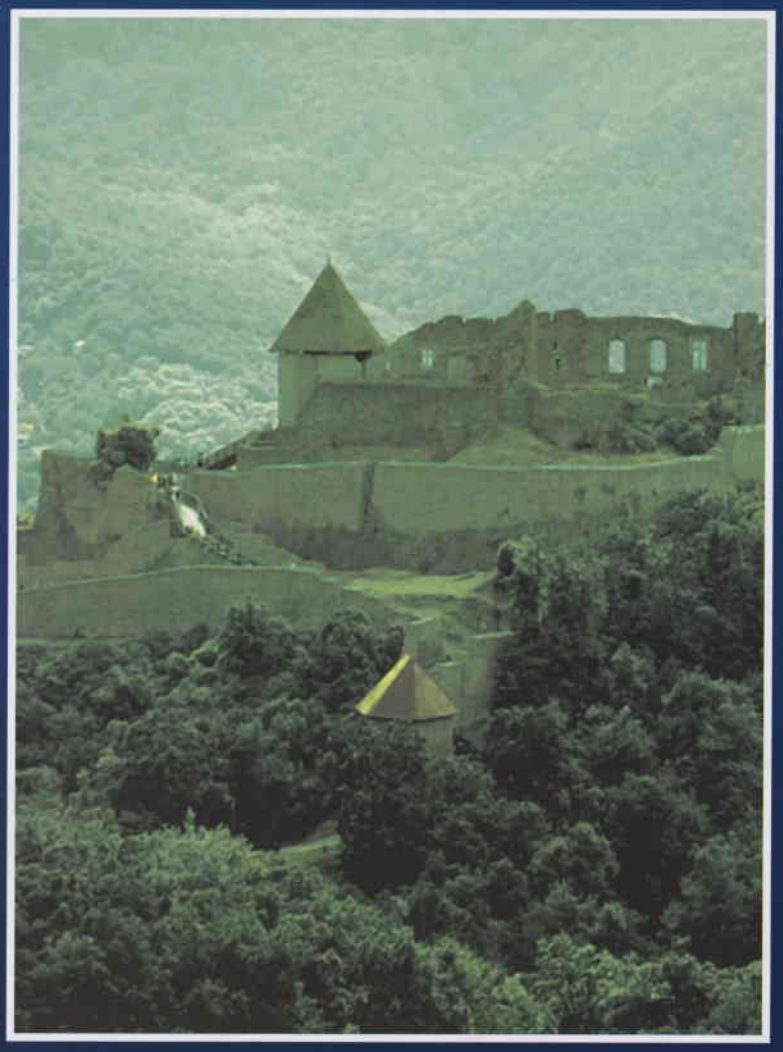
The Hungarian Journal of

VASCULAR DISEASES

2006/suppl/1

1st Central European CVI conference



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VRT304/SEP06

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3. M. MARSHALL, D. LOEW, AND C. SCHWAHN-SCHREIBER: Hydroxyethylrutosides (oxerutins) in the treatment of CVI stage I an II (CEAP 3 and 4)

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Érbetegségek
The Hungarian Journal of Vascular Diseases

Scientific Journal of the Hungarian Society for Angiology and Vascular Surgery and of the Cardiovascular and Interventional Radiological Society of Hungary

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Foreword

The Journal of the Hungarian Society for Angiology and Vascular Surgery, together with the sponsorship of Novartis Consumer Health Ltd., have launched a new series of scientific meetings, the Central European Chronic Venous Insufficiency Conferences. This is the first occasion that Czech, Polish, Slovak and Hungarian colleagues have gathered to inform each other about the magnitude of this problem in their countries, the solution possibilities available to them and their plans for the future. As we all know, there are well-known experts is all of these countries and we are near geographically so we can learn a lot from each other. We have a great deal of experience and these possibilities for sharing information have not been used until now as well as they should be.

Certainly there are very many patients in each country, but we do not know exactly how many and how serious their illness is. It is not known what therapeutic possibilities are stressed in one country and which ones in another. We need to inform each other about new developments and enhance our joint experience. We all hope this conference serves to shape a closer relationship and better information exchange. This information can result in better therapeutic modalities and results, which of course is the ultimate aim of this meeting.

I would like to remind you that in 1335 there was a conference at the invitation of King Robert Karoly of Anjou with the participation of two further kings, John of Luxemburg from Bohemia and Kazmer the Great from Poland here at Visegrad. That discussion lasted for three weeks and was succesfull. We are not kings and this conference did not last as long, but it will be held severals times and we all hope that it will be fruitful and rewarding for every participant.

This conference relies on the participation of 160 of the most acknowledged specialists and scientists of the region, who have dedicated themselves to CVI patient cure. Our objective is to get therapeutic methods and people closer as well.

Visegrad, 19 May 2006

Imre Bihari M. D.
Editor

Chronic venous insufficiency: global importance and strategy

PROF. VLADIMIR SEFRANEK M. D., PhD.

The present report focuses on the chronic venous disorders of the leg (CVDL). This term is used to encompass the following clinical presentations or their combinations: venous symptoms and signs, oedema, teleangiectasias, reticular veins, skin changes and venous ulcer (1).

CVDL is one of the most prevalent medical conditions. It has been estimated to occur in 10% to 40% of adults. Several types and clinical presentations of varying severity have been included in these figures. In medical literature and terminology we can also find other terms used for defining this condition: chronic venous insufficiency (CVI) and chronic venous disorders (CVD). Chronic venous insufficiency of the lower limb is a poorly defined term and means a different set of symptoms and signs to different clinicians. To some it means all venous disorders that are not acute venous thromboses, occlusions and injuries. To others it implies venous disease causing symptoms in the leg, including swelling (venous oedema) and the skin changes of lipodermatosclerosis and ulceration (3).

Currently we can define chronic venous insufficiency as deteriorated venous blood drainage due to organic and functional damage of the venous system of the legs leading to venous stasis and hypertension.

The main causes of chronic venous insufficiency are (2, 15):

– obstruction of isolated segments or more diffuse regions of the deep venous system of the legs (approximately 20% of CVI cases),

– reflux (approximately 80% of cases) in several parts of the venous system of the legs caused by structural and/or functional damage of the venous wall and valves. These changes may occur in superficial veins, the deep venous system, or perforating veins; damage to these separate components of the venous system of the leg may be isolated or occur in two or all three components respectively.

From the aetiological point of view we can differentiate three types of CVI (15):

– Congenital (congenital venous malformations e.g. Klippel-Trénaunay disease).

– Primary CVI (natural history of the disease may lead to numerous forms and varying degrees of severity of CVI).

– Secondary CVI (after injury, deep venous thrombosis, external compressions by tumours, entrapment etc.).

Chronic venous disorders of the leg (CVDL) encompass the following clinical presentations:

– Venous symptoms (heavy or restless legs, night cramps, venous claudication etc.).

– Clinical signs (oedema, skin changes – lipodermatosclerosis, atrophy, ulcers).

Obstruction of the deep venous system of the leg may be in rare cases of congenital origin. We can find hypoplasia and aplasia of some segments of the deep venous system worsening the venous outflow from the leg. In the vast majority of cases the obstruction is acquired due to deep venous thrombosis. It is necessary to add that obstruction in these cases is nearly always combined with reflux. Structural and

functional damage of the venous wall and valves may be caused by congenital hypoplasia or aplasia, or acquired (primary or secondary) due to essential chronic venous disease or deep venous thrombosis, in rare cases also because of superficial venous thrombosis.

Venous hypertension and stasis is the main pathophysiologic cause of changes leading to clinical symptoms and signs of CVI: cyanosis, oedema, hyperpigmentation, skin and subcutaneous tissue induration, lipodermatosclerosis, 'atrophie blanche', corona phlebectasia, cutaneous ulcers etc. Valvular insufficiency may hinder normal venous pump function that is the main mechanism of venous drainage of the lower extremities.

Venous hypertension and stasis activate a cascade of changes involving endothelial cells, microcirculation and extracellular tissue. It has been demonstrated that in capillaries there arises the accumulation of leucocytes, their adhesion and their deposition into the tissue. Also erytrocyte aggregation and subsequent partial obstruction and loss of capillaries may lead to severe damage of the microcirculation in CVI. The release of inflammatory mediators, enzymes, cytokinins and superoxide radicals are also compounds of these processes. Deposition of leucocytes (macrophages and T-lymphocytes) into the tissue leads to lipodermatosclerosis. It is also known that an increase of growth factors (VEGF) leads to neovascularization in lipodermatosclerosis. There is also an antioxidative defence system failure at a cellular and tissue level causing venous wall destruction. Worsening of the situation may be caused also by a negative influence on the hemostasis and activation of intravascular coagulation. Ambulatory venous hypertension caused by both deep venous or superficial venous reflux on the macrovascular level leads to microangiopathy on the microvascular level. Tissue necrosis with skin and subcutaneous tissue ulcerations arise due to the activation of leucocytes sequestered in the cutaneous microcirculation. The effect of bioflavonoids is based on the decrease of the level of endothelial activation. The capillatroscopic view of these changes is very instructive. In the moderate grade of changes we can see the microoedema around capillaries that are dilated and tortuous. In more severe changes we can see the occlusion of capillaries by formed cells (sequestered leucocytes and aggregated erythrocytes). The nutrition of the cutaneous and subcutaneous tissue is at a very low level ('atrophie blanche') ending with tissue necrosis and a venous ulcer formation.

Varicose veins are a very important component of the complex clinical picture of CVI. They may arise as a part of a congenital venous malformation (e.g. Klippel-Trénaunay disease), or they are acquired and arise primarily or secondarily. Primary varicose veins are due to an essential venous wall weakening and its gradual and progressive dilatation in limited segments of the superficial venous system leading to the organic and functional disorder of venous valves and venous blood reflux. The final step in the pathogenesis is the venous hypertension development leading to dilatation or further parts and segments of superficial leg veins. Secondary varicose veins may develop due to existing deep venous hypertension (hypoplasia or aplasia of the deep venous valves and/or perforating veins or their destruction after deep venous thrombosis).

Classification of chronic venous insufficiency has been developing since the 1970s. The first clinically applicable classification was introduced in 1978 by Widmer in Switzerland on the basis of the Basle III Study. The author of the next relatively popular classification was Porter in 1988. A modern classification of venous disorders, CEAP Classification, was introduced in 1995 by the American Venous Forum in Hawaii. Widmer's Classification is practical, more widespread in German-speaking countries and in central Europe. This classification strictly differentiates between 'uncomplicated' varicose veins and more severe types of the disease. Clinical conditions can be divided into three grades (I-III). Varicose veins according to *Widmer's Classification* are also divided into three groups (teleangiectasias, reticular veins, and trunk varicosities). *Porter's Classification* divides the clinical conditions of CVI into four clinical classes: 0 asymptomatic, 1 mild CVI, 2 moderate CVI and 3 severe CVI. *CEAP Classification* is considered the most appropriate classification for modern clinical use. The scoring system of this classification avoids the difficulty of confusing morphological and functional terms. However, it will probably need certain modifications to improve its practicality and usefulness (2). CEAP Classification uses four categories: C (clinical signs – class 0-6), E (aethiology – Ec congenital, Ep primary, Es secondary), A (anatomic distribution – As superficial veins, Ad deep veins, Ap perforating veins), and P (pathophysiologic dysfunction – Pr reflux and Po occlusion).

The epidemiology of chronic venous insufficiency has been very well studied during the last decades. The prevalence of varicose veins in adults in Western populations is 25% to 33% in females and 10% to 20% in men. The incidence is higher in women than in men but may be constant at different ages. The risk of acquiring varicose veins in women increases with the number of pregnancies and obesity. The evidence in men is not so strong. Genetic predisposition and lifestyle (westernization) are well-known risk factors but the epidemiological evidence is lacking. The frequency of venous skin changes in population increases with age and is more common in women. The prevalence of open ulcers is 0.3%. The female to men ratio is 2-3:1. The risk of ulcers is associated with varicose veins and deep venous thrombosis as well (2).

The diagnostics of chronic venous insufficiency have changed recently thanks to the great progress in ultrasound modalities. Diagnostic procedures are performed for several purposes – to determine the venous origin of symptoms and

GSV reflux & anatomy
Diameter of the GSV
Distance of the GSV from the skin
SSV reflux & anatomy of the SPJ
Perforator incompetence / location
Patency of the deep venous system
Evidence of prior deep venous thrombosis
Deep venous reflux

Table I. Diagnostics of CVI. Features evaluated on duplex ultrasound scanning. GSV: greater saphenous vein. SSV: shorter saphenous vein. SPJ: sapheno-popliteal junction.

