7 days with 30- to 40-mm Hg graduated compression stocking.

Sclerotherapy - ask the experts

Chairpersons: E. Rabe (Germany), A. Scuderi (Brazil)

Sclerotherapy and surgery

B. PARTSCH (Austria)

Surgery has been the main form of treatment for large varicose veins for many years. Due to the development of foam and the combined use of duplex ultrasound, there has been a renaissance of sclerotherapy in the last 10 years. Not every patient is suited to a stripping operation of large varicosities. An alternative treatment is attractive in older patients or patients with concomitant diseases like diabetes, adiposity, history of deep vein thrombosis, or even the presence of a venous ulcer. Recurrent varicose veins after a primary stripping operation are more found more frequently than has been suspected for many years. Due to a higher complication rate, redo surgery is unpopular. In these patients, ultrasound-guided foam sclerotherapy offers a safe, comparatively simple, and inexpensive alternative to conventional surgery. Although foam sclerotherapy has many advantages, there will always be patients who are better treated by surgery. Varicose veins of large diameter are less successfully treated by sclerotherapy. Varicose convolutes located subcutaneously often leave unsightly patches of indurated and hyperpigmented skin after sclerotherapy, and are easily treated by stab-avulsion phlebectomy. Ultrasound-guided foam sclerotherapy is another useful tool in the treatment of large varicose veins.

Echoguided sclerotherapy and foam

A. CAVEZZI (Italy)

Sclerosing foams (SF) are mixtures of gas and liquid solution with surfactant properties, affording full control of drug concentration inside the vein and contact time with the endothelium. Cabrera proposed the use of a microfoam of sodium tetradecyl sulfate and polidocanol for sclerotherapy in 1993. Many authors subsequently reported different methods for foam production. Sclerosing foam is characterized in part by the following parameters:

- Type and concentration of sclerosant
- Type of gas, ratio of liquid to gas
- Additional nonactive substances
- The method of preparation
- The time after processing
- Bubble size distribution

The microfoam has a number of unique physical properties. Bubble size, fluid-to-gas ratio, and foam breakdown rate are all highly important. New measurement techniques were developed to define the essential differences between microfoams, foams, and froths, depending on the diameter of bubbles:

- Froth >500 µ
- Foam >300-500 µ
- Microfoam <250 µ

Microfoams are characterized by:

- Density
- Stability
- Bubble size distribution

Density is controlled by the ratio of fluid to gas. Stability is dependent on viscosity, dissolved gas, temperature, and bubble homogeneity. Bubble size distribution measurement is complex, and must also be performed quickly. Use of sclerosing foam is an appropriate procedure in the therapy of varicose veins. Sclerosing foam is a powerful tool in expert hands, and in general more effective than the liquid form of sclerosants. It is necessary to have good skills in conventional liquid sclerotherapy before starting with foam sclerotherapy.

The differences between polidocanol and STS

M. MALOUF (Australia)

Venous sclerotherapists worldwide use polidocanol (POL) and sodium teradecil sulfate (STS). These are two highly effective and trusted detergent sclerosants for treating varicose and spider veins. In liquid form STS is two to three times more potent than POL, but their clinical effect is approximated when made into a foam. Chemically POL is a synthetic long-chain fatty alcohol related to lignocaine. It contains ethyl alcohol and phosphate buffers. STS is a synthetic long-chain fatty acid salt stabilized in benzyl alcohol and sodium phosphate, and preserved with a variable level of carbitol. The two sclerosants contain different ionic/non-ionic properties, behave differently in micelle formation, and there is a difference in the stability of their respective sclerosing foams. There are major clinical differences in the use of these two sclerosants. Pain on injection with STS is commonly noted, and sometimes severe. POL is almost painless on injection, related to its local anesthetic property. The likelihood of developing anaphylaxis or allergy is quoted as being over 20 times higher with STS than with POL. A higher concentration of POL liquid is needed to achieve the same potency and perhaps efficacy of sclerosis compared with STS liquid. Foaming augments the potency of both solutions to reach equivalent clinical efficacy. Recent clinical trials were performed comparing these two sclerosants, for the treatment of esophageal varices and later for the treatment of varicose veins and spider veins of the legs (including the Australian Polidocanol Study 1991-94 and Goldman's presentations 1998 and 2002). These studies found the efficacy of both sclerosants to be equal. Concerning the frequency and severity of complications, such as allergy, pigmentation, and injection ulceration, the Australian trial showed that POL produces much fewer and less severe complications compared with STS. Many sclerotherapists who have used both sclerosants have favored POL for the above reasons. Others prefer using the sclerosant that they are used to and accept a higher rate of pain, potential complications, and possible anaphylaxis.

Side effects induced by incorrect techniques (of sclerotherapy)

J. J. GUEX (France)

Thrombotic complications of sclerotherapy are usually not related to an incorrect technique, but sometimes to the wrong indication or lack of respect of contraindications. The importance of compression after sclerotherapy to prevent deep venous thrombosis is likely, but evidence is scarce. Extensive superficial reactions, sometimes considered to be superficial thrombophlebitis, can be observed after injection of too-strong sclerosing agents. The incidence of necrotic complications has dramatically decreased due to the evolution of the technique. They are attributed either to intra-arterial or at least to extravascular injections. Severe necroses were mostly observed after injection of junctions without duplex guidance. The latest reports from insurance companies in France indicate no severe necrosis. The safety of ultrasound-guided sclerotherapy has been sufficiently demonstrated. Obviously, the open needle allows one to keep access to the vein and to double-check reflux of blood in the line and position of the needle in the vein. Small necroses are due to extravascular injections in fragile areas such as the ankle or the anteromedial aspect of the lower leg. Visual troubles are worrisome complications, even if no case of lasting visual impairment has been reported so far. We have observed that these were mostly observed after foam or air block injections, and mostly after treatment of reticular or spider veins. The responsibility of air bubbles and not foam seems likely. In all cases, attention must be paid to prepare foam at the last minute in order to use it during its stability period. Poor results of sclerotherapy can be attributed to either tactical or strategic mistakes. In the latter group we find a lack of preliminary assessment of the whole venous system, while in the first group the main cause is poor technique. Poor results which can be considered as side effects are matting and pigmentation. Good understanding of the disease and good training should limit their frequency to almost zero.

Chronic venous insufficiency-foam sclerotherapy

Chairpersons: L. R. Villalonga (Cuba), M. Sato (Japan)

Foam of polidocanol 3% versus 1% in greater saphenous vein sclerotherapy: preliminary results

C. HAMEL-DESNOS, F. A. ALLAERT, J. P. BENIGNI, G. BOITELLE, F. CHLEIR, P. OUVRY, M. SCHADECK, P. R. DESNOS (France)

A previous study showed that foam of 3% polidocanol (POL) provides better results than liquid form for sclerotherapy of the great saphenous vein (respectively 85% versus 35% reflux free). This randomized double-blind study investigates whether a lower concentration of POL (1%) may provide the same result with a better tolerance. One hundred and fifty-eight patients with great saphenous vein (GSV) reflux were included (diameter between 4 and 8 mm) and randomly allocated to the two treatment groups. A first injection of 2.5 mL was performed 10 cm below the saphenofemoral junction by direct puncture under duplex assistance. In case of unsuccessful spasm, injections may be repeated up to three times (maximal injected volume: 7.5 mL). Only one treatment was performed. Two or three injections were required for two thirds of the patients. The success rate was 80% at 6 months (18 recanalizations/144 patients) and 75% at 1 year. One deep venous thrombosis was observed. The study is still blinded until the end of the trial (February 2006) but the results are in favor of an equivalence between the two concentrations of foam.

Reference:
Hamel-Desnos C, Desnos P. R. Wollmann JC, Ouvry P, Mako S, Allaert FA. Evaluation of the efficacy of polidocanol in the form of foam compared with liquid form in sclerotherapy of the greater saphenous vein: initial results. *Dermatol Surg.* 2003; 29:1170-1175.