Parameter	Arterial	Venous	Neuropathic
Location	Foot	Ankle	Pedal planta MT-phalang. joints
Pain	Intensive	Moderate	None
Ulcer bottom	Fibrinous exsudate, necroses	Fibrinous exsudate, granulations	Granulations, callous
Other changes	Trophic changes of skin (A)	Trophic changes of skin (V)	Hypestesia
Pulses	Weak or none	Normal	Usually normal

Table II. Different diagnostics for leg ulcers.

signs and in case an analysis of venous morphology and function is necessary. These evaluations provide information on which the decision-making about the treatment modalities may be based. Venous disorders may affect venous emptying in two ways: reflux or obstruction. Diagnostic procedures available at the present time are as follows: history, physical examination and clinical tests (e.g. Trendelenburg), measuring of the extremity, several methods of ultrasound (CW Doppler, duplex ultrasound scanning and colour-coded duplex scanning [CCDUS]), plethysmography and its modifications (PPG, LRR etc.), and venography (ascending or descending). CW Doppler investigation in venous disease has recently started to be considered out of date. Duplex ultrasound scanning is, on the other hand, considered to be the gold standard for evaluating venous disease. All three anatomic components (superficial, deep and perforating veins) can be assessed. In the majority of patients this is the only diagnostic investigation necessary! Plethysmography also has not been considered so important for the accurate diagnostics of venous disorders in recent years. It can be useful when both reflux and obstruction are identified by duplex US in order to identify the predominant pathophysiologic component. Venography has been used very rarely in the last few years because of the influence of duplex ultrasound scanning. This modality is necessary when complex reconstruction procedures (surgical or endovascular) are planned: patients with severe obstruction or incompetence of the deep venous system (16). Features evaluated on duplex US scanning are shown in **table I**. In deciding the correct treatment it is necessary to have the possibility to distinguish clearly among several leg ulcers (see **table II.**).

Principles of treatment of chronic venous insufficiency

Conservative treatment is satisfactory in the vast majority of cases (compression, exercise, lifestyle, venous drugs). In more severe cases of the disease it is necessary to consider more radical possibilities of treatment (surgery, endovascular treatment). The first task in the treatment is reflux and venous hypertension elimination. It is necessary to eliminate the reflux in all three departments of the leg venous system (superficial, deep and perforating veins). In haemodynamically significant symptomatic varicose veins it is necessary to indicate surgery of varicose and perforating veins. Less frequently there can be a necessity to perform reconstructive surgery of the deep venous system in cases of severe valve incompetence. We can perform valve correction, transplantation or transposition. In cases of significant deep venous system obstruction due to extensive deep venous thrombosis there is a possibility to solve the problem of venous outflow using bypass techniques. Local treatment of venous ulcerations and skin changes is also a very important component of the complex management of CVI.

Conservative treatment is an essential and basic part of all treatment modalities and it is necessary to apply the main principles of this treatment also in cases treated surgically or endovascularly. The main components of conservative treatment are medication treatment (venoactive drugs, antibiotics, topical treatment of ulcers and skin changes), compression treatment and sclerotherapy. Details of these methods of treatment will be presented in further papers of the symposium.

Correction of superficial reflux is a further principle. (The old axiom that all important venous reflux is in the deep system is no longer tenable). Surgery of varicose veins and incompetent perforating veins is composed of the ligation and stripping of the greater saphenous vein (GSV), crossectomy, ligation of the short saphenous vein (SSV) if necessary and surgical mini-stab avulsion of varicose veins. Surgical stripping of the GSV has been substituted by minimally invasive endovascular ablation methods (radiofrequency or laser techniques). Incompetent perforating veins must be ligated to thereby improve the skin and subcutaneous tissue perfusion. Classic *Linton* or *Cockett* operations

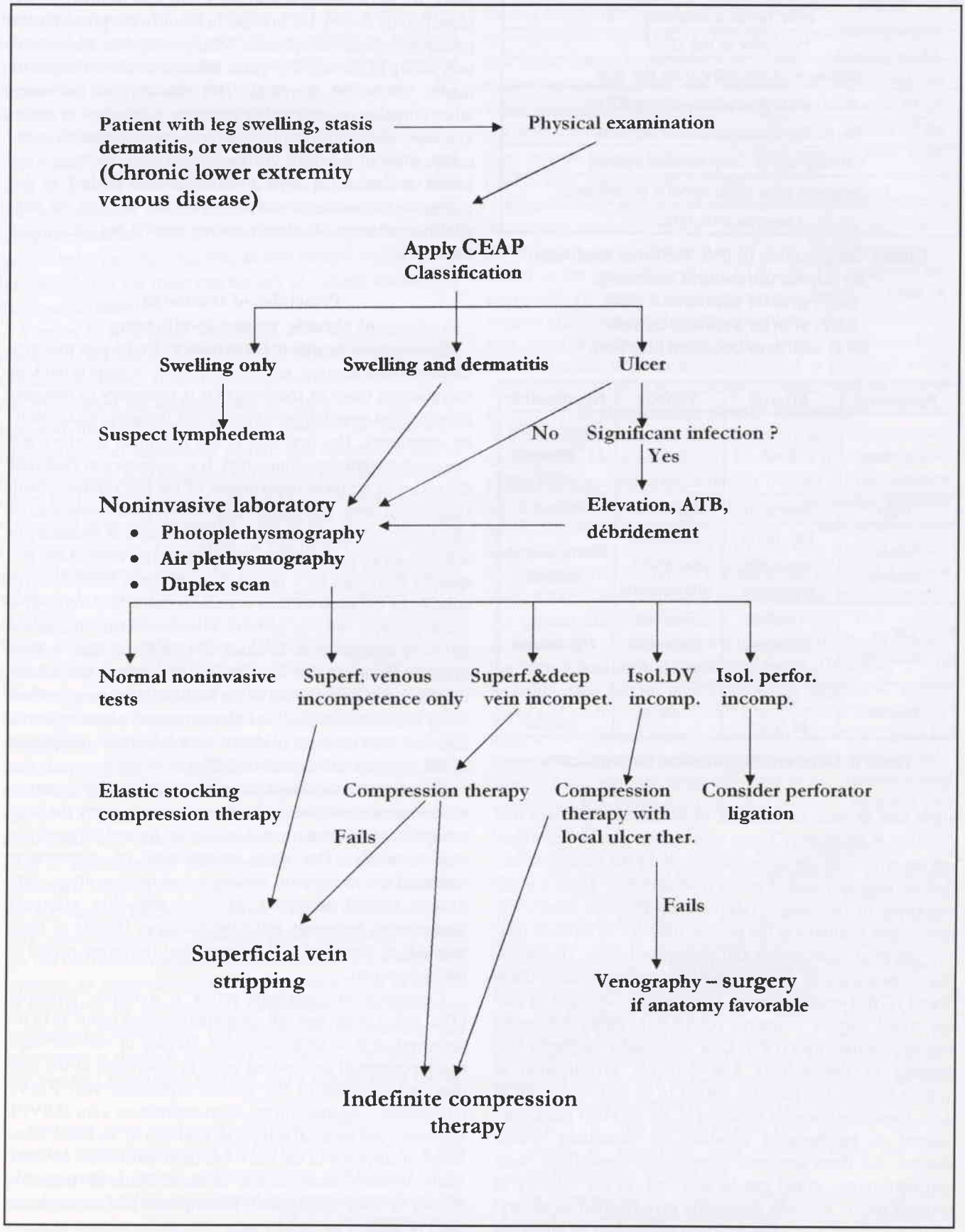

Figure 1. CVI – Evaluation and conservative management.

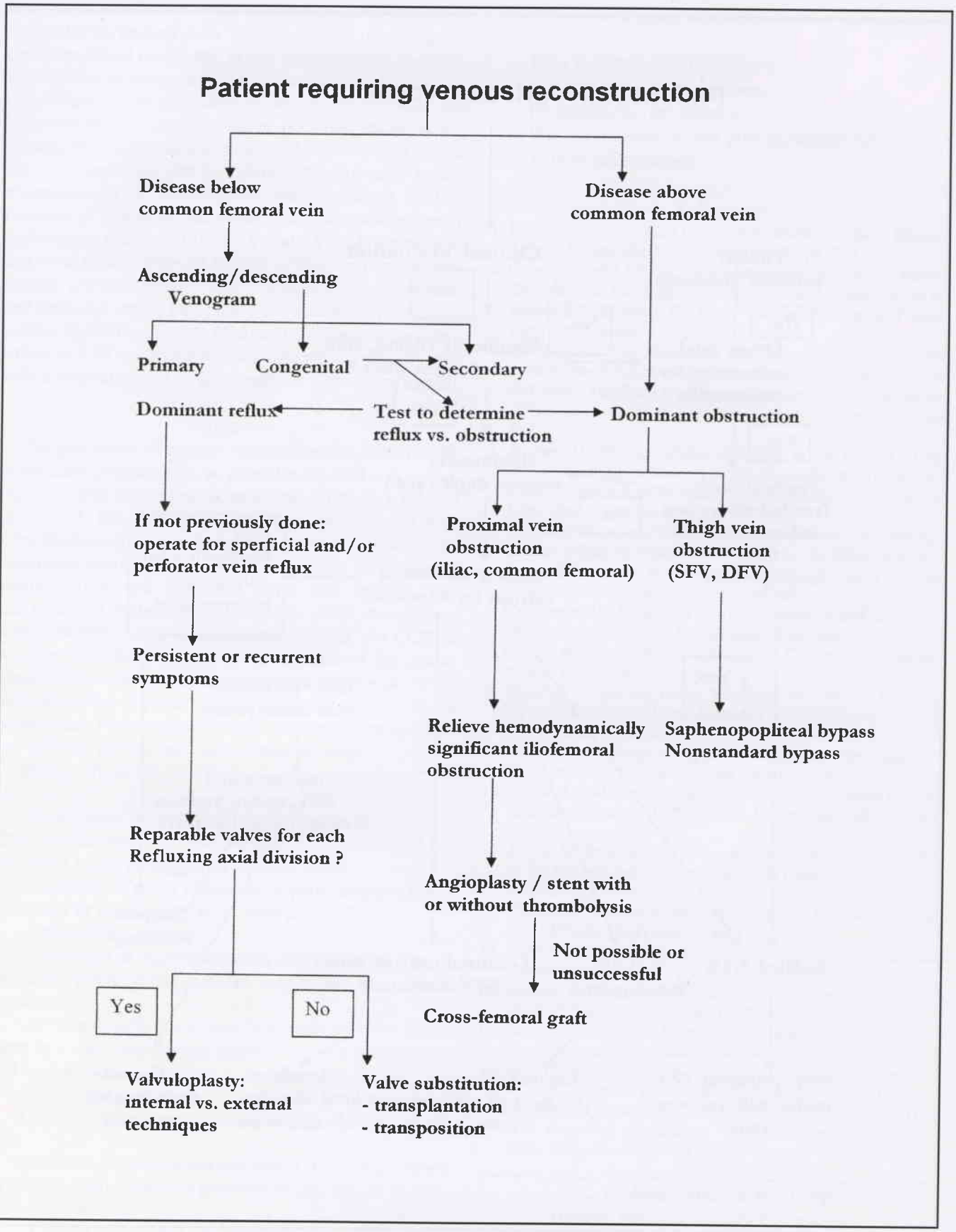

Figure 2. CVI – Surgical treatment.

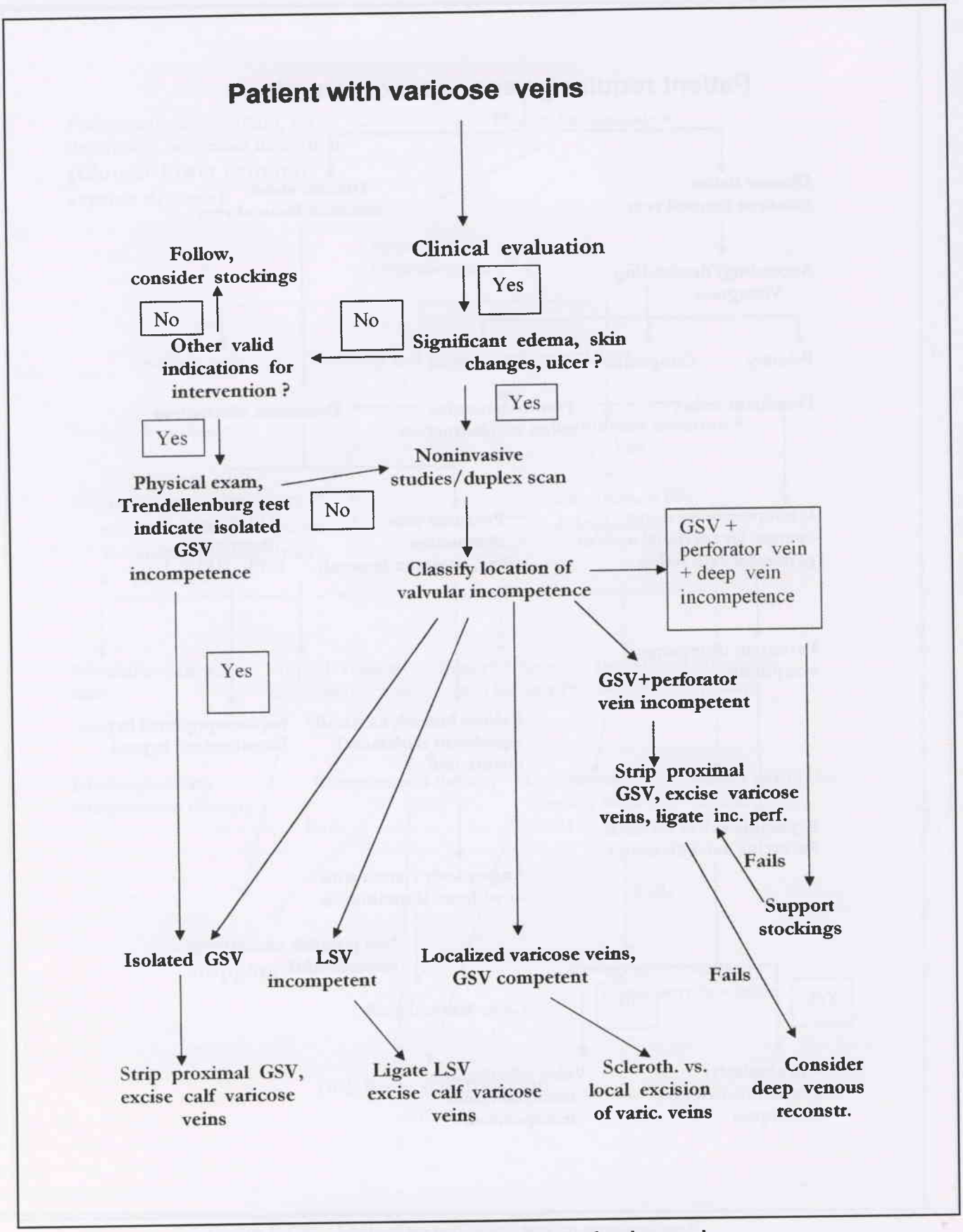

Figure 3. Algorithm of the management of varicose veins.