Clinical and hemodynamical outcomes of duplex-guided foam sclerotherapy: a 24-month follow-up study

R. GONZALES ZEH, S. BARAHONA-CRUZ (Chile)

In this prospective open study, 143 patients were included and 175 procedures were performed : 106 on the GSV and 69 on the SSV. All patients were treated by duplex-guided injection using polidocanol 3% with Tessari's technique. The volume of the injection was calculated for each patient depending on the diameter of the vein (mean: 7 mm for GSV and 5 mm for SSV) and the length of the reflux. At 1 year, reflux was observed in 9.4% of the GSV-treated and in 4.3 % of the SSV-treated patients. At 2 years, reflux was observed in 14% of the GSV-treated and in 10% of the SSV-treated patients. One case of DVT was observed at 1 week by systematic duplex.

Indications and outcome of greater saphenous vein foam sclerotherapy

F. VIN (France)

Foam sclerotherapy of the great saphenous vein is indicated in cases of a venous diameter less than 7 mm. Previous studies have shown that recanalization occured in 50% of the treated veins if the initial diameter is above 8 mm. Two hundred eighty limbs were treated. A first injection of 3 cc of polidocanol 3% (1/4 air) was performed, and if needed, a second procedure was performed 2 weeks later (3 cc at the upper third of the thigh and 2 cc at the lower third). Occlusion was obtained at the first session of treatment in 85% of the cases and at the second session in 92.8% of the cases. At 1 year, 79.9% of the patients had a GSV occluded, 12.7% did not and, 7.4% were lost of follow-up. Few complications were observed: one case of DVT and 3.3% of venous inflammation.

Chronic venous insufficiency - echo guided sclerotherapy

Chairpersons: A. Frullini (Italy), P. M. Canongia (Brazil)

With the participation of:

A. I. SHIMANKO, M. L. DIBIROV, A. J. VASILIEV, S. A. SOLOMATIN, N. A. POSTNOVA, S. V. TSURANOV (Russia), A. CORNU-THENARD (France), N. CROCETTI, D. PAOLICELLI, C. MINGARELLI (Italy), T. ALBERTI, M. VASSALLO, J. MEJIAS, L. RODRIGUEZ (Venezuela), N. MORISSON, D. NEUHARDT (USA), J. BRODERSEN, J. RICHTER (Germany)

Duplex-guided sclerotherapy with a sclerosant agent or foam is used for the treatment of great or small saphenous vein insufficiency, and incompetent perforating veins with open trophic ulcerations. Rare superficial venous aneurysms are normally treated surgically; however, a series of nine cases of venous aneurysms treated with echosclerotherapy represents a promising alternative procedure.

Catheter-directed echo-guided sclerotherapy by percutaneously inserting an angiography catheter under echographic guidance with positioning distal to the ostial valve and slowly injecting foam while removing the catheter seems even more effective and controlable. The primary success rate is 89%; 3-months follow-up shows a closing rate of 93% (Alberti et al). The KAVS catheter was designed to reduce the side effects of the slerosing agent (pigmentation, superficial phlebitis, skin necrosis, visual disturbances, deep venous trombosis). By inflating a distal balloon at the saphenofemoral junction, foam can be injected under duplex ultrasound without entering the deep venous system. The amount of foam is reduced by aspiration at the end and only the foam which is interacting with the venous wall is left. It has been mentioned that sclerotherapy is never completely controllable; there is always a loss of the agent to the deep system by collaterals and perforating veins.

In order to prevent side effects, it is important to have an idea of the maximal volume of foam that can be injected. A table with two parameters (vein diameter and vein length to be sclerosed) helps to define the needed volume. Several influencing factors such as position of the patient and spasm of the vein during injection have to be taken into account.

The introduction of foam and technical improvements are turning duplex guided sclerotherapy into a valuable method comparable to other surgical and non-surgical techniques (endovascular radiofrequency and laser venous closure).

Miscellaneous

Chairpersons: J. Sas (Argentina), F. R. Bastos (Brazil)

Sclerotherapy and thrombophilia

C. HAMEL-DESNOS, J. L. GILLET, F. A. ALLAERT, P. R. DESNOS (France)

The authors of this large multicenter prospective randomized study in ninety-four patients with thrombophilia treated different types of varicous vein disorders with sclerotherapy under anticoagulant treatment. The patients were randomized to two groups, one treated with low-molecular-weight heparin and the other with oral anticoagulation with warfarin. There was no occurrence of clinical deep or superficial thrombosis during and after the procedures. Protection with low-molecular-weight heparins or warfarin appears a useful tool to use in this kind of patient.

It will be necessary to perform randomized studies under ultrasonic control to demonstrate the efficacy of anticoagulation therapy in patients with thrombophilia treated for varicous veins disorders.

The use of foam sclerotherapy during varicose vein surgery

J. F. UHL, M. LEFEBVRE-VILARDEBO, D. CRETON (France)

The combination of venous surgery and foam sclerotherapy in the same surgical session can help us to treat complex cases of venous insufficiency like inaccessible veins, lymph and venous dystrophies, popliteal cavernomas, venous recurrences with good results.

LYMPHEDEMA

Compression Therapy in Lymphoedema,

In the framework of the SIGVARIS symposium.

J. L. CATALDO (Brazil)

According to conservative estimates, several million people in Brazil suffer more or less from some form of lymphedema. Most patients have inadvertently learnt details about the disease and the appropriate modes of treatment from therapists. Throughout the entire course of medical studies, little attention is devoted to diseases of the lymphatic system, and consequently doctors in Brazil have little acquaintance with the problems of lymphedema. Because of the increasing numbers of surgical operations, the incidence of lymphedema has certainly increased, but improvements in treatment and refined therapeutic techniques have done much to lessen the burden of the disease. The treatment of lymphedema must include a range of the therapeutic options such as:

- Hygiene/skin treatment
- Manual whole-body and segmental lymphatidrainage
- Compression therapy with bandages and then with custom-made compression stockings
- Special physical exercises
- Diet
- Psychological motivation

ULCERS

Venous ulcers – clinical and compression management of venous ulcers

Chairpersons: J. Hafner (Switzerland), M. Avramovic (Argentina)

Biotechnologies in the treatment of venous leg ulcers: fibroblast and keratinocyte autograft

L. CORCOS, D. DE ANNA, L. DONEGA, F. PELLEGRINI, P. COLAMUSSI, P. KUWORNU, C. POGGI, D. ZAGNI (Italy)

The autologous skin graft represents the basis for the modern surgical treatment of vascular leg ulcers. At the present time biotechnologies make it possible to take a small skin fragment with a 2-to 3-cm^2 biopsy, which is divided into the two essential components: dermatocytes and keratinocytes. Extensive tissue layers (100 to 200 cm^2) are then developed in vitro and are separately implanted on the ulcer surface. The authors performed a clinical trial, using biotechnologies on 210 ulcerated legs over the last 3 years. Half of the ulcers had typical venous origin and were related to CVI. The procedure was divided into two steps: in the first, typical surgical procedures for CVI were performed. The second step was much longer and more difficult: a small skin graft was taken from the anterior region of the patient's elbow. Next, it was divided in the biology laboratory into the two main components – dermatocytes and keratinocytes. Separated keratinocytes were allowed to multiply in a hyaluronic acid bed, and were then implanted in the debrided ulcer surface after 4 weeks. A clinical follow-up of all cases was performed at a mean of 14 months (range: 3 months to 3 years).

Reduction in ulcer size of more than 25% was observed in 80.6% of treated ulcers. Reduction of more then 50% of initial size was observed in 66% of treated. Only in 6 cases was total wound healing observed. Perhaps in the future this method may replace the traditional Tiersch method.

Laser treatment in chronic leg ulcers

P. CASONI (Italy)

A wide variety of methods have been tried, but few have been assessed in randomized trials. The aim of this study was to test whether the topical use of a laser source such as Diode 810 nm can improve healing time. Of 180 leg ulcers, over 3 years a group of 44 homogeneouscases with non-healing vascular leg ulcers were randomized 2 weeks after conventional treatment (multilayer bandage, elastic stockings, and non ad pancement). Patients continued treatment with the bandage changed twice a week and randomized to receive laser Diode 810 nm treatment 60/100 J/cm^2 (n=22 Group A) or a simple nonadherent dressing (n=22 Group B) The main end point for this trial was the time to complete healing. A comparison of images and of life tables up to 3 months of treatment was made.

At the end of the study 60% of group A (treated with laser plus occlusive dressing) and 35% of group B (without laser source) had completely healed. Life table analysis showed a significant difference (P=0.032).

Thus, it is now possible to consider a new method of treating leg ulcers.

Surgical treatment of non-healing venous ulcers-crural fasciectomy versus shave therapy

C. SCHWAHN-SCHREIBER (Germany)

Long-term results after shave therapy of venous leg ulcers resistant to other treatment

In the framework of the Symposium of the German speaking phlebological societies of Austria, Germany and Switzerland.

H. J. HERMANNS (Germany)

Surgical treatment by shave therapy by crural fasciectomy are indicated in venous ulcers that are still nonhealed after 1 year of optimal treatment. In fact, in these two retrospective studies, the mean duration of operated venous ulcers was around 15 years before surgery. Shave therapy is the removal of the ulcer and of the surrounding epifascial fibrotic tissue by a dermatome (dermatolipectomy). Crural fasciectomy is the removal of the ulcer and of the surrounding fibrotic tissue together with the underlying fascia (dermatolipo-fasciectomy) with a scalpel. In both procedures, the defect is immediately covered by a mesh split skin graft. The results in term of complete healing are equivalent with the two procedures. At 1 year, complete healing rates are between 61% and 64%, and around 75% to 80% at several years of follow-up. Postoperative treatment included compression therapy for life, intermittent pneumatic compression therapy at home, manual decongestive massages, and education of the patient. Currently, shave therapy is the method of choice. Crural fasciectomy is indicated in cases of important tendon necrosis.

Short-stretch or multilayer elastic bandaging in venous ulceration? Results of a randomized clinical trial

P. J. FRANKS, C. J. MOFFATT, The Wound Healing Nursing Research Group (United Kingdom)

The purpose of this trial was to compare the use of a Cohesive Short Stretch System-**CSSB** (Actico-Activa Healthcare, Flexiban-Activa Healthcare) with a generic 4-layer bandage system-**4LB** (Flexiban-Activa Healthcare, Setocrepe-SSL, Elset-SSL, Coban-3M) in the management of chronic venous ulceration. In all, 156 patients met the entry criteria and were randomized from the 12 clinical centers with median (range) ulcer size of 4.33 (0.33 to 123.10) cm^2. Analysis revealed that after 24 weeks a total of 111 (71%) of patients had complete ulcer closure, 32 (21%) had withdrawn from the trial, 12 (8%) remained with open ulceration and one patient had died. Of the 74 patients randomized to 4LB, 51(69%) had ulcer closure on treatment compared with 60/82 (73%) on CSSB. Intention-to-treat analysis reduced a hazard ratio for healing of 1.08 (95% CI 0.63 to 1.85, *P*=0.79). Withdrawal rates were similar between groups (15, 20% 4LB, 17, 21% CSSB). Ulcer closure rates for patients treated with CSSB were similar to those for patients managed by the 4LB system in this trial. Both systems appear to be equally effective in healing chronic venous ulcers.

LECTURE

Efficacy of a compression stocking for therapy of chronic venous ulcer compared with bandages

M. JÜNGER (Germany)

One hundred and thirty-four patients with venous leg ulcers were included in this study (prospective, multicenter, open-labeled, randomized, active controlled study with blinded assessment of the primary end point). Exclusion criteria were infected ulcer or obesity. U-Stocking (Venotrain® ulcertec) or bandages applied for at least 8 hours per day over 12 weeks. The primary end point was the healing rate after 12 weeks as assessed by planimetric measures. The secondary outcome variables were duration until healing, extent of ulcer healing, experience of use, and patient compliance. As a result, therapy with the U-Stocking produced a significantly higher rate of complete healing of 47.5% (29/61) versus 31.7% (19/60) with bandages, one-sided *P*=0.0129 (95%-CI for differences: 4.3% to 28.5%). Mean duration until healing was 46 days in both groups. Time required for application of the U-Stocking was a mean of 5.4 min (SD 5.4) versus 8.5 min (SD 6.5) for bandages, *P*=0.0001. So, the U-Stocking was superior to bandages in compression therapy for venous ulcer.

LECTURE

New technical method (mixtures of gas) in the production of Tessari's sclerotherapy-foam and postsclerotherapy compression

L. TESSARI (Italy)

The author has reported new technical procedure for the production of the sclerosing foam. New foam is consists of a mixture of the sclerosant solution and soluble/biocompatible gas (CO_2). This foam allows greater safety and favors the transendothelial release of these self maintaining and facilitating the homogeneous contact of the sclerosant with the endothelium for a longer time. For postsclerotherapy compression, the author used the Struva® stockings by Medi (Struva® 23 or Struva® 35).

Chairpersons: L. Norgren (Sweden), P. Mendonça (Brazil)

Ultrasonic treatment of infected leg ulcers: preliminary results

A. L. LA ROSA, R. M. MOIA, M. R. BUFFONI, M. Y. YUSUF, C. B. BLUS, L. P. PERVERSI, P. M. MARONE (Italy)

Ultrasound is known to have two properties of dissection on biological tissues and can damage bacterial cells through two mechanisms, cavitation and heating. The authors developed a Debridement Ultrasonic System to treat leg ulcers and simultaneously obtain a local bactericidal effect. The purpose of this study was to evaluate the efficacy and time consumption of radical ultrasonic debridement in the treatment of leg ulcers, the degree of the bactericidal effect in vivo, and the effective killing action of cavitation alone in an experimental model.

Fifteen patients (3 males, 12 females) presenting with infected leg ulcers underwent ultrasonic debridement: 7 ulcers were treated with a steel probe (group I), and 8 ulcers with a titanium probe (group II). A gross examination of intraoperative results of ultrasonic debridement of ulcers, with respect to surface appearance after fibrin and necrotic tissue removal was performed between groups I and II. The ultrasonic local bactericidal effect was investigated between group I and II, with culture immediately after ultrasonic procedure and after 24 and 36 hours. The killing action of cavitation alone, using a titanium tip in pulsed mode, was studied with sonication of a suspension of *S. Aureus* at 30 s, 45 s, 1 min, 1.30 min, with external refrigeration of samples, maintained at a temperature of 37° C.

At gross observation, all 15 ultrasonically treated patients showed a radical debridement of ulcers after only one procedure, with no significant difference between group I and II. Ultrasonic debridement was rapid with a medium time duration of 9 s per cm^2 and minimally painful. A complete bactericidal effect in group I resulted in 6 out of 7 ulcers after only one procedure, and maintained after 24 and 36 hours. In group II only 1 ulcer experienced complete bacterial killing. The sonication of *S. Aureus* in vitro at 30 s and 45 s revealed insignificant bacterial killing; at 1 min there was 48.80% killing due to cavitation. Ultrasonic exposure of the sample at 1.30 min increased bacterial killing to 56.96%.

Ultrasound seems very promising in the debridement of the leg ulcers, with favorable results for rapidity and treatment with minimal pain. The study suggests that the higher bactericidal power of the steel probe tested in vivo depends on its greater aptitude to develop heat as opposed to the titanium probe.