seem to be obsolete. A newer minimal invasive method of subfascial perforating vein ligation (SEPS) offers significantly improved results (8). In less frequent cases of refractory oedema or ulcers caused by severe deep venous obliteration there is the possibility to reduce venous stasis and hypertension and improve tissue perfusion using bypass techniques. Similar situations caused by severe deep venous valve incompetence can be influenced using valve repair, transplantation or transposition. Other adjuvant modern methods of treatment encompass laser and radiofrequency endovenous ablation of the GSV and SSV, ultrasound-guided foam sclerotherapy of truncal varicosities ('endosclerotherapy'), physiotherapy – exercise to mobilize the articular and muscular venous pumps, use of mechanical (pneumatic) pumps, hydrotherapy etc. **Figures 1-3.** illustrate the algorithms of CVI management using diagnostic evaluation and both conservative and surgical methods of treatment as well.

Summary

The prevalence of chronic venous disorders (10% to 40% of the adult population) is so great that the total cost including the actual cost of healthcare + time off work + reduced quality of life represents a heavy social burden. CEAP Classification of venous disorders helps to define individual conditions more exactly, avoids difficulties of confusing morphological and functional terms and enables optimal treatment method decision-making. Out of several diagnostic modalities duplex ultrasound scanning and CCDUS are now considered to be the gold standard for evaluating venous disease. All three anatomic components of the ven-ous system (superficial, deep and perforating veins) can be assessed. Plethysmography and venography are considered obsolete and are used only in special cases.

What is IN in the treatment of venous disorders of the leg:

– Assessment of quality of life (it was the symptoms of CVI, not the varicose veins themselves, that affected the quality of life in patients with varicose veins).

– Day-case surgery / minimally invasive surgery (radiofrequency or laser energy GSV ablation, SEPS).

– Compression therapy.

– Correction of superficial reflux (the old axiom that all important venous reflux is in the deep system is no longer tenable).

– Getting surgery of varicose veins right first time (treatment by a specialist vascular surgeon, not by a non-supervised trainee!)

– Ultrasound guidance + IV foam sclerosans injections.

What is OUT in the treatment of venous disorders of the leg:

– Nihilism of patients and physicians (GPs) in questions of varicose vein treatment possibilities (recidivism of varicose veins etc.)

– Clinical assessment of varicose veins alone; venography.

– Extensive stripping of the below-knee segment of the GSV.

– High ligation of the GSV alone.

– Linton and Cockett operations.

– Hyperbaric oxygen therapy.

– Waiting for ulcer to heal prior to intervention.

– Truncal sclerotherapy.

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RA GYÓGYSZERKÉSZÍTMÉNY MEGNEVEZÉSE: Venoruton Forte 500 mg tabletta MINŐSÉGI ÉS MENNYISÉGI ÖSSZETÉTEL: 500 mg O-â-hidroxietil-rutozid (oxerutin) tablettánként. GYÓGYSZERFORMA: Tabletta: zöldes-sárga színű, pettyes, korong alakú, domború felületű, egyik oldalán mélynyomású Zyma logo, másik oldalán "CV" jelzéssel ellátott tabletta. Törési felülete zöldes-sárga színű. KLINIKAI JELLEMZŐK: Terápiás javallatok: A krónikus vénás elégtelenség következtében kialakuló, (gyakran jelentős) visszér tágulat, valamint együtt jelentkező vénás keringési zavar, vénás eredetű trophikus bőrelváltozások, lábszárfekély kezelésére. A kísérő oedema csökkentésére. A vénás elégtelenség során fellépő tünetek [pl. fáradt, nehéz lábak, görcsök, paraesthesia, és "nyugtalan" lábak (restless leg)] enyhítésére. A krónikus vénás elégtelenség kezelése során alkalmazott rugalmas kötés hatásának javítása. Aranyér tüneteinek megszüntetése. Diabeteses retinopathia. Adagolás és alkalmazás: Krónikus vénás elégtelenség: Kezdő adag: naponta 2 x 1 tabletta. A fenntartó kezelés: naponta 1 x1 tabletta tabletta. Aranyér-betegség: megegyezik a krónikus vénás elégtelenség és komplikációi kezelésére javasolt adagokkal. Diabeteses retinopathia: 1800-3000 mg oxerutin naponta. Kiadhatóság: II/1 csoport Orvosi rendelvényre kiadható gyógyszerkészítmények (V). Ellenjavalatok: Ismert túlérzékenység a termék bármely összetevőjére. A terhesség első trimesztere (ld. 4.6. pont). Szív, vese- illetve májbetegség következtében kialakuló alsó végtagi oedema kezelésére nem javasolt. Gyógyszerkölcsönhatások és egyéb interakciók: gyógyszerkölcsönhatást nem jelentettek. Terhesség és szoptatás: a terhesség első három hónapjában történő alkalmazását kerülni kell. A készítmény hatásai a gépjárművezetéshez és gépek üzemeltetéséhez szükséges képességekre: nincs arra utaló adat, hogy a készítmény befolyásolná a gépjárművezetést, vagy a gépek kezelését. Nem kívánatos hatások, mellékhatások: Ezek főként gasztrointesztinális zavarok (flatulencia, hasmenés, gyomor fájdalom, gyomorrontás), fejfájás, szédülés, fáradékonyság, bőrviszketés, hőhullám és pruritus voltak, melyek gyorsan megszűnnek a kezelés abbahagyásakor. Túladagolás: tünetekkel járó túladagolást nem jelentettek.GYÓGYSZERÉSZETI JELLEMZŐK: Segédanyagok: makrogol 6000, magnézium-sztearát. Inkompatibilitás: nem ismeretes.Felhasználhatósági időtartam: 5 év. Különleges tárolási előírások: legfeljebb 30°C-on. Nedvességtől védve tartandó. Csomagolás típusa és kiszerelése: 30db, 60 db tabletta PVC/Al blisztерben és fáltkartonban. Megjegyzés: (egy kereszt) A FORGALOMBA HOZATALI ENGEDÉLY JOGOSULTJA: Novartis Hungária Kft., Consumer Health, Budapest. A FORGALOMBA HOZATALI ENGEDÉLY SZÁMA: OGYI-T 5299/01/02, Alkalmazási előírás OGYI-eng. száma: 15.624/55/2003 Bruttó fogyasztói ár: 2130 Ft, TB támogatás 0 Ft, beteg által fizetendő 2130 Ft. Az árak 2006.október 01-től a következő árváltoztatásig érvényesek. Kérjük olvassa el a részletesebb alkalmazási előírást is!

VRT301/SEP06

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Chronic venous insufficiency care in Hungary

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In Hungary an epidemiological study was performed in 2000 (1) as a thorough investigation into the prevalence of chronic venous insufficiency, including the distribution of the various types of varices and chronic venous insufficiency and the major factors contributing to their development.

Definition of varicosity

The subjects of this survey were varices, which are, according to the most widely-accepted definition: dilated, elongated, tortuous segments of the superficial venous system with incompetent valves that allow retrograde flow (5, 7). All visible veins under the skin were considered in our study, including spider veins and dilated but asymptomatic vessels as well (8). Further signs of chronic venous insufficiency were also investigated (12, 13). In other studies, spider veins or teleangiectasias and smaller reticular veins (C1) are often excluded (4, 5).

Method

General practitioners were invited to participate in the data collection for this epidemiological survey conducted in practices located in Budapest and the vicinity. Recruited investigators completed a training course before receiving the survey forms. Patients presenting complaints unrelated to venous diseases or pathological conditions of the lower extremity were eligible.

The surveyed population

The survey was conducted on 566 individuals aged 14 to 92 years. The age-distribution of the study was dominated by the 50-60 year-old age group, whereas the number of individuals younger than 30 or older than 80 years of age was small. The mean age of the study population was 49.6 years; the male-to-female ratio was 216 to 350. It is important to note that *two thirds of other studies collected data from fewer than 800 subjects* and only one third of them made larger-scale epidemiological investigations (4, 8, 12). For this reason our study and the smaller ones only give a tentative result for the nation as a whole.

The prevalence of chronic venous disease

The prevalence of chronic venous disease was rather high, 57.1 (323/566) in this population. Prevalence data from foreign countries are scattered over a wide range according to ethnicity and geographical location from 2.1 to 90.4% (12, 13). In recently published large-scale studies higher prevalences were found than in former ones: the *Bonn Venen Study* reported 90.4% which is exceptionally high in the literature (12). Similar high prevalence 77.3% was found in *Italy* as well (collecting data from all regions of the country) (6). A *multicentre French study* excluded spider veins (C1) which account for the highest number of cases, and therefore their results were much lower: in women 50.5%, in men 30.1% (4). The *Brazilian* study defined varicosity in the same way, and their mean result was 47.6% (11).

In Hungary, a large-scale survey was reported by *Bonyhádi et al.* in 1974 (2). This survey was conducted in Budapest; the screening of 3005 adult citizens yielded a 38 per cent prevalence of varicosity. The potential causes of this relatively large difference (compared to the 57.1 per cent

Age	<20	21-30	31-40	41-50	51-60	61-70	71-80
Prevalence	12.5	4.7	44.1	68.4	69.8	69.2	82.1

Table I. Prevalence of varicosity according to age groups.

prevalence found in our study) are abundant and include a dissimilar definition of varicosity, among others. Unfortunately, neither of their two publications (2, 3) contain any definition of the condition regarded as 'varicose'. Furthermore, *Bonyhádi et al.* surveyed only the 30-60 year-old age group and in other words, disregarded populations of a higher or lower than average risk of developing varicosity. In our survey, the prevalence of varicosity was 62.1 per cent in the 30-60 year-old age group. The difference between the 38 per cent prevalence found in 1974, and the recently ascertained mean of 57.1% is thought to reflect the unfavourable influence of changes in living conditions, lifestyle, occupational health, and physical activity levels. Therefore it is important to bear in mind the possibility of a real increase in the prevalence of varicosity among the inhabitants of Budapest.

Age

Stratifying the study population into age groups reveals the definite influence of age on occurrence. While the prevalence of varicosity is as low as 12.5 per cent in young people under 20 years of age, it is as high as 82.1 per cent in the elderly population (71-80 year-olds). **(Table I.)**

Body weight

The mean body weight was 66.7 kg for females and 79.0 kg for males. The proportion of overweight individuals was 28.1 per cent. This group was characterized by a higher (76.7 per cent) prevalence of varicosity. Body weight increases with age and it is therefore possible that the influence of excess weight is only an indirect reflection of the impact of aging. Reversing this dilemma yields the opposite question: is the role of weight gain only secondary? According to our results, advancing age and weight gain are independent risk factors in terms of developing varicosity. On the one hand, the influence of excess weight is evident in the 51-60 year-old age group: the prevalence of varicosity in normal and overweight individuals was 59.7 vs. 73.7 per cent ($p<0.01$). On the other hand, the age-related increase in prevalence is apparent in the subgroup with normal body weight.

Physical activity

The distribution of the study population by level of physical activity was as follows: 26.2 per cent pursued a sedentary occupation, 30.7 per cent were blue-collar workers, and 2.8 per cent were engaged in physically demanding sports. Jobs involving a lot of standing are associated with a higher incidence of varicosity for obvious reasons. This is in agreement with the 64.9 per cent prevalence of varicosity found in individuals employed in such jobs, compared to the 54.3 per cent prevalence associated with sedentary work. Lower extremity varicosity was ascertained in 76.1 per cent of blue-collar workers.

	Parity				
Number of births	0	1	2	3	>3
Prevalence	40.3	66.1	71.9	91.9	75.0

Table II. Prevalence of varicosity according to number of parities.

Pregnancy and hormonal influence

Two hundred and two of the 350 female participants had children. Nulliparity was associated with a 40.3 per cent prevalence of varicosity, which afflicted 73.7% of parous women. Therefore, childbirth is an evident risk factor in lower extremity varicosity ($p<0.005$). **(Table II.)** As suggested by the similar prevalence of varicosity among males and nulliparous women, female gender itself does not seem to increase the propensity for this form of venous disease. Childbirth, however, is a significant risk factor. At the same time, however, it is pregnancy – and not delivery – that facilitates the development of varicosity. Literature data are less conclusive as regards the unfavourable impact of pregnancy and the indifference of gender (10). Naturally, these findings may reflect the cumulative effect of several factors (e.g. civilised lifestyle and pregnancy); however, our results clearly demonstrate the contributory role of pregnancy in the pathogenesis of varicosity.