The debridement of hard-to-heal leg ulcers by means of Versajet

G. MOSTI, M. L. IABICHELLA, P. PICERNI, A. MAGLIARO, V. MATTALIANO (Italy)

Debridement is a mandatory step for promotion of healing in necrotic and sloughy ulcers. The authors' experience with the Versajet Hydrosurgery System (Smith & Nephew), a new tool for mechanical debridement of exudating ulcers, based on a Fluidjet technology that, using the Venturi effect, excises and aspirates the unwanted tissue, were presented.

Observation was performed in a group of 104 patients with nonhealing venous leg ulcers. In the majority of the cases (n=75) the debridement was achieved in 1 step; 2 and 3 treatments were required in 24 and 7, respectively. The Versajet procedure is quick (mean time per treatment: 5 min); it considerably shortens the in-hospital time by roughly 5 days as it shortens the debriding time from 6.1 to 1.4 days and promotes a quicker healing process. The debridement is selective, removing only the tissue centered in the working end and sparing the healthy tissue. Debriding with Versajet is highly effective in reducing the bacterial burden of the ulcer bed from 1 860 260 to 7 816 CFU cm^2. The pain caused by Versajet is well tolerated, especially when set for gentle debridement; the pain level valued with a visual analog scale was 4.3. Compared with usual debridement with gauze and saline solution, the pain is the same or less. If multiple treatments are required, the combined use with moist dressings is synergistic, as the dressings soften the necrotic tissue, thus facilitating the following Versajet debridement. The results show that Versajet may be considered a new, very effective tool for ulcer debridement, allowing a quick, selective, with minimal pain and bleeding debridement; it considerably decreases the bacterial burden and leaves a flat surface ready for the skin graft.

Compliance and measurable results of applying compression

In the framework of the JOBST Symposium.

M. JÜNGER (Germany)

The author presented the results of hemodynamic examination of patients with different stages of CVI. He showed that improvement of venous outflow directly correlates with maximal walking pressure and resting pressure of the compression bandages. The author presented a new compression system: Ulcercare® (Jobst, BSN) for treatment of patients with CVI CEAP 6 class. Ulcercare® consists of two below-knee stockings which provide 40 mm Hg ankle pressure. This combination is very effective and comfortable for use in patients with active venous ulcers. Also, the author presented new compression leggings. In spite of absence of foot compression, these leggings significantly improve venous return.

LECTURE

Study of the effect of five different methods of compression in the treatment of venous leg ulcers

In the framework of the SIGVARIS Symposium.

E. O. BRIZZIO (Argentina)

Thirty-five patients with active venous leg ulcer were included. The five different types of compression were used over 6 months:

A) Sigvaris Stocking AD (Delilah) with minimum compression (15-20 mm Hg)
B) Sigvaris Stocking AD (862) with medium compression (20-30 mm Hg)
C) Sigvaris Stocking AD (863) with high compression (30-40 mm Hg)
D) Four-layer short stretch bandage
C) Inextensible CircAid Boot.

At the end of treatment 27 ulcers were closed and 8 ulcers were active. There was no significant difference between types of compression.

Editor's comment: This study was underpowered.

THROMBOSIS

LECTURE

Vascular endothelial growth factor gene therapy accelerates venous thrombus resolution and recanalization

K. G. BURNAND (UK)

After observing the rise in the expression of the vascular endothelial growth factor (VEGF) during venous thrombus resolution, this group from the UK designed this study in mice, creating a thrombus in the interior of vena cava which was injected with adenovirus VEGF (adVEGF) in different concentrations. They observed that treatment with adVEGF reduced thrombus size and increased recanalization. This could form the basis of a novel treatment of deep vein thrombosis in humans.

Thrombo-embolic pathology- surgical management

Chairpersons: F. A. Allaert (France), M. Portiho (Brazil)

Combined open and endovascular recanalization of symptomatic chronic iliofemoral venous thrombosis

G. S. ODERICH, A. A. NOEL, H. BJARNASON, P. GLOVICZKI (USA)

Six consecutive patients who underwent combined open and endovascular recanalization of chronically occluded (n=5) or stenosed (n=1) iliofemoral veins were retrospectively reviewed.

There were 4 males and 2 females with a mean age of 41 years (range, 30 to 49 years). Five patients had thrombophilia and all were treated with oral anticoagulants and compression stockings. CEAP classification was class 4 in three patients, class 5 in one, and class 6 in two. Two patients had associated inferior vena cava (IVC) occlusion and two patients had bilateral iliofemoral vein occlusions. All patients underwent open common femoral vein exposure, femoral vein endophlebectomy, bovine pericardial patch venoplasty, and stenting of the occluded/stenosed venous segments. There was one early iliofemoral vein occlusion due to poor inflow, which was successfully treated with thrombectomy, arteriovenous fistula, and femoral vein stent. Mean follow-up was 25 months (range, 1 to 63 months). All patients showed clinical improvement and both class 6 patients had healed ulcers at 2 and 3 months, respectively. At the last follow-up, CEAP classification was class 3 in 3 patients and class 5 in 3 patients. Two patients had late unilateral iliofemoral occlusions and one had femoral vein restenosis, yet only one of these 3 had mild recurrent symptoms. One patient who had IVC and

bilateral iliofemoral recanalization developed unilateral iliofemoral vein occlusion and failed attempted recanalization. Another patient with femoral vein restenosis was successfully treated with a stent, and the third patient with asymptomatic iliofemoral vein occlusion was treated conservatively. Early results of combined open and endovascular recanalization of chronically occluded or stenosed iliofemoral veins demonstrate significant symptom improvement, despite recurrent thrombosis or restenosis in three of eight recanalized iliofemoral segments in 6 patients. Open endophlebectomy and patch venoplasty may provide adequate venous inflow and allow endovascular treatment of patients previously considered unsuitable for iliofemoral vein stenting.

Thrombolytic therapy and thrombectomy of acute venous thrombosis

G. R. ASKERKHANOV, M. A. KAZAKMURZAEV, I. S. ISMAILOV (Russia)

One hundred and five patients with acute iliofemoral venous thrombosis were treated with thrombolytic therapy with subsequent thrombectomy in 44 cases. Different methods of thrombolytic therapy with streptokinase were used. In conclusion the author underlined that the combination of the thrombolytic therapy with early thrombectomy radically removes thrombus, preserves competence of valves, and decreases the rate of rethrombosis.

Intermittent pneumatic compression of the foot and calf improves the outcome of catheter-directed thrombolysis using low dose urokinase in patients with acute proximal venous thrombosis of the leg

S. HOSHINO, T. OGAWA, H. MIDORIKAWA, K. SATO (Japan)

Twenty-five patients with proximal DVT were divided into two groups: 10 patients underwent catheter-directed thrombolysis (CDT) and 15 patients had a combination of CDT with intermittent pneumatic compression (IPC). In this group a temporary vena cava filter was implanted for 3 to 7 days. The pulmonary embolization was assessed by pre- and postoperative angiography. There was no symptomatic pulmonary embolization in either group. In the CDT+IPC group, new asymptomatic pulmonary emboli and small thrombi in the vena cava were found. In spite of the initial thrombolysis, results in the CDT+IPC group were best. The author concluded that combination of the CDT and IPC gave the best results compared with CDT alone, and was not associated with increased risk of symptomatic pulmonary embolization.

Acute pulmonary thromboembolism. Emergent treatment with rt-PA

A. LIMURIS, N. FISTAS, C. H. EFTIMIADES (Greece)

Twenty patients with pulmonary thromboembolism were treated with rt-PA infusion.The thrombolytic therapy with rt-PA was started with a 10-mg bolus intravenous injection for 4 min and slow infusion of 40 mg for 60 min. Pulmonary angiography was performed in all cases. After full thrombolysis all patients received low-molecular-weight heparin for 7 days and then oral anticoagulants. Three patients died as a consequence of right heart fealure. In the other cases good results were achieved.

Mini-invasive treatment of chronic venous insufficiency

N. SALIMZHANOV (Russia)

A total of 1110 patients with chronic venous insufficiency were treated. Complex examinations including X-ray phlebography, phlebotonometry, duplex scanning, and radionuclide phlebography were performed. The author used a combination of the different mini-invasive methods such as microphlebectomy, SEPS, and sclerotherapy. For rehabilitation the author used medical compression, stockings, intermittent pneumatic compression, and venotonics. In all cases good functional and cosmetic results were achieved.

Surgical considerations for acute and chronic pulmonary thromboembolism

M. ANDO, T. NISHIBE, M. YAMASHITA, M. SATO, R. HOSHINO, Y. KONDO (Japan)

Eighteen patients with acute pulmonary thromboembolism and 93 patients with chronic postembolic pulmonary hypertension were operated on. In 18 cases pulmonary embolectomy was performed, and in 93 cases thromboendarterectomy using deep hypothermia and circulatory arrest. All patients had pulmonary hypertension with pressure ranging from 30 to 70 mm Hg (mean 45 mm Hg). The author concluded that emergency thrombectomy with cardiopulmonary bypass was an effective operation for restoration of the pulmonary artery (1 patient died). Surgical treatment of patients with chronic occlusion of the pulmonary artery is more dramatic. Twelve patients died of heart and respiratory failure, but 77 showed good clinical results.

System inflammatory response syndrome in patients with deep venous thrombosis

V. SOROKA, P. CHECHULOV (Russia)

System inflammatory response syndrome (SIRS) is a well-known medical problem. SIRS can predict outcomes in patients with vascular inflammatory diseases. We investigated the score of SIRS criteria (WBC, temperature reaction, tachypnea, and tachycardia) in patients with acute deep thrombosis (DVT) and evaluated the rate of the complications, such as recurrent thrombosis, pulmonary embolism, and chronic venous insufficiency. In addition to the SIRS score we assessed the level of procalcitonin. In the majority of the cases SIRS was identified. Patients who had two or more positive SIRS criteria had recurrent thrombosis and pulmonary embolism ($P<0.01$). The risk of this complication was well-correlated with a high level of procalcitonin (mean 2±0.4). The author concluded that levels of procalcitonin are a good predictor of SIRS and early thromboembolic complications.

Purulent deep vein thrombophlebitis of the leg: surgery or not?

C. RANDON (Belgium)

The author presented a clinical case, and 12 cases from the literature, of the treatment of purulent DVT. Different therapeutic modalities were discussed. Most cases of purulent DVT can be managed by conservative treatment. Broad-spectrum antibiotics are added based on cultures; if negative and other sources of infection are excluded, they are started on an empirical basis and given for at least 6 weeks (amoxiclav with an aminoglycoside). Surgical therapy for purulent DVT consists of a thrombectomy or thrombolysis in patients with cerulea alba dolens, and in young patients with thrombosis of the common femoral or iliac vein to avoid CVI. The incomplete removal of the thrombus (remnants of the thrombus due to adherence at the vein wall) more then 2 weeks after onset of the DVT is a disadvantage in both procedures. Deep phlebectomy is the only operation where every septic focus is removed, but has a high risk of morbidity and mortality due to the extent of the operation. If septicemia persists after 4 weeks of broad-spectrum antibiotics, a surgical thrombectomy or thrombolysis is performed. If the clot can not be removed, a full excision of the affected vein is indicated.

Endovascular treatment of venous disorders

In the framework of the joint meeting UIP/Brazilian Society of Angiology and Vascular Surgery.

Chairpersons: L. Moura, A. Frankini, G. Pitta, F. Miranda Jr (Brazil)

This was a didactic session about current practice in Brazil.

F. Miranda Jr made a review of the history of iliac vein compression (May-Thurner/CockettSyndrome), revision of symptoms and signs, and his personal diagnostic experience in the field of echocolor Doppler (sensitivity 73% and positive predictive value 91%). He also presented some data from the literature in endovascular treatment of compression of the iliac vein with PTA and stenting: primary and secondary permeability with deep vein thrombosis (DVT; 52% and 90%) and without DVT (60% and 100%).

A. Von Ristow recounted his personal experience in the treatment of proximal venous thrombosis with thrombectomy. He mentioned the goals (prophylaxis of potentially lethal DVT or pulmonary embolism, prophylaxis of post-thrombotic syndrome, and treatment of severe DVT), indications (impeding venous gangrene, phlegmasia cerulea alba and dolens) and the specific importance of duplex scan and angio CT in diagnostic investigation. He also presented the results of his personal technique (insertion of temporary vena cava filter; surgical exposure of ipsilateral vessels; proximal thrombectomy; angioplasty/stenting if indicated; distal thrombectomy; creation of an A-V fistula; closure of the fistula 30 to 45 days later by endovascular methods) in 52 cases (9 isolated lower cava, 17 lower cava + distal veins, 18 iliofemoral + distal veins, 8 femoral + distal veins). In this series the frequency of this procedure in patients with DVT was 7.1% and the early results were: good in 41, partial rethrombosis in 9, 1 amputation, and 1 death. The late results in 43 of the patients were: good in 33 and light post-thrombotic syndrome in 10. He concluded that venous thrombectomy is a safe and effective procedure.

Finally, C. Peixoto gave his personal point of view on the treatment of proximal vein thrombosis by catheter thrombolysis with rt-PA (2 mg/h over 18-24 hours). He reported 85% of clinical success (patency > 90% with concomitant iliac stent) and emphasized the importance of the experience with this technique to achieve good results.

ASSESSMENT OF TREATMENT EFFICACY

Quality of Life

SERVIER Session on the Quality of Life

Chairpersons: G. Jantet (France), S. Park (Korea)

- Epidemiological results of the RELIEF study across different continents. G. Jantet (France)
- Multilingual validation of a CVD-specific questionnaire of QoL: the example of the CIVIQ in Spain. F. S. Lozano (Spain)
- QoL changes in patients with chronic venous disease: comparison of the CIVIQ and the SF12. J. J. Guex (France)
- Relationship between signs, symptoms and quality of life in patients with chronic venous disease. M. Perrin (France)
- Change in the quality of life in patients with chronic venous disease: results of a 6-month study using MPFF*. P. L. Antignani (Italy)

The objective of this new analysis on the cross-sectional RELIEF Study was to compare demographic, clinical, and quality of life characteristics of patients with chronic venous disease in different continents. RELIEF was held in general practices from 18 countries in Europe, Asia, and Latin America. Patients diagnosed with clinical class C0s to C4 according to the clinical, etiological, anatomical, pathophysiological (CEAP) classification, over 18 years of age, male or female, of any race, whether wearing compression stockings or not, were enrolled in the study. Venous reflux was detected by means of a pocket Doppler. Symptoms (sensation of swelling, cramps, leg heaviness) were assessed on a 4-point scale, pain was rated on a visual analogue scale (VAS), edema was estimated by measuring leg circumference, and quality of life (QoL) by using the Global Index Score (GIS) of the CIVIQ. Comparison between continents used Chi^2 tests or the Fischer exact test for discrete variables, and the Kruskal-Wallis test for continuous variables.

A total of 3948 patients were enrolled in this analysis. Patients were mainly Caucasian (77.9%), and female, (81.1%), with a mean age 45.5 years, and mean duration of CVD of 12.4 years. Differences were seen in Asia (A) where patients' mean age (41.6 years) was significantly lower than in Europe (E) and Latin America (LA) (P<0.0001). The proportion of men in Asia (40.1%) was far higher than in Europe (15%) and in Latin America (13.5%), (P=0.001). Moreover, Asian patients waited less than their European or Latin American counterparts before seeing a doctor (5.1 years in A versus 13.6 years in E and 11.7 years in LA, P<0.001). Asian patients in the great majority declared having no family history of venous disease (84%), versus only about 26% in Europe and in Latin America (P<0.001) where declarations were similar (P=0.6).