Females are exposed to *further hormonal influences,* including oral contraceptives (OC) and postmenopausal hormone replacement therapy (HRT). In this survey, 43.1 per cent of females (151/350) were regular OC users; 90 of these 151 women had varicosity and 61 did not. In the subgroup of nulliparous women, OC use was not associated with a higher risk of varicosity (the prevalence of which was 31.6% in nulliparous OC users and 51.7% in non-users; N. S.). Thus our data do not confirm the contributory role of hormonal contraception, but on the contrary, suggest a preventive effect. The *Edinburgh veins study* led to the same conclusion (9).

Twenty-five females were receiving HRT. No association could be found between hormone replacement and varicosity, as the prevalence of the latter was almost identical among women receiving / not receiving HRT (64.0 vs. 64.3%).

As	No.	%	Type of vein
1	182	57	Teleangiectasia, reticular vein
2	28	8.5	Greater saphenous vein
3	18	5.6	Lesser saphenous vein
4	71	22	Side branch varicosity
Ap	24	7.4	Perforator insufficiency

Table III. CEAP classification of varicosity. Distribution of anatomical findings of the survey.

Types of varicosity

The prevalence of individual types of varicosity was also explored. In many cases different types of varicosities were found, when the more severe ones were taken into consideration. **Table III.** summarises the dominant forms of lower extremity varicosity. These proportions are similar to ones in other studies (6, 12).

As in Hungary there is no other epidemiological study and as our results show very similar data to many other surveys we have extrapolated the percentage for the whole Hungarian population to better understand the significance of this disease. Importantly, more than the half the cases are comprised of patients with 'spider' veins or reticular varicosity, usually treated by sclerotherapy and not surgery. In the famous *Edinburgh Vein Study* where 867 women and 699 men were examined the prevalence of spider and reticular veins was over 80% of participants. Therefore they regard this type of varicosity 'the norm' in their population (8). The prevalence of truncal varicosity is also remarkably high and justifies surgery in approximately 10 per cent of the adult Hungarian population – this corresponds to many hundreds of thousands of people.

If we sum up exactly the percentage of the greater and lesser saphenous, half the side branch and half the perforator insufficiency varicosities, they make up about 15%, more than one sixth of adult population. In Hungary there are about 8 million adults, half of whom have varicosity which means 4 million people. Finally about 1-1.5 million could be *operated on* for varicose veins. Every year only 15 000 varicectomies are performed is state hospitals and about the same amount in private clinics. It seems there is a lot more work to be done.

Teleangiectasias and reticular veins and about half the side branch and perforator varicosities, are suitable for *sclerotherapy*. This means more than one third of the adult population. In other words about 2-3 million adults are possible subjects for sclerotherapy in Hungary. We do not have any relevant data about the number of sclerotherapy interventions, but according to our survey performed in 2000 the number of sclerotherapy treatments is under 50 000 a year. According to the severity of chronic venous insufficiency the following results were found (**Table IV.**).

C	No.	%	Types
c0	238	42.8	No clinical sign
c1	176	31.1	Spider veins, reticular varices
c2	57	10.1	Common varicose vein (GSV, LSV)
c3	40	7.1	Edema
c4	39	6.9	Pigmentation, dermato-sclerosis, eczema
c5	10	1.8	Scar of healed ulcer
c6	6	1.0	Open crural ulcer

Table IV. Clinical findings of the survey according to CEAP classification.

Advanced chronic venous insufficiency

These are C4-C5 and the most severe is C6. If the percentages are summed up they make 9.7%, roughly one tenth of the adult population. This means less than 800 000 people. They should probably be operated on to improve their condition or their avoid complications.

There is an important data about the severe chronic venous insufficiency cases. A little more than half the chronic venous insufficiency people (5.1%) had deep venous thrombosis and a little less than half of them (4.6%) did not. This means that almost half the severe chronic venous insufficiencies *could be prevented* by a simple varicectomy.

Open crural ulcer was found in 1% of the adult population, which is similar to the results of other studies where incidence was between 1.0 and 1.5% (5, 13). In the Bonn Vein Study it was reported that in the last decades with active health care the former similar results were decreased to 0.7% (C5-6) (12).

In Hungary to cure or help patients with varicosity and chronic venous insufficiency almost every method which is known in the wider world is used: operations not only with hook but with laser and other instruments, sclerotherapy including foam sclerotherapy, compression treatment with sophisticated dressings in ulcer cases and different medicines and ointments as well. In our opinion the level of service is quite high throughout the country but the amount of treatments are not as many as would be necessary.

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Chronic venous insufficiency in Slovakia

PROF. MÁRIA FRANKOVICOVA M. D., PhD.

Introduction

Even the Ebers papyrus dating from 1550 B. C. (Wondrák, 1959) mentions dilated veins. Hippocrates (460-377 B. C.) utilized compression bandages and recommended the perforation of varicose veins. Roman consul Gaius Marius was operated on for varices. The operation was performed without anaesthesia. As the surgeon was about to operate on the other extremity, Marius refused it, because the pain was greater than the benefit of the operation Plutarch 50-120, A. D. (Bergan, 1992.). Aristoteles, Claudius Galen, Trendelenburg, Madelung, Babcock, Linton, Cockett etc. described, operated on and sclerotized varicose veins.

In Slovakia the issue of CVI is the subject of various professional events. Within the framework of the Slovak Medical Society, several specialist societies can be found: the Slovak Angiologic Society, the Slovak Society of Vascular Surgery, the Slovak Dermatological Society – Section of Phlebology and Wound Healing, the Slovak Society of Radiology – Section of Vascular Interventional Radiology.

Slovak specialists working today in the treatment of CVI

1. *Angiologists:* prof. Viera Štvrtinová M. D., PhD., Ewald Ambrózy M. D., PhD., Július Kmec M. D., PhD., Andrej Dzupina, M. D., PhD.

2. *Vascular surgeons:* prof. Vladimir Šefránek M. D., PhD., prof. Július Mazúch M. D., DrSc., prof. Július Vajó M. D., PhD., prof. Mária Frankovicova M. D., PhD., František Arendárcik M. D., Peter Labaš M. D., PhD.

3. *Dermatologists:* Tibor Danilla M. D., PhD., Darina Jarcušková M. D., PhD., Jagienka Jautová, M. D., PhD.

4. *Radiologists:* Pavol Lesny M. D., Ivan Vulev M. D., Katarína Kriegerová M. D., PhD.

When evaluating and analysing chronic venous insufficiency thoroughly, it is advisable to consider it from the point of view of the professional, the point of view of the patient and that of the manager-strategist.

The professional point of view has been divided into that of the angiologist, vascular surgeon, dermatologist and radiologist.

1. CVI from the angiologist's point of view (prof. Viera Štvrtinová M. D., PhD.)

In 2004 the International Epidemiologic survey 'Triangle' was carried out in Slovakia, and focused on a better understanding of the triangular relationship between subjective symptoms, objective signs and the quality of life of patients with CVI. The survey was supported professionally by the Slovak Angiologic Society of the Slovak Medical Society. The survey was aimed not only at diagnosing patients with CVI among general practitioners, but also at analysing the prevalence of individual clinical stages of CVI.

Ninety-nine general practitioners from Slovakia were involved in the 'Triangle' survey and 3134 patients were examined. Adult patients with subjective symptoms or objective signs of CVI were included. The observation lasted 20 days. The patients were classified using CEAP classification.

Based on the epidemiologic survey in Slovakia, it was found that:

a/ the most frequent CVI symptoms of the subjects were varicose veins (54%) and swollen legs,

	Men		Women		Total
	Absolute number	%	Absolute number	%	Sum. of absolute numbers
Ischemic disease of lower limb	362	7.0	60	1.26	428
Other arterial diseases	210	4.1	120	2.34	330
Venous insufficiency	*603*	*11.76*	*971*	*18.94*	*1574*
Other venous diseases	982	19.16	1272	24.81	2254
Other diseases	235	4.58	305	5.96	540
Total	*2392*	*46.6*	*2734*	*53.30*	*5126*

Table I.

	Men		Women		Total
	Absolute number	%	Absolute number	%	Absolute number
Venous insufficiency in the group	*603*	*11.7*	*971*	*18.9*	*1574*
Grade I	90	14.9	200	20.5	290
Grade II	381	63.1	485	49.9	866
Grade III	132	21.9	286	29.4	418
Total	*603*		*971*		*1574*

Table II.

b/ 77% of the subjects complained of heaviness or pain in the legs,

c/ swollen legs occasionally in the evening, every evening or even morning were claimed by 69% of the subjects,

d/ 56% of the subjects felt inhibited about revealing their legs due to CVI.

Angiological patients
(Július Kmec, M. D., PhD., 2004, Košice)

We present the profile from the Košice region examined by J. Kmec M. D., PhD., who was the president of the Slovak Angiologic Society for many years. **Table I.** shows that women comprised two thirds of the 5126 patients with venous insufficiency.

Angiological patients
(Július Kmec, M. D., PhD., 2004, Košice)

In the group of 5126 patients, 1574 were patients with chronic venous insufficiency. According to the degree of venous insufficiency verified objectively by digital photoplethysmography, Grade II of chronic venous insufficiency prevails both in men and women.

This finding is important especially from the prognostic point of view, because insufficient medical or surgical treatment causes progression of the disease to Grade III with serious clinical consequences and significant impairment of the patient's quality of life. **(Table II.)**

2. Chronic venous insufficiency: from the vascular surgeon's point of view

In Slovakia radical treatment of CVI is the subject of the following fields: general surgery, vascular surgery.

The Slovak Society of Vascular Surgery, whose president is prof. Šefránek M. D., DrSc., organizes the annual Slovak Congress of Vascular Surgery, where special attention is paid to the treatment of CVI. The vascular surgery register of Slovakia shows that in 2004 there were 3856 operations performed on the venous system, with 3801 operations for varicose veins, 22 venous thrombectomies, 29 patients with endoscopic ligation of perforating veins, and the correction of the deep venous system was performed four times. The Slovakia has over 5 million inhabitants and there are three specialized institutions for vascular surgery with 78 beds (318 beds are needed).

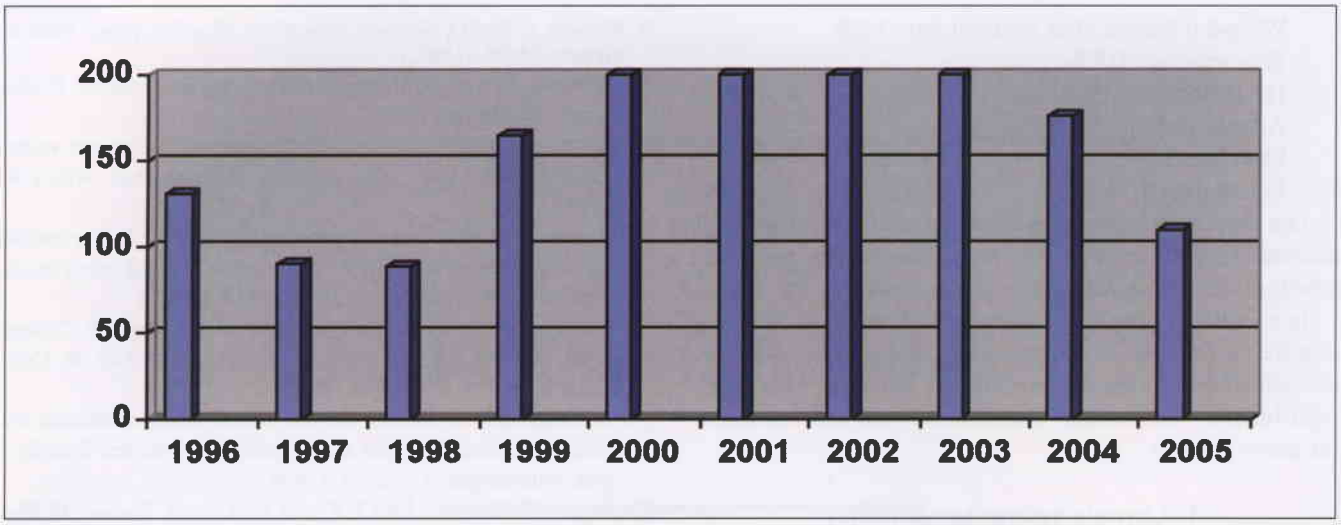

Figure 1.

Vascular surgery in the Slovakia at present:

– National Cardiovascular Institute in Bratislava – Department of Vascular Surgery,

– Department of Vascular Surgery – Cyril and Metod Hospital, Petrzalka, Bratislava,

– East Slovak Cardiovascular Institute in Košice – Department of Vascular Surgery.

CVI operations are also performed in departments of general surgery

– Vascular Surgery Unit, Prešov,
– Division of Vascular Surgery, Liptovsky Mikulaš,
– Vascular Surgery Unit, Banska Bystrica,
– Division of Surgery, Lucenec,
– Department of Surgery, Zilina,
– Division of Vascular Surgery, Nitra.

The table shows the aforementioned departments according to the number of CVI operations.