Although Asian and Latin American patients were classified in less severe CEAP categories (% in C0s-C2: 70.8 in A and 66.3 in LA, P=0.768) than European patients (% in C0s-C2: 61.2, P<0001), they were suffering more from symptoms and had a worse quality of life (P<0.001 versus Europe). Sensation of swelling was the most reported symptom in LA, while in Asia it was cramps. It seems through this analysis that the behavior towards CVD was different depending on the continent considered. Men in Asia consulted more frequently and earlier than patients (mostly women) from Europe and Latin America. Symptom perception is continent-dependent, and so is the impact of the condition on the QoL.

The validation program of the Spanish version of CIVIQ, presented by F. S. Lozano, was performed in two steps: 1) qualitative validation which assesses conceptual equivalence between the French source version and the Spanish CIVIQ. 2) psychometric

validation regarding validity, reliability, and responsiveness of the instrument.

Four hundred and seventy-six patients completed the CIVIQ. The patients' mean age was 46 years (+ 12) with 11.3% men and 87.6% women. Distribution of patients into the CEAP clinical classes was as follows: 2.3% in CoS, 25.9% in C1, 43.6% in C2, 19.8% in C3, and 8.4% in C4. The 4-dimension structure of the CIVIQ was retrieved in the Spanish version, with a restriction for the social dimension. This is most probably due to cultural bias. The cross-sectional validity was ensued. The Spanish CIVIQ has demonstrated its capacity to discriminate among the different severity groups of illness at baseline (Spearman's correlation coefficients >0.30). So was the clinical longitudinal validity, with good correlations between variation in the CIVIQ scores and clinical score changes across a 6-month treatment with an oral micronized phlebotropic drug (MPFF*, Laboratoires Servier, France). Reproducibility was excellent, with all intraclass correlation coefficients >0.70, and so was responsiveness with mean changes for all dimensions statistically significant in clinically improved patients (P<0.000 for all the CIVIQ dimensions).

The CIVIQ can be used independently in Spain for assessment of treatment outcomes in chronic venous disorders or for measurement of the impact on QoL of the condition. Psychometric properties of the Spanish CIVIQ have met the cross-cultural validation criteria. As for the four other languages validated the same way (English for Singapore and India, German for Austria, Polish, and Portuguese) the Spanish CIVIQ might be used either as a global index or a multidimensional profile.

J. J. Guex demonstrated that the generic SF-12 is a useful tool for the assessment of QoL changes in patients with CVD, while the CVD-specific instrument CIVIQ seems to be more responsive to the physical repercussions of the disease. Comprehensive assessment of QoL should include both generic and disease-specific measures using fully validated tools. Translation and cultural adaptation of QoL questionnaires into different languages and countries must follow internationally established criteria.

On the other hand, the management of chronic venous disorders with phlebotropic drugs should greatly improve the QoL of patients, particularly at the early stages of the disease.

In a multivariate analysis performed to assess the impact of demographic data, reflux, signs, and symptoms on the quality of life of patients with chronic venous disorders, M. Perrin showed that age, female gender, BMI, ankle circumference, presence of reflux, and assignment to C3 and C4 CEAP clinical classes had a significant impact on QoL, with a variation of less than 3 GIS points on the CIVIQ. On the other hand, symptoms of chronic venous disorders, especially heaviness in the legs and pain, were found to significantly (P<0.0001) alter patients' QoL, with a decrease of 7 to 14 points on the GIS for each symptom.

In conclusion, in as much as MPFF* improves venous symptoms, as evidenced through the RELIEF study in patients C0s to C4, such prescription may be recommended to improve QoL.

According to P. L. Antignani, the relationship between symptoms, signs, and the quality of life of patients with CVD has never been analyzed in a single study. This triangular relationship remains to be better evaluated. This could be the aim of further trials using the revised CEAP classification for the description of signs, validated scales for the assessment of symptoms, and generic and specific QoL scales for the evaluation of disease impact on patients' health.

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Health-related quality of life in patients suffering from lower limb lymphedema

In the framework of the thematic session: epidemiology and socioeconomics.

P. J. FRANKS, C. J. MOFFATT, D. C. DOHERTY, A. F. WILLIAMS, P. S. MORTIMER (UK)

Health-related quality of life (QoL) has already been examined in patients suffering from arm lymphedema, but rarely in patients with lower-limb lymphedema. The aim of this study was to determine the validity and the accuracy of MOS-SF36 quality of life scale, and other scales measuring the pain (McGill short form) and the functional ability (Barthel index) in patients with lower-limb lymphedema. Patients included were 164, 70.7% of whom were female and mean age was 76.9 years. The SF 36 questionnaire appeared to be the most appropriated scale in this patient group. The SF 36 measured a deficit in all quality of life scores, especially the physical domain, the social domain, and the emotional field. The QoL was lower in females than in males, but this difference was not statistically significant. After 24 weeks of follow-up, treatment led to a significant improvement in 6 of 8 scores of the SF 36. Patients treated by bandages exhibited the greatest benefit in all different scores of the SF 36, compared with patients treated with hosiery or with patients not treated.

SF 36 appeared to be appropriate in evaluation of QOL in patient with lower-limb lymphedema, especially for testing the impact of different treatments in this population.

Ascribing leg symptoms to chronic venous disorders. The construction of a simple scoring system

In the framework of the thematic session: epidemiology and socioeconomics.

P. H. CARPENTIER, C. POULAIN, A. CORNU-THENARD, R. FABRY, F. CHLEIR, B. GUIAS, C. BETTAREL BINON, G. MISEREY (France)

The aim of this work was to develop a simple venous symptom scoring system. The scoring system has to discriminate between different etiologies of symtoms and to be applicable in clinical practice. Two groups of patients were selected from different institutional or private vascular centers. One group (n=123) had documented chronic venous disorders without any arterial, neurologic, or rheumatologic comorbidity. The second group (n=94) had arterial, rheumatologic, or neurologic diseases but no venous disorders. They filled out a 54-item questionnaire characterizing leg symptoms. Six out of 54 symptoms were associated with the highest likehood ratio of having venous disorders in the first group of patients: type of symptoms (heaviness or sensation of swollen legs); associated symptoms (itching, restless legs or phlebalgia); worsened by warmth or improved by exposure to cold environment; absence of worsening by walking; site of the symptoms (whole leg); increasing throughout the day. These 6 items were combined and analyzed on ROC curves to test their specificity and sensibility. The most efficient score was obtained by combining four items: type of symptoms; associated symtoms; worsened by warmth or improved by exposure to cold environment and absence of worsenning by walking. If the score was >3 (3 or 4 criteria/4), the specificity was 95% and the sensibility 76% for having chronic venous disorders. If the score was <1 (0 criteria/4), the specifity was 94% and the sensitivity 67% for not having chronic venous disorders. This venous symptom scoring system was subsequently validated in two new series of patients.

The 4-criteria scoring system is able to efficiently discriminate patients with chronic venous disorders. Reproducibility in real clinical conditions and applicability in other countries are therefore needed.

LECTURE

Determinants of pressure exerted by medical compression stockings

W. BLÄTTLER (Switzerland)

The force exerted by Medical Compression Stockings (MCS) was measured with the Zwick dynamometer, the pressure exerted on the leg with the Sigat instrument. Leg circumference was determined with the Perometer and local radius calculated from computer tomographic slices. Three types of stockings were tested: Sigvaris Glamour (23-32 mm Hg), Sigvaris 503 (23-32 mm Hg) and Neo Durelna (30-40 mm Hg). Twenty-eight healthy volunteers took part in various experiments, both under static and dynamic conditions. The pressure measured at the leg/MCS-interface corresponded to that determined on the dynamometer, provided it was assessed at an area where the local radius was close to that of the ideal round leg. Tissue characteristics and type of MCS had no influence. Leg circumference showed no appreciable variation with movements (average change at b=+0.08cm, b1=-0.56cm, c=0.01cm, d=+0.49cm). Consequently, only small effects on global interface pressures were observed. However, significant variations of local radii and interface pressures were found along the leg circumference, eg, at the c-site the local radius varied between 50 and 250 mm. Stockings reduced the variation of radius to 80 to 140 mm. With a Sigvaris 503 stocking on the leg the interface pressure along the circumference varied between 20 and 40 mm Hg. So, the MCS tested exerted the predefined pressures on the leg. Muscle activity was not associated with appreciable changes of leg circumference, but with significant variations of local radii. Therefore, the global interface pressures showed only minimal changes while the local pressures varied importantly. Thus, interface pressure measurements obtained at one single site only may lead to erroneous. The presented data obtained with MCS do not support the existence of a substantially different working and resting pressure.