As vascular surgeon I would like to present the results of operations for CVI in the Department of Vascular Surgery of the East Slovak Cardiovascular Institute.

Recently published studies from our department on the radical treatment of varicose veins include topics such as:

1. surgical complications of operations for lower limb varicose veins,

2. limb threatening complications of varicose vein surgery.

Department of vascular surgery VÚCH, a. s. Košice 1st Surgical Clinic of P. J. Šafarik University Košice

Surgery on the venous system 1996-2005 is summarised in **figure 1.** From 1996 to 2005 1675 patients were treated surgically.

Preoperative examinations required in our institute:

Internal preoperative examination, haemocoagulation examination, gynaecological examination in women, duplex or colour ultrasonography / patients are examined by an angiologist or radiologist.

Accurate preoperative mapping is part of the surgeon's preparation for the best therapeutic results.

Patients who visited our department have been divided into 3 groups:

Group I – patients with intradermal teleangiectases and subdermal reticular veins (C1),

Group II – marked varices combined with marked reticular and intradermal varices combined with insufficient perforators (C2-C3),

Group III – large trunk and collateral varices combined with skin changes (C4-C6).

Radical treatment depends on the exact location of varices, their size, place of reflux and insufficient perforators. The following procedures or a combination of them were indicated:

– Classical surgical treatment: 840.
– ELVES: 150.
– Sclerotherapy: 355.
– Sclerolaser: 87.
– Vasculight: 15.

Surgical treatment:

– Crossectomy: 92%.
– Total stripping of v. s. magna: 66%.
– Limited stripping of v. s. magna: 34%.
– Ligation of perforators: 40%.
– Extirpation of collateral varices: 68%.

Complications after surgery:

– Paresteses: 4.7%.
– Residual varices: 8.0%.
– Lymphorrhea: 1.4%.
– Headache: 1.6%.

– Wound infection after crossectomy: 1.2%.
– Skin necrosis: 0.9%.
– Haematomas: 15.0%.
– Allergy to Heparin: 0.1%.
– Phlebitis: 2.0%.
– Skin burns: 2.7%.

Our current treatment is a combination of radical surgery, sclerotherapy, laser therapy, and conservative measures, which involve drug and compression therapy.

In conclusion, as a vascular surgeon I would like to mention the fact that in our Department three serious iatrogenic complications of varicose vein surgery from other health establishments were treated: one femoral vein and two femoral artery injuries.

3. Chronic venous insufficiency from the patient's point of view

a/ Patients face subjective difficulties and often social problems as well.

b/ What do Slovak patients expect?

– Rapid relief,
– prevention of the progression of the disease,
– stable efficiency in the long-term administration of medication.

Patients do not want to have swollen legs, spasms and to feel functional discomfort.

Conclusion

In conclusion, the epidemiologic study in Slovakia has confirmed the high incidence of chronic venous diseases.

Treatment should be started early and it should be complex

a/ radical procedures – surgical methods and sclerotherapy,

b/ conservative methods, compression stockings and treatment with venoactive drugs.

In should be emphasized that care of CVI patients requires both time and multidisciplinary professional cooperation.

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CVI care in the Czech Republic

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The Czech Republic belongs to those European countries where management of patients with vascular disorders started to interest doctors relatively early. Prof. Bohumil Prusik (1886-1964) is considered to be the founder of Czech angiology. He started his vascular studies before the 2nd World War and as early as 1928 he performed the first angiography in Prague.

Physicians interested in angiology were formerly organised together with cardiologists in the Czech Society of Cardiology. Starting in 1994 the Czech Society of Angiology was created and at present it consists of about 400 members.

While vascular surgery was recognised in the Czech Republic more than 20 years ago, vascular medicine-angiology was established only recently (in 2004) as one of the independent branches of internal medicine, parallel to cardiology, nephrology, gastroenterology etc. Up to now more than 40 physicians have finished their postgraduate educat-ion and have obtained their diplomas in angiology. Accord-ing to the conception of angiology we expect to have in the first line one physician specialised in angiology for 50,000-100,000 inhabitants. Furthermore, at the second level, specialised vascular centres with complex multidisciplinary care will be created – one for 500,000-1 million inhabitants.

Is it known from the National Health Information System that the cardiovascular group of diseases is the most threatening for the Czech population. It is associated with the highest morbidity and the most frequent hospitalisation. Cardiovascular diseases are the cause of more than half of all deaths in the country.

Bobek, 1961 (Klatovy)	11%
Weddell, 1966 (Cardiff)	11%
Hackel, 1971 (Wurzen)	18%
Coon, 1973 (Tecumseh)	11%
Beaglehole, 1975 (New Zealand)	15%
Fischer, 1978 (Tubingen)	15%
Winkler, 1980 (Dippoldiswalde)	14%
Evans, 1999 (Edinburgh)	36%

Table I. The frequency of varicose veins in epidemiological studies.

The importance of chronic venous insufficiency is not related to the high mortality but to the high number of people with the disease and the socio-economic impact of its manifestations. The frequency of varicose veins found in different studies varies widely (**table I.**). One of the first epidemiological studies in European countries which focused on varicose veins was performed in the district of Klatovy in the Czech Republic and published in 1961 by prof. Bobek from Pilsner University (1).

The socio-economic impact of chronic venous diseases is evident for example from data about working incapacity. The highest numbers of lost working days due to cardiovascular diseases in the Czech Republic are not caused by myocardial infarction or other heart diseases but by chronic venous disorders – varicose veins, venous ulcers etc. These represented about 50% of all cardiovascular cases in 2003 (**table II.**).

	n (cases)	Days (mean)
Arterial diseases	134	53
Venous diseases	1034	27
Myocardial infarction	117	143
Chronic ischaemic heart disease	553	63
Cardiovascular diseases (total)	2235	60

Table II. Lost working days in selected groups of patients with cardiovascular diseases per 100, 000 inhabitants. (Czech Health Statistics Yearbook, 2003.)

	Before HR	During HR infusion
N (measurements)	120	160
Capillary filtration coefficient	0.007 + 0.004	0.005 + 0.003

Table III. Effect of hydroxyethylrutisodes on capillary filtration in the legs of patients with chronic venous insufficiency.

The development of varicose veins is associated with venous hypertension, failure of valves in the veins and inherited weakness of vein walls, which is perhaps the most important factor in their pathophysiology. The weakness of vein walls allows progressive venous dilation even at normal venous pressures, followed by valve failure as a secondary event. One of the first studies confirming the different structure of varicose veins was performed by physicians from the Institute of Clinical Experimental Medicine in Prague and published by Svejcar et al. in 1963 (3). Varicose veins as well as normal veins from patients with varicose veins were shown to have had a decrease in collagen and an increase in muscle cells and hexosamines, compared to normal veins.

Venoactive drugs in the management of patients with chronic venous insufficiency were introduced in the 1960s and there were certain controversies with regard to the effectiveness of these substances. The declared action of these drugs – based on experimental findings – may be summarised into the following items:

1. the decreasing of venous distensibility,
2. the decreasing of capillary permeability,
3. the protection of endothelial cells.

With respect to clinical conditions, hydroxyethylrutisodes were one of the first venoactive drugs to have a documented effect on capillary permeability (4).

Using venous occlusion plethysmography, capillary filtration in the lower limbs of patients with chronic venous insufficiency followed after a single administration of this

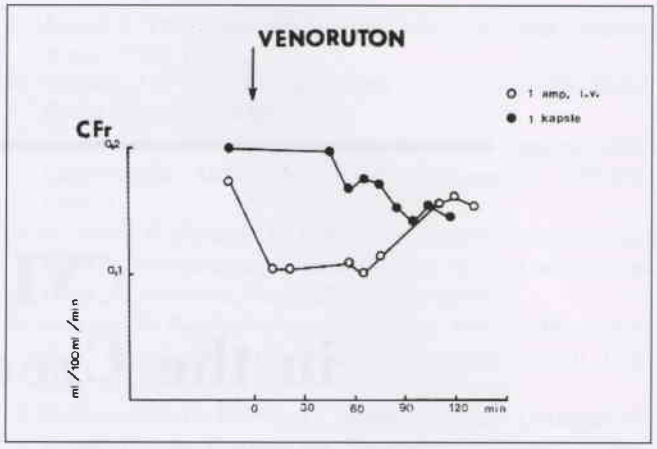

Figure 1. Mean capillary filtration rate after 500 mg i.v. and 300 mg oral hydroxyethylrutisodes.

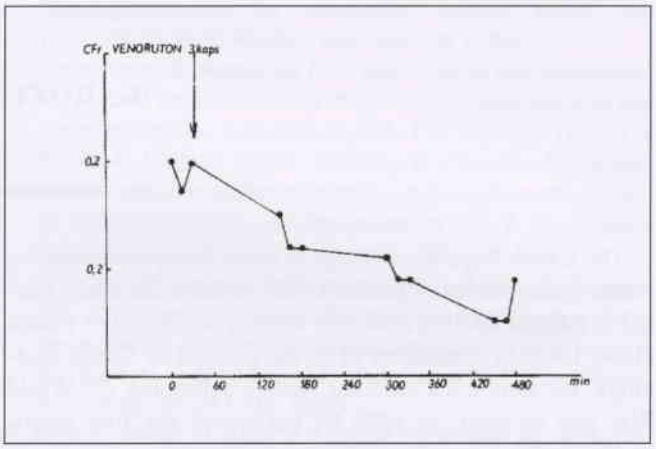

Figure 2. Dynamics of decreased capillary filtration rate during 8 hour follow-up after oral administration of HR (900 mg).

compound. As **table III.** shows the mean value of capillary filtration of fluid in the legs of patients with chronic venous insufficiency was significantly reduced after the administration of an infusion with hydroxyethylrutisodes.

The decreased capillary filtration rate after hydroxyethylrutisodes can be interpreted as the influence on capillary permeability. Observations of the dynamics of changes after oral and intravenous administration revealed certain differences (**figure 1., figure 2.**). Intravenous administration produced an almost immediate decrease in capillary filtration to a level that remained stable until about 120 min after injection. After oral administration, the decrease appeared later and continued throughout the entire period of measurement (5).

Conclusions:

1. Chronic venous insufficiency represents a severe socio-economic problem in the Czech Republic.

2. Chronic venous insufficiency has been shown to be the most frequent cause of working incapacity among patients with cardiovascular diseases.

3. Three examples of previous Czech contributions to our knowledge of chronic venous diseases were presented.

4. Current therapeutic approaches provide multiple possibilities in how to influence the development of chronic venous diseases. Pharmacotherapy focuses on substances which have evidence of effectiveness in these cases.

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VRT302/SEP06

1- G.B. Agus, C. Allegra, G. Arpaia, G. Botta et al.: Guidelines for the diagnosis and treatment of Chronic Venous Insufficiency, International Angiology, 2001. vol. 20.suppl. 2 to No.2.

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3- M. MARSHALL, D. LOEW, AND C. SCHWAHN-SCHREIBER: Hydroxyethylrutosides (oxerutins) in the treatment of CVI stage I an II (CEAP 3 and 4)

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CEAP & CVI care: Diagnosis and patient pathway optimalisation

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Introduction

Chronic Venous Insufficiency (CVI) is a frequent disease with various forms of etiology. The signs and symptoms are different and the treatment also depends on the origin and stage of the disease. Because of these complications the classification is also difficult; however nowadays we have one that is accepted worldwide. Proper understanding of the pathophysiology, knowledge of the diagnostic tools and the treatment options could help us to decrease the occurrence of this endemic disease.

Background

Chronic Venous Insufficiency is a progressive disease classified by CEAP. One of the major determinants of CVI is venous reflux caused by insufficient venous valves of either the superficial, the deep veins or the perforator system.

If we would like to analyse the incidence of the pathophysiological origin of CVI we can find that 81% is reflux, 2% is occlusion and 17% is a combination of both. However the risk of signs and symptoms can increase by 3.5 times in the latter case. Thus it is unquestionable that the clarification of reflux is essential.

Tests for CVI

There are simple and expensive tools available for the diagnosis of CVI such as percussion – Schwartz-test, Valsalva maneuver with ultrasound, CW Doppler, duplex sonography, photo-air-strain gauge plethysmography, simple or MR venography, ambulatory venous pressure measurement (AVP), intravascular ultrasound (IVUS).

Figure 1. Percussion test.

– Percussion test: easy to use, no device is necessary. Useful, but just a screening test for the superficial venous system in clinical practice (**figure 1**).

– Valsalva maneuver. The sudden increase of intraabdominal pressure can cause reflux especially in the proximal vein, that we can measure either with CW Doppler or duplex sonography. The lack of a standardised way of producing intraabdominal pressure, and the difference in reflux in the horizontal position give certain limitations to this method.

– The manual squeeze test with Doppler (or duplex sonography) control can identify reflux segmentally (**figure 2**). A more standardised method is when pneumatic cuffs

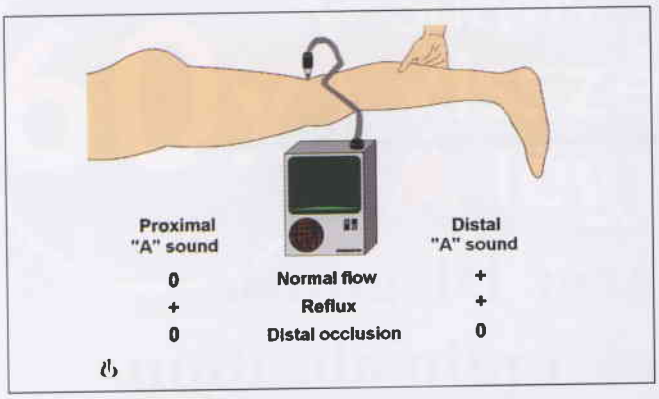

Figure 2. Manual squeeze (calf and thigh) test with CW Doppler testing "A"ugmentation sound of popliteal vein.

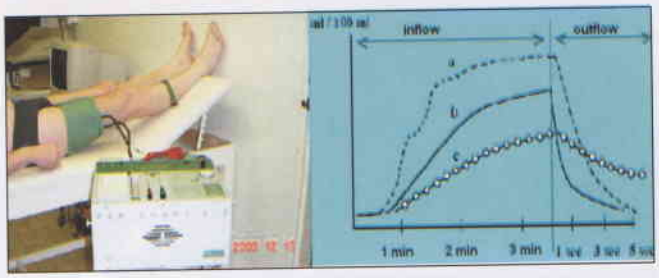

Figure 4. Strain gauge plethysmography can measure the blood volume change of the leg. Compression on thigh level can block only venous return to the heart. Curve "a" varicosity. Inflow is more. Outflow is normal. Curve "b" inflow and outflow are normal. Curve "c" iliac thrombosis. Inflow is lower than the normal volume. Outflow is slower.

are used to empty veins below the transducer. Nowadays this is considered the best way in clinical practice. These tests can measure reflux in individual veins.

It is also possible to measure the 'total leg' reflux:

– The most useful measurement of air plethysmography is the venous filling index (VFI).

– Photo plethysmography (PPG) can measure the venous reflux time which is shorter in the case of reflux (**figure 3**). It is very useful for testing superficial vein insufficiency. Unfortunately using a tourniquet to block superficial venous reflux cannot give accurate enough data about deep venous insufficiency.

– Strain gauge plethysmography (**figure 4**), venography or MR venography are useful for the control of pelvic outflow or obstruction.

As the time of reflux cannot be enough to determine the degree of CVI, some calculate other values also (e.g. reflux time, venous filling index, volume of reflux, total limb reflux volume).

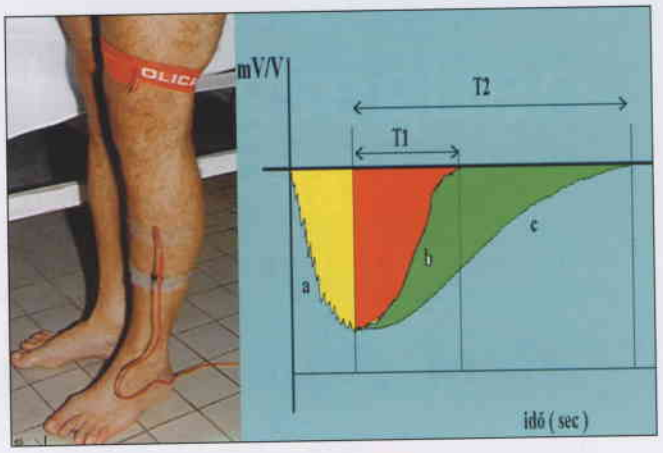

Figure 3. Photo plethysmography. Refilling time (RT) normal value is < 20 sec. The "a" curve is the emply phase of the leg veins, "b" and "c" curves are the fast or normal refilling periods of the veins. RT is faster in case of reflux.

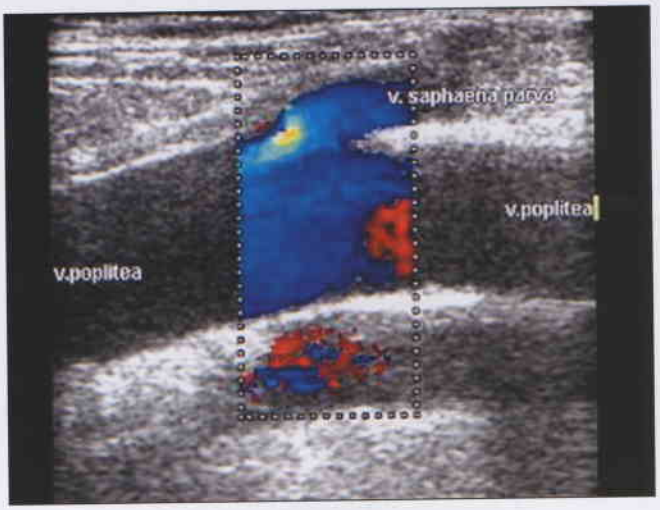

Figure 5. Colour duplex sonography of the sapheno-popliteal junction.

– The most popular tool is duplex sonography, which is capable of showing the anatomical situations (size and diameter of the vessel, location of the occlusion, the condition of the veins and valves) (**figure 5**) and capable of measuring the malfunction (e.g. reflux) of the venous system (**figure 6**).

Unfortunately there is no standardised method for testing patients for CVI with ultrasound devices in Hungary.

Currently we suggest a form using an US Vascular Lab. This form seems useful for evaluating the venous system of the lower extremity in CVI using the compressibility, the augmentation, the phasicity of the venous flow, and the results of the Valsalva maneuver. (**Table I., II.**)

Unfortunately none of these tests can give a perfect correlation to the severity of CVI alone, and performing all the above-mentioned tests is extremely time-consuming.

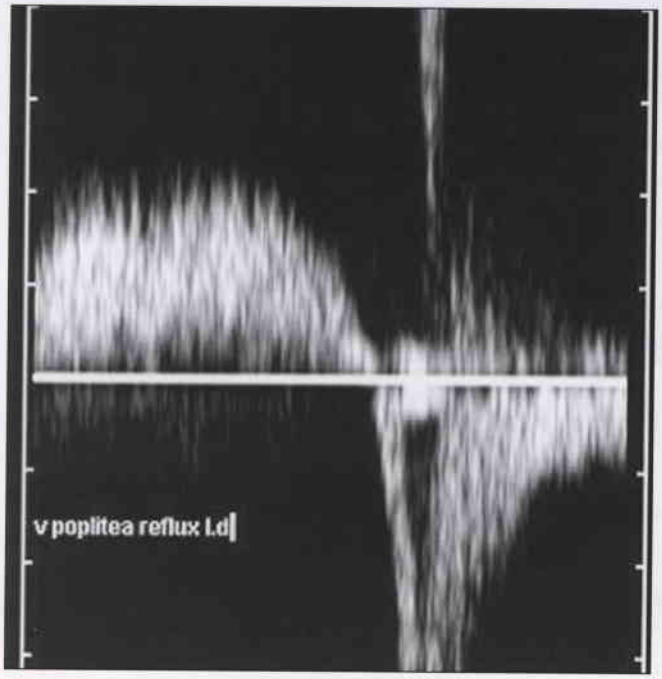

Figure 6. Pozitive curve because of manual squeeze and negativ spike after release showx reflux in the popliteal vein.

Compressibility	normal = 1, partial loss = 2, total loss = 3	
Location	*Right*	*Left*
Common femoral		
Profunda femoral		
Femoral (upper)		
Femoral (distal)		
Popliteal		
Posterior tibial		
Gastrocnemius		
Soleus		
Greater saphenous		
Lesser saphenous		

Table 1.

Algorithms

Thus if we would like to classify the patients for the different tests most effectively, we have to divide them according to CEAP (CEAP C1-3/C4-6) advised by an expert panel and age (young/old).

– Young CEAP C1-3 grade patients are more likely to have superficial vein insufficiency only which is suitable for vascular surgery or other interventions. The most common devices to identify CVI are duplex sonography and PPG in clinical practice together with clinical examinations.

Figure 7. White blood cell trapping can harm the endothelium of veins.

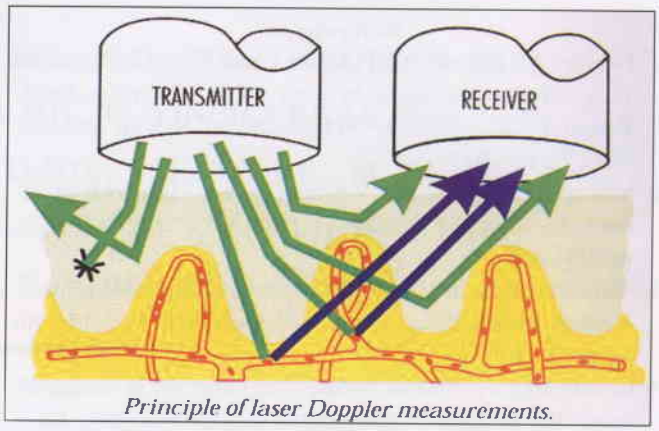

Figure 8. Laser Doppler can measure skin capillary flow.

– Similar tests are necessary for the old CEAP C4-6 grade patients, who are less likely to be available for deep venous reconstruction because of the general condition of their health.

– The young CEAP C4-6 grade patients are the best candidates for extended investigations using all the available methods mentioned above, to discover the deep and superficial vein disturbances for the correct conservative and reconstructive treatment.

It is certain that future improvements in easier and less invasive vascular procedures (in the venous field) will demand more complex examinations. A greater understanding in the microcirculatory changes of CVI is also expected in the future (**figure 7**). It could help us find the necessary devices and lab tests when examining the more vulnerable cases. Nowadays Laser Doppler can help us in finding the microcirculatory disturbances (**figure 8**).

It is important not the forget that peripheral arterial disease is also able to cause a worsening in the condition and so it is also essential to make a general arterial check-up.

In certain cases performing histological tests to differentiate from skin cancer is necessary.

	Augmentation		Phasicity		Valsalva	
	Right	*Left*	*Right*	*Left*	*Right*	*Left*
Common femoral						
Femoral					1. normal 2. partial loss 3. total loss	
Popliteal						
Post. Tibial						
Peroneal						

Table II.

Conclusion

General acceptance and optimal use of these tools could give us an economical and effective treatment for our CVI patients.

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Venoruton (HR) new observations and clinical studies. A new life for HR.

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Key Words

Venous Disease, Varicose Veins, Chronic Venous Insufficiency, Venoruton, Elastic Compression, Edema, Veins, Venous Microangiopathy

Introduction

New information about Venoruton has been evaluated by our research group and is briefly presented in this chapter.

1. The endothelial cells model

Damage to endothelial cells (e-cells) is common in vascular disorders and in reactions associated with transplantation. An elevated number of circulating e-cells indicate diffuse endothelial damage in a variety of disorders. In chronic venous insufficiency (CVI) the number of e-cells is abnormally increased and this can be considered an important indication of endothelial damage. A group of 23 subjects with two levels of CVI (severe and very severe with previous ulcerations) with increased e-cell count (seen by microscopy) was studied and treated for 4 weeks with oral Venoruton (1 g/day) to evaluate the effects of treatment on the circulating e-cells (blood taken from a peripheral leg vein). Comparable (age and sex distribution) groups (normal and CVI subjects) were followed up as controls. After 4 weeks there was a significant decrease in e-cells both in subjects with CVI and in those with very severe CVI and a history of previous ulcerations. This study suggests that e-cells may play a significant role in venous disease both being an indication of severe disease and a further problem. The use of Venoruton appears to decrease the number of circulating e-cells.

This study suggests the important role of this compound in protecting the endothelium and offers new potentially important therapeutic options not limited only to venous disease.

Source: Circulating endothelial cells in venous blood as a marker of endothelial damage in chronic venous insufficiency. Improvement with Venoruton. M. R. Cesarone MD., G. Belcaro MD., PhD., MD., L. Pellegrini MD., A. Ledda MD., G. Vinciguerra PhD., A. Ricci MD., G. Gizzi MD., E. Ippolito MD., F. Fano MB., M. Dugall MD., G. Acerbi MD., M. Cacchio MD., A. Di Renzo, M. Hosoi MD., S. Stuard MD., M. Corsi MD. *Clin Appl Thrombosis Hemostasis,* In Press, April 2006.

2. Venoruton vs Daflon: Venoruton is better than Daflon in CVI (considering the evaluation of the effects on quality of life in chronic cases)

This independent study investigated the differences in efficacy between Venoruton and 500 mg micronised diosmin + hesperidin (D+H) (Daflon) in patients with chronic venous insufficiency (CVI), evaluating venous-related quality of life (Ve-QOL). A first group of 90 patients with severe venous hypertension (CVI, ankle swelling) was randomized for treatment with oxerutins or D+H. The oxerutin group received oral oxerutins (2 g/day); the D+H group received 3 (500 mg) tablets daily every 8 hours for 8 weeks. A second group of 122 comparable patients was included in a registry following the same study format. The 2 treatments were administered with the same methods and procedures. Clinical conditions were comparable. All patients completing 8 weeks of treatment were included in a registry. Specialists or general practitioners included patients when they considered that clinical conditions were compatible with treatment indications using 1 of the 2 treatments on the basis of their evaluation and experience. When cases were compatible with the registry, the prescribing physician communicated the case to our monitoring centre. Patients were evaluated without interfering with their treatment. The main target of evaluation for this study was the change in Ve-QOL (range, 0-100) induced by treatment. A specific Ve-QOL questionnaire was used for this study. Ve-QOL score is a specific expression of the changes in QOL induced by CVI in patients between 35 and 75 years old (defined in our population studies) in which no other significant clinical disease is present (as a confounding factor affecting QOL). Two hundred and twelve patients completed the 2 parts of the study. The treatment groups were comparable in age and gender distribution. The mean age was 42 years (SD+/–5.5) in the oxerutins group and 41.5 (SD+/–6) in the D+H group. There were no differences in the severity of CVI between the treatment groups at inclusion. A significant decrease (46.8%, $p<0.05$) in Ve-QOL score; that is, improvement, was observed in the oxerutins group. The change in Ve-QOL was significantly less in the D+H group (15.5%). In conclusion, CVI, venous microangiopathy, and edema were significantly improved by the treatment with oxerutins; the improvement in QOL was significantly greater in the oxerutins group. The comparison with D+H indicates that oxerutins are comparatively more effective on Ve-QOL and on signs/symptoms of CVI.