What pressure do we need to compress leg veins?

In the framework of the Symposium of the German speaking phlebological societies of Austria,Germany and Switzerland.

B. PARTSCH.(Austria)

In nine healthy volunteers and five patients with incompetent small saphenous vein, the external pressure necessary to narrow or to occlude leg veins was investigated. The pressure necessary to narrow the veins was 30 mm Hg in the sitting position and 35 mm Hg in the standing position. Venous occlusion occured for an external pressure of 50 to 60 mm Hg in the sitting position, 75 mm Hg in the standing position and 20 to 25 mm Hg in the suppine position. Only pressures reached by short-stretch bandages while walking can intermittently compress and occlude the veins leading to a reduction in deep venous reflux and to an improvement in venous hypertension. A complete occlusion of the superficial veins after sclerotherapy or surgery may be achieved by addition of local pressure pads to the bandages.

Fascinating compression therapy

H. PARTSCH (Austria)

The effects of compression can be summarized in 4 points:

- **Immediate edema reduction**. This was demonstrated in patients with CVI but also in normal subjects by water plethysmography. This is the reason for the immediate venous pressure changes under short-stretch bandages (about 30% in 2 hours). In patients with DVT, leg circumference was mesured before and after 9 days of treatment either by bed rest, elastic stockings or Unna boot. After 9 days, the leg circumference decreased significantly in the group treated with elastic stockings or Unna boot (without any significant difference between these two systems of compression) but was not significantly reduced in the group treated by bed rest.
- **Immediate pain relief in DVT**. This can be measured by the 100-mm visual analogic scale of pain or by the Lowenberg test (difference between the pressure tolerated on the healthy side and the pressure tolerated on the DVT leg). Bandages induced better pain relief in patients with DVT than stockings.
- **Reduction of ambulatory venous hypertension**. Thigh compression as exerted with class II thigh-length compression stockings (15 mm Hg) is not able to reduce venous diameter, venous reflux, or venous hypertension. With a compression of 40 to 60 mm Hg on the thigh, exerted by short-stretch bandages, considerable hemodynamic improvement, including reduced venous reflux, can be obtained in patients with severe deep vein incompetence. Intermittent venous occlusion can be achieved when external pressure is higher than the intravenous pressure. This can be achieved by inelastic bandages, as the working pressure of inelastic bandages is superior to that obtained by elastic bandages.
- **Increase in arterial flow**. Sustained compression reduces the arterial flow and is contraindicated in patients with peripheral arterial disease. Intermittent compression, achieved by inelastic bandages, enhances arterial flow by reduction of ambulatory venous hypertension, reduction of edema, and release of vasoactive substances from endothelial cells.

Further reading:

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- Delis KT, Nicolaides AN. Effect of intermittent pneumatic compression of foot and calf on walking distance, hemodynamics, and quality of life in patients with arterial claudication: a prospective randomized controlled study with 1 year follow-up. *Ann Surg.* 2005;241:431-441.

Reporting standards for outcomes following treatment of venous C0s-C3 patients

In the framework of the Joint round table of the UIP-Société Française de Phlébologie, in cooperation with the American College of Phlebology, the American Venous Forum, and the Société Française d'Angiologie.

Chairperson: J. J. Guex (France)
Moderators: P. Gloviczki (USA), M. Schadeck (France), F. A. Allaert (France), J. P. Benigni (France)
Expert panel: M. Perrin (France), S. Zimmet (USA), B. Eklof (Sweden), F. Chleir (France)

The study and treatment of C0s-C3 patients was the subject of this interesting session. This group of patients are the most numerous in the population with chronic venous insufficiency, do not have an obvious outcome, as do those with ulcer healing, and can be treated by radically different methods that have very different goals.

J. J. Guex pointed out the necessity of new evaluation criteria that should take into account first, the primary reason for the patient's visit (pain, esthetical reasons) which would be the "main patient criterion" and second, the patient reported outcomes (PROs) after treatment because, as he said, if the patient is not satisfied after treatment, this is equivalent to failure.

M. Perrin summarized the venous severity scores (VSS) with their three different parts: Venous clinical severity score (VCSS), Venous disability score (VDS), and Venous segmental disease score (VSDS). After a revision of these he stated that the VSS is an outstanding tool for assessing the outcomes of treatment for the higher classes of CEAP classification. However, for C0s-C3 another tool should be developed.

The Quality of life (QoL) aspect was discussed by F. Chleir, recommending the integration of QoL analysis into clinical trials on CVD and into our everyday practice in order to evaluate treatment outcomes. There was agreement between the panel that the actual QoL test could not be ideal for this group of patients. They pointed out that the ideal QoL survey should be practical, sensitive to changes, especially to clinically important ones, and to the patient's assessment of the significance of these changes.

Finally, S. Zimmet and J. J. Guex presented a new venous survey that claims to be easy to use, a research-and office-based tool, and evaluated for validity, reliability, and responsiveness. This new venous survey is a self-evaluation test for the patient that includes preoperatively: main concern, rate of leg discomfort, rate of the appearance of the legs, limitation of activities due to the venous problem, moment of clinical severity, comparison to 1 year earlier, emotional problems caused by the veins, sensation of health risk related to the veins. Postoperatively the patient has to perform a new evaluation that includes several of the previous points and a self evaluation of the treatment. Finally there is a part for physician evaluation. This new survey will be included in the Société Française de Phlébologie Website to try to collect new proposals to improve it before its official validation and presentation.

Joint symposium UIP/Argentinean Society of Phlebology

Chairpersons: O. Andoniades (Argentina), N. Rosli (Argentina)
Secretary: J. Fernandez (Argentina)
Speakers: A. Schapira (Argentina), J. Fernandez (Argentina), E. Tkach (Argentina), A. Avramovic (Argentina), V. Spano (Argentina), J. Ciucci (Argentina), D. Lesnik (Argentina)

This panel of experts from the Argentinean Society of Phlebology presented their experience in different aspects of modern phlebology. Prof Schapira presented his saphenous preservation technique in varicose vein surgery, pointing out the necessity of preoperative mapping.

A different way to perform foam sclerotherapy was presented by Dr Tkach, with his turbulence sclerotherapy technique, which consists in introducing and extracting the foam mixed with blood repeatidly. This way, as he says, foam can contact a major vein surface and therefore be more effective.

Sclerotherapy in the treatment of venous ulcers was thoroughly presented by Dr Avramovic, who emphasized the importance of a complete clinical checkup in order to eliminate other possible causes of leg ulcers.

Finally, Prof Ciucci presented the algorithm for lymphedema treatment practiced in his centre, which includes a multidisciplinary approach with the collaboration of endocrinology, dermatology, psychology, and physiotherapy. He remarked on the necessity of pharmacologic treatment of lymphedema, including eradication of pain.

VI

MISCELLANEOUS

Results of the UIP consensus conferences in the last 4 years

Chairpersons: C. Allegra (Italy), H. Partsch (Austria)
With the participation of:
A. Caggiati (Italy), venous anatomy
P. Coleridge-Smith (UK), duplex anatomy
B. Eklof (Sweden), refinement of the CEAP classification
H. Partsch (Austria), evidence-based compression therapy
P. Coleridge-Smith (UK), new consensus on venous hemodynamics
C. Allegra (Italy), UIP Phlebological Schools

This panel of experts has presented the consensus guidelines on terminology achieved by the venous societies in order to create a common language when dealing with venous disease.

Venous anatomy was presented by Prof Caggiati (*J Vasc Surg.* 2005;41:719-724) while Prof Coleridge-Smith defined the duplex anatomy (in press in *Eur J Vasc Endovasc Surg*). The revision of the CEAP classification, including a refinement of the C classes and an introduction of an "advanced" and a "basic" CEAP version, was presented by Prof Eklof (*J Vasc Surg.* 2004;40:1248-1252).

Prof Partsch presented the evidence that compression therapy has an important role when dealing with venous disease.

Prof Coleridge-Smith presented the outlines of new consensus on venous hemodynamics currently in preparation.

Phlebology

In the framework of the Joint Symposium UIP/Brazilian Society of Phlebology and Lymphology.

Chairpersons: J. B. Thomaz , A. Scuderi, F. Miranda Jr (Brazil)

This was a didactic session about current practice in Brazil.

Celso Figuerôa gave a complete review of anatomy and physiology of pelvic varices, and their possible role in the recurrence of varicose veins in the lower limbs. He also mentioned the great difficulty of diagnosis and the importance of clinical suspicion.

João Júlio Dittmar presented his personal experience in the surgical management of varicose veins in the lower limbs, and emphasized the need for cosmetic care and immediate compression: crossectomy, GSV and/or SSV stripping, ligation of perforators, and phlebectomies, all with minimal incisions.

Anacleto Carvalho provided a review of ulceration: incidence in relation to ambulatory venous pressure, types of venous insufficiency with ulceration (superficial, deep, and perforator systems), venous hypertension, and microcirculation changes. There are many frequently used technical surgical procedures, but his personal experience is with cutaneous and venous disconnection techniques (ulcer surgical resection with ligation of the feeding varicose veins, granulation, and finally cutaneous grafting). He also discussed the more frequent relapse causes; lymphagitis, infections, and treatment abandonment.

Solange Gomes gave a review of history, definition of sclerosing agents and sclerosing power, mechanism of action and classification of chemical, physical, and combined agents with advantages and disadvantages.

Finally, José Calasso focused his presentation on the more frequent sclerotherapy complications and possible forms of their treatment: pigmentation, cutaneous necrosis, temporary edema, pain, and thrombophlebitis.

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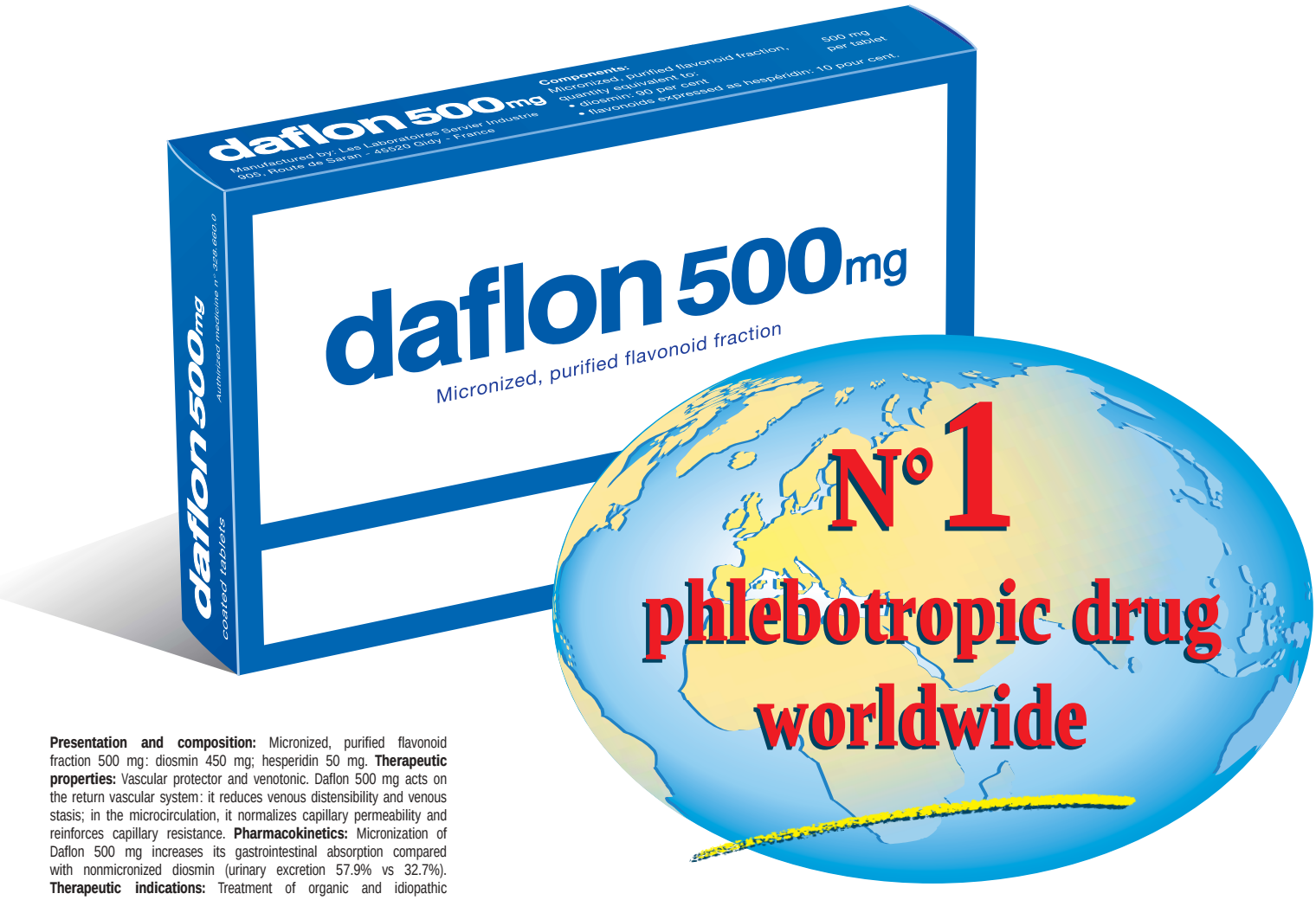
daflon® 500mg

Micronized purified flavonoid fraction

A micronized form and a comprehensive mode of action for better clinical efficacy



Presentation and composition: Micronized, purified flavonoid fraction 500 mg: diosmin 450 mg; hesperidin 50 mg. **Therapeutic properties:** Vascular protector and venotonic. Daflon 500 mg acts on the return vascular system: it reduces venous distensibility and venous stasis; in the microcirculation, it normalizes capillary permeability and reinforces capillary resistance. **Pharmacokinetics:** Micronization of Daflon 500 mg increases its gastrointestinal absorption compared with nonmicronized diosmin (urinary excretion 57.9% vs 32.7%). **Therapeutic indications:** Treatment of organic and idiopathic chronic venous insufficiency of the lower limbs with the following symptoms: heavy legs; pain; nocturnal cramps. Treatment of hemorrhoids and acute hemorrhoidal attacks. **Side effects:** Some cases of minor gastrointestinal and autonomic disorders have been reported, but these never required cessation of treatment. **Drug interactions:** None. **Precautions:** *Pregnancy:* experimental studies in animals have not demonstrated any teratogenic effects, and no harmful effects have been reported in man to date. *Lactation:* in the absence of data concerning the diffusion into breast milk, breast-feeding is not recommended during treatment. **Contraindications:** None. **Dosage and administration:** *In venous disease:* 2 tablets daily. *In acute hemorrhoidal attacks:* the dosage can be increased to up to 6 tablets daily. *As prescribing information may vary from country to country, please refer to the complete data sheet supplied in your country.*

Chronic venous insufficiency

2 tablets daily

Hemorrhoidal disease

up to 6 tablets daily

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