Source: Venoruton vs Daflon: evaulation of effects on quality of life in chronic venous insufficiency. *Angiology,* 2006 Mar-Apr; 57(2): 131-138. M. R. Cesarone., G. Belcaro, L. Pellegrini, A. Ledda, G. Vinciguerra, A. Ricci, A. Di Renzo, I. Ruffini, G. Gizzi, E. Ippolito, F. Fano, M. Dugall, G. Acerbi, U. Cornelli, M. Hosoi, M. Cacchio.

3. Prevention of edema and flight microangiopathy with Venoruton (HR) in patients with varicose veins

The aim of this open study was the evaluation of the effects of HR (Venoruton) at a dose of 1 g/day on the prevention and control of flight microangiopathy and edema in subjects with varicose and moderate chronic venous insufficiency flying for more than 11 hours. Patients with varicose veins, edema, but without initial skin alterations or complications, were included. Measurements of skin laser Doppler (LDF) resting flux (RF) venoarteriolar response (VAR), ankle swelling (RAS), and edema were made within 12 hours before and within 3 hours after the flights. The resulting edema after the flights was evaluated with a composite edema score (analogue scale line). A group of 20 subjects was treated with HR (1 g/day, starting 2 days before the flight and 1 g for every 12 hours on day of travel). Another group of 18 subjects formed the control group. The length of the flights was between 11 and 13 hours; all seats were in coach class. Fifty patients were enrolled and 38 patients were able to be evaluated at the end of the trial. The 2 groups (treatment and control) were comparable in age and sex distribution. The decrease in RF was significant in both groups with a higher flux at the end of the flight in the HR group ($p<0.05$). The venoarterioral response was decreased at the end of the flights; the decrease was lower in the HR group ($p<0.05$). The increase in RAS and edema score were significantly lower in the HR group. In conclusion HR is useful for reducing the level of microangiopathy and the increased capillary filtration and in controlling edema in patients with venous disease in long flights. The higher level of flux and VAR and the reduction in edema indicate a positive effect of HR on the microcirculation. This study confirms that HR prophylaxis is effective in controlling flight microangiopathy associated with edema.

Source: Prevention of edema and flying microangiopathy with Venoruton (HR), (0-[beta-hydroxyethyl]-rutisodes) in patients with varicose veins. 1.: *Angiology,* 2005 May-Jun; 56(3): 289-293. M. R. Cesarone, G. Belcaro, A. Ricci, R. Brandolini, L. Pellegrini, M. Dugall, A. Di Renzo, G. Vinciguerra, G. Gizzi, U. Cornelli, B. M. Errichi, M. Corsi, E. Ippolito, R. Adovasio, M. Cacchio, S. Stuard, C. Larnier, C. Candiani, F. Cerritelli.

4. Venoruton: rapid relief of signs/symptoms in CVI and venous microangiopathy

The aim of this independent study was to demonstrate the rapidity of the clinical action of HR (0-[beta-hydroxyethyl]-rutisodes), Venoruton (Novartis Consumer Health) in patients with chronic venous insufficiency (CVI). Two groups of patients with venous hypertension and microangiopathy were treated with HR (1 or 2 g/day, for 8 weeks). Twelve patients (age 56.4; range 44-66; M:F = 6:6) were included in group 1 (1 g/day) (moderate CVI and microangiopathy); 10 patients (age 57.4; range 42-67; M:F = 5:5) in

group 2 (2 g/day) with more severe CVI and microangiopathy. Average ambulatory venous pressure (AVP) was 58.6 (range 50-65) with a refilling time (RT) shorter than 10 seconds. There were no significant differences in AVP and RT between the 2 groups, but the duration of the disease was longer in group 2: 3.5 years (SD 2.0) in group 1 and 6.4 years (SD 3.3) in group 2. All included subjects completed the study and no dropouts were observed. In both dose groups there was a progressive decrease in laser Doppler resting flux (RF), indicating improvement in microangiopathy and a significant decrease in capillary filtration (RAS) associated with a significant improvement in analogue scale line score (ASLS) and edema. Although the effect in the 2 g dose group was more rapid on the microcirculatory parameters with a significant effect on RF and RAS after 4 days (effect of 1 g per day after 8 days and 6 days, respectively), there was no difference in the time taken to reach a significant clinical improvement (ie, the ASLS and the edema score): 4 days in both groups. Venous microangiopathy and edema were improved by the treatment with HR within a few days. The effects were visible with both dosages, in both severity groups.

Source: HR, 0-(beta-hydroxyethyl)-rutisodes; (Venoruton): rapid relief of signs/symptoms in chronic venous insufficiency and microangiopathy: a prospective, controlled study. *Angiology,* 2005 Mar-Apr; 56(2): 165-172. M. R. Cesarone, G. Belcaro, L. Pellegrini, A. Ledda, G. Vinciguerra, A. Ricci, G. Gizzi, E. Ippolito, F. Fano, M. Dugall, G. Acerbi, M. Cacchio, A. Di Renzo, S. Stuard, M. Corsi.

5. Flight microangiopathy on long-haul fligths: prevention of edema and microcirculation alterations with Venoruton

The aim of this study was the evaluation of the effects of Venoruton (HR) on the prevention and control of flight microangiopathy and edema in subjects with varicose veins flying for more than 7 hours. A group of 80 patients with varicose veins, edema, and initial skin alterations due to chronic venous hypertension were included. Measurements of skin laser Doppler (LDF) resting flux (RF), PO_2 and rate of ankle swelling (RAS), were made before and after the flights (within 2 hours before the flights and within 2 hours after the flights). The length of the flights was between 7 and 9 hours; all seats were in economy class. The two groups (treatment and control) were comparable in age and sex distribution. The variation (decrease) in PO_2 was significant in both groups. In subjects treated with HR the decrease in PO_2 was smaller ($p<0.05$). The decrease in LDF-RF was significant in both groups with a higher flux at the end of the flight in the treated subjects ($p<0.05$). The venoarterioral response was decreased at the end of the flights. The decrease was less evident in the treatment group ($p<0.05$). The increase in RAS was significant in the control group while it was limited in the HR group. In conclusion, HR is useful for reducing the increased capillary filtration and in controlling edema in patients with chronic venous disease in long-haul flights. HR is effective in controlling flight microangiopathy associated with edema.

Source: Flight microangiopathy on long-haul flights: prevention of edema and microcirculation alterations with Venoruton. *Clin Appl Thromb Hemost,* 2003 Apr; 9(2): 109-114. M. R. Cesarone, G. Belcaro, G. Geroulakos, M. Griffin, A. Ricci, R. Brandolini, L. Pellegrini, M. Dugall, E. Ippolito, C. Candiani, E. Simeone, B. M. Errichi, A. Di Renzo.

6. Venoruton in comparison with diosmin+hesperidin in chronic venous insufficiency and venous microangiopathy

The aim of this independent study was to investigate differences in efficacy between HR (0-[beta-hydroxyethyl]-rutisodes) and D+H (500 mg diosmin+hesperidin) in patients with chronic venous insufficiency (CVI). A first group of 90 patients with severe venous hypertension (CVI, ankle swelling) were randomized into an HR or a D+H group. The HR group received oral HR (2 g/day, 8 weeks); the D+H group received a 500 mg tablet 3 times daily for 8 weeks. A second group of comparable patients was included in a registry following the same study format. Patients were openly included; the 2 treatments were administrated with the same methods and procedures. Clinical conditions were comparable to those described in the randomized study. Patients treated for at least 8 weeks were included in the registry. A number of physicians (specialists or general practitioners) included patients when they considered that clinical conditions were compatible with using 1 of the 2 treatments on the basis of their personal evaluation and experience. When cases were compatible with the registry, the prescribing physician communicated the case. Patients were evaluated without interfering with the treatment. The main targets of evaulation were skin flux at rest (RF), strain-gauge-derived rate of ankle swelling (RAS), and analogue symptoms score (ASLS). Ninety subjects completed the study in the first group; 122 in the second, registry group (total of 212 patients). The first and second (registry) groups and the 2 treatment groups were comparable in age and sex distribution. The pooled mean age was 42 years (SD +/–5.5) in the HR group (46+62 patients) and 41.5 (SD +/–6) in the D+H group (44+60 patients). Considering pooled data there were no differences in microcirculatory parameters between the pooled treatment groups at inclusion. A significant decrease ($p<0.05$) in RF and RAS was observed in the HR group at 8 weeks. The decrease in resting skin flux and in capillary filtration was associated with a significant improvement in signs/symptoms (analogue scale line) from an average of 9.4 (range 3-10) to 3.3 (4-6) ($p<0.05$). Significantly smaller variations were observed in the D+H group. The decrease in RF was 47.6% in the HR group vs 15.7% in the D+H group. The decrease in RAS was 40.9% in the

HR group vs 12.8% in the D+H group. The decrease in ASLS was 64.8% in the HR group vs 12.9% in the comparative group. In conclusion venous microangiopathy and edema were improved by the treatment with HR both in the randomised study and in the pooled analysis. The comparison with D+H indicates that HR is comparatively more effective both on the microcirculatory parameters and on the signs/symptoms of CVI.

Source: HR, 0-(beta-hydroxyethyl)-rutisodes, in comparison with diosmin+hesperidin in chronic venous insufficiency and venous microangiopathy: an independent, prospective, comparative registry study. *Angiology,* 2005 Jan-Feb; 56(1): 1-8. M. R. Cesarone, G. Belcaro, L. Pellegrini, A. Ledda, A. Di Renzo, G. Vinciguerra, A. Ricci, G. Gizzi, E. Ippolito, F. Fano, M. Dugall, G. Acerbi, M. Cacchio.

Innovation projects

7-Jet-lag

A recent study has indicated that brain edema following long-haul flights can be associated with signs/symptoms of jet-lag. Some hypertensive patients treated with ca-antagonist or ace-inhibitors may develop a different degree and localisation of edema, including brain edema associated with jet-lag symptoms. The anti-edema protection offered by Venoruton (both when used as a single agent and when linked to caffeine) indicate the positive action of this compound on this common syndrome. Further studies are in progress involving the evaluation of minimal brain edema with MRI and CT scans after long (>10 hrs) flights.

8-Caffeine

This in association with HR has shown in a pharmacological model (including iontophoresis) a marked reduction in the abnormal increase in skin flux seen in CVI and venous hypertensive microangiopathy. Dose-ranging studies are now in progress.

9-Pycnogenol

The association HR-pycnogenol to produce a super-venous drug is under evaluation. Specific action of this higher-efficacy, high-dose compound is under preclinical and clinical assessment in situations in which CVI has an important edema component (i.e. CVI associated with diabetes and hypertension requiring treatment).

10-Oncology

The effect of HR on circulating endothelial cells is under evaulation in situations (i.e. radio and chemotherapy) when the increased number of endothelial cells due the to treatment is associated with important side effects. A formulation of Venoruton has already been approved for the prevention of damage due to radiotherapy.

11-Cold

On the basis of a preliminary study conducted in the Department of Pediatrics, University of Virginia School of Medicine, Charlottesville we have evaluated the use of HR in the early treatment of cold.

Background: the University of Virgina Study. Rutisodes are naturally occurring flavonoids (diet) with documented effects on capillary permeability and edema. The purpose of this study was to assess the effect of troxerutin on the symptoms of the common cold. Ninety-four volunteers with common cold symptoms were recruited. Volunteers were randomized to either active treatment (n = 49) with troxerutin (50 mg) and Zn gluconate (25 mg) or control treatment (n = 45) with 10 mg Zn gluconate. Symptoms were assessed by subjective symptom score prior to treatment and then daily for the next 4 days. The total symptom score over the 4 days of study treatment was 27.7 +/– 2.0 (mean +/– SEM) and 33.0 +/– 2.6 in the active and control groups, respectively (p = 0.10 unpaired t-test). The total daily symptom score on day 1 was reduced by 11% compared to baseline in the active group and by 1% in the control group (p = 0.03). Evaulation of the effect of treatment on individual symptoms revealed a significant effect on rhinorrhea. The total rhinorrhea score over the course of the study was 3.7 +/– 0.4 in the active group compared to 5.1 +/– 0.5 in the control group (p = 0.025, unpaired t-test). Daily rhinnorhea scores were significantly lower in the active group on study days 1 and 3. Based on this preliminary study, the possibility that the rutisodes might provide a safe and effective treatment for rhinorrhea in the common cold deserves systematic evaulation.

Source: Treatment of the common cold with troxerutin. R. B. Turner, S. L. Fowler, K. Berg. *APMIS,* 2004 Sep; 112(9): 605-611. Department of Pediatrics, University of Virginia School of Medicine, Charlottesville.

Episodes of cold in CVI patients treated with HR in the San Val. CVI epidemiological, prospective study

Flavonoids have an important effect on capillary permeability and edema. This study was performed to assess the effect of HR treatment (1 g in a period of 3 months in winter) on the occurrence, signs and symptoms of flu and cold.

A group of 93 CVI patients were included within a venous epidemiological study in which HR was used as the main treatment (45) in comparison with stockings (48). All subjects completed the study and the two groups were comparable.

After three months flu and cold symptoms were significantly decreased in the HR group (–32% considering the days of disease for flu and –38% considering cold). Signs/symptoms evaluation (according to Turner) indicated (subjective symptom score before treatment and then daily for the next 4 days) a total symptom score over the 4 days of study treatment of 26 (2.0) in the HR group and 34 (4)

in controls. Daily rhinorrhea scores were lower in the HR group on days 1-4. This pilot study suggests the possibility that HR may offer safe and effective treatment for colds and possible protection against flu. The actions of HR in this field should be investigated in a larger study.

Conclusion

Venoruton has several potential, important actions which have never been completely explored and exploited. New studies offer new potential clinical and preventive applications.

Also HR, and flavonoids in general (originally present in large quantities in our primitive diet), are not only useful in venous diseases but in a range of clinical diseases and preclinical, preventive applications on the basis of physiological and evolutionary consideration.

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VRT303/SEP06

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Chronic venous insufficiency: compression therapy and physiotherapy

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The present report focuses on two important therapeutic modalities used for the management of chronic venous disorders of the leg (CVDL) – compression therapy and physiotherapy. We would like to answer following questions: do compression therapy and exercise really improve tissue circulation? How can we define the methods themselves? What are the possibilities in the treatment of CVI? What are the limitations and contraindications of compression therapy and physiotherapy?

The treatment of chronic venous insufficiency relies on three main methods: sclerotherapy, surgery and compression therapy (1).

Before proceeding to the basic facts about compression therapy and physiotherapy in chronic venous insufficiency (CVI), we have to analyse some essential facts about the pathophysiology of venous disease. Superficial venous insufficiency is usually connected with a dilatation of superficial veins and valve incompetence – the greater saphenous vein (GSV) or the short saphenous vein (SSV) and their branches leading to a back and forth flow of venous blood. Correcting the reflux through the venous junction is therefore crucial for the treatment of varicose veins. Deep venous insufficiency may be present in several ways:

– primary incompetence when deep veins and valves become dilated and incompetent (primary varicosis of the deep venous system,

– secondary insufficiency due to superficial venous insufficiency,

– postthrombotic syndrome (vein wall and valves destroyed by deep venous thrombosis).

Incompetent perforating veins enable backward blood flow from the deep into the superficial veins. This backflow explains the features of stasis, characteristic of chronic venous insufficiency, which predominates at the medial aspect of the ankle. Altered microcirculation: reflux in venous trunks creates venous hypertension with an impact on the microcirculation, forcing intracapillary fluid to diffuse into the intersticial space. The subsequent development of oedema and extravasation of blood cells (degradation of hemoglobin) enables a rise in hemosiderin, which causes hyperpigmentation. Tissue injury and damaged lymphatic drainage play an important role in the development of the late manifestation of chronic stasis in the legs.

The role of compression in phlebology is obvious when we realise that fluid exchange between capillaries and the intersticial space and lymphatic drainage of protein-rich exsudates creates a state of dynamic equilibrium. A disruption of this equilibrium leads to oedema formation or sub-aponeurotic stasis. There are numerous factors causing disturbances to this equilibrium:

– increased transmural capillary pressure (venous thrombosis, muscle-vein pump insufficiency in CVI),

– disrupted equilibrium between the capillary and tissue oncotic pressure, causing oedema due to liver and renal disease,

– low tissue pressure (lipoedema),

– increased capillary permeability (inflammation, diabetes, reperfusion),

– disrupted lymphatic flow (trauma, inflammation, lymphoedema).

These disturbances may respond favourably to medical compression therapy.

What are the fundamental principles of compression therapy? We have to realise that external pressure leads to a reduction in the vein diameter. This results in an increase in venous velocity and improves venous drainage from the legs. In an upright position, compression increases orthograde flow in incompetent veins and decreases reflux.

Enhancing the efficacy of the venous pump is an important therapeutic principle in the management of chronic venous insufficiency. The effects of compression therapy on venous hemodynamics at the microcirculatory level include accelerated blood flow in the capillaries, reduction of capillary filtration and increased reabsorption due to enhanced tissue pressure and an improvement in local lymph drainage. Reduction in blood volume in the legs leads to a shift of blood into the central vascular compartments of the body and to an increase in the preload to the heart and increased cardiac output. Caution is necessary in patients with severe cardiac failure! During pregnancy this shift of blood may influence the maternal and foetal heart rate.

Classification of chronic venous insufficiency has been developing since the 1970s. The first clinically applicable classification was introduced in 1978 by Widmer in Switzerland on the basis of the Basle III Study. The author of next relatively popular classification was Porter in 1988. A modern classification of venous disorders, CEAP Classification, was introduced in 1995 by the American Venous Forum in Hawaii. Widmer's Classification is practical, more widespread in German-speaking countries and in central Europe. This classification strictly differentiates between 'uncomplicated' varicose veins and more severe types of the disease. Clinical conditions can be divided into three grades (I-III). Varicose veins according to *Widmer's Classification* are also divided into three groups (teleangiectasias, reticular veins, and trunk varicosities). *Porter's Classification* divides the clinical conditions of CVI into four clinical classes: 0 asymptomatic, 1 mild CVI, 2 moderate CVI and 3 severe CVI. *CEAP Classification* is considered the most appropriate classification for modern clinical use. The scoring system of this classification avoids the difficulty of confusing morphological and functional terms. However, it will probably need certain modifications to improve its practicality and usefulness. CEAP Classification uses four categories: C (clinical signs – class 0-6), E (aethiology – Ec congenital, Ep primary, Es secondary), A (anatomic distribution – As superficial veins, Ad deep veins, Ap perforating veins), and P (pathophysiologic dysfunction – Pr reflux and Po occlusion).

Classification of CVI from the point of view of compression therapy enhances some aspects presumably in the compartments of superficial and perforating veins – varicose veins:

– venous trunks (GSV, SSV); massive reflux in trunks is frequent without visible varicose veins,

– accessory trunks (lateral and medial saphenous vein),

– incompetent perforators,

– nonsaphenous veins,

– reticular network,

– teleangiectasias.

Mechanism of action of compression therapy:

1. decrease of oedema,
2. softening of lipodermatosclerosis,
3. decrease in venous volume (narrowing of veins),
4. increase in venous velocity,
5. blood shifts into central compartments,
6. reduction of venous refluxes,
7. improvement in venous pumping,
8. influence of arterial flow,
9. improvement in microcirculation,
10. increase in lymph drainage.

Compression therapy can be divided into two phases:

a/ Therapeutic phase:

– reduction of oedema,

– venous ulcer healing.

b/ Maintenance phase:

– to keep improved tissue condition,

– long-term treatment.

Basic types of compression therapy (for the hemodynamic effect see also figure 1):

a/ Passive compression:

– produced by inelastic bandages which counteract the increase in muscle volume resulting from muscle contraction,

– totally inactive during rest: 'resting pressure',

– effective during muscle contraction: 'working pressure'.

b/ Active compression:

– delivered by an elastic orthosis,

– leg is compressed both at rest and during exercise,

– powerful recoil forces of the elastic fibres exert an active pressure on the limb,

– muscle contraction increases the compression effect.

Compression materials can be divided into several groups:

1/ Inelastic materials:

– Zinc plaster bandages (Unna's boot) are the classic example of a completely non-elastic material. It is necessary for them to be applied by trained staff and to remain on the legs from several days to several weeks.

2/ Continuous-use elastic bandages and dressings:

– remain on the patient's legs even during bedrest. Must be changed sometimes (after 2 days or after several weeks, on average once a week).

– indication: for more severe forms and grades of CVI at the beginning of treatment until rich decongestion,
– only short-stretch materials (70% extensibility),
– specially trained personnel required.

3/ Daytime-use elastic bandages or dressings:

– applied by the patient in the morning and not removed before going to bed,
– indication: less severe congestion,
– material: medium and long-stretch bandages,
– low working pressure – while walking stretch during the contraction of the muscles,
– compression stockings are a form of daytime-use elastic dressing (hosiery).

4/ Compression enhancement:

– variously shaped foam rubber pads help us to modify the local contact pressure,
– these pads are used wherever a particularly high contact pressure is desirable,
– it is especially useful with venous ulcers.

The basic rules of compression therapy are as follows:

– not to be applied to an ulcer where there is also an arterial component,
– dressing must be firm – resistance to calf muscles is necessary,
– dressing must be applied without gaps,
– the pressure is to decrease continually from distal to proximal,
– the basic bandage should end at the level of the head of the fibula. Bandages crossing the knee or thigh have only been used in special indications,
– an adequate number of layers must be applied to ensure adequate pressure from the bandage.

The medical textile industry started early in the 20th century when doctors had empirically identified the beneficial medical effects of compression therapy. Industrial progress allowed the development of knitting and weaving machines and the use of latex allowed the manufacture of elastic products. Germany, Switzerland and France are currently the leading producers of medical stockings and bandages in the world. International consensus has been reached over the question of technical standards of stockings (RAL-GZ 387).

Compression stockings are divided into four compressive classes:

– class I: 18-21 mm Hg,
– class II: 25-32 mm Hg,
– class III: 36-46 mm Hg,
– class IV: over 58 mm Hg.

Physicians treating CVI have to know the indications of medical compression in these individual compression classes and to be familiar with the prescription of stockings and bandages for individual patients.

The main indications of compression therapy in venous disease:

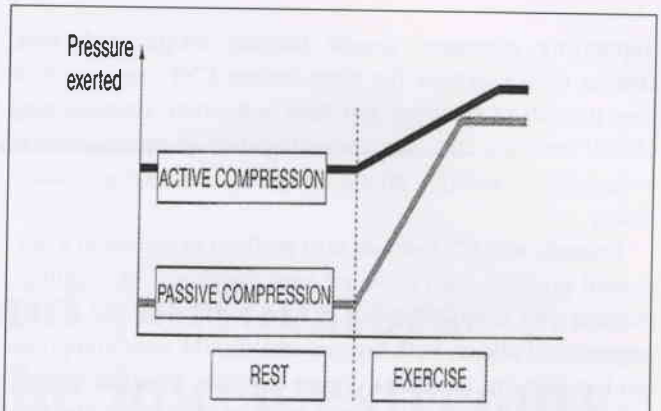

Fig. 1. - Pressures delivered by passive and active compression at rest and during exercise.

Figure 1. Pressures delivered by passive and active compression at rest and during exercise.

1. acute deep venous thrombosis,
2. superficial thrombophlebitis,
3. post-surgery or after sclerotherapy,
4. chronic venous insufficiency (grades I-III of Widmer's Classification, CEAP C3-C6),
5. varicose veins during pregnancy,
6. important varicose veins (C2) with subjective fatigue.

Other techniques of compression and other indications:

1. intermittent pneumatic compression,
2. mercury bath compression,
3. compression for long-term bedridden patients,
4. compression during commercial air travel,
5. elastic compression in sports medicine.

The main contraindications of compression therapy:

1. severe occlusive arterial disease with ABI < 0.55; the resting pressure induced by compression must never be greater than the arterial perfusion pressure,
2. severe congestive heart failure (compression may cause subsequent cardiac preload).
3. textile allergies.

Physiotherapy and exercise

Physiotherapy must be an essential component of the complex treatment of CVI. It is also necessary to teach patients with CVI the importance of exercise and for them to accept it into their lifestyle. It is well-known that venous hypertension and stasis are due to obstruction or reflux in deep or superficial veins and failure of the venous pump function (the main mechanism of venous outflow from the legs). The main purpose of physiotherapy therefore is the improvement of leg venous outflow supporting venous pump function. Walking is the simplest exercise for improving muscle-venous pump and venous retum. Patients with CVI should perform temporary elevation, 'stepping', repeated standing on tiptoe (while standing for a longer time).

Supporting measures should include weight reduction, change of occupation (in more severe CVI), reduction of long periods of standing, flat-fleet correction, strengthening of calf muscles and regular participation in sports such as swimming, cycling, hiking, jogging and cross-country skiing.

Patients with CVI should also perform exercises in a horizontal position with elevated legs: 'walking' or 'cycling'. Regular and deep breathing in time to the exercise is very important. Patients with leg oedema should wear compression bandages or stockings during exercise. Physical therapy at home might include a cold bath or showering the legs with cold water.

Summary

We have been looking for the answer to the question stated at the beginning of the paper: 'Does compression therapy and exercise (physiotherapy) really improve tissue circulation?'.

It is obvious that both methods of treatment can dramatically improve the condition of leg perfusion in patients with severe and moderate venous disease. Therefore both these methods of treatment are unavoidable components of complex CVI management. Compression therapy may dramatically improve tissue perfusion reducing oedema and lipodermatosclerosis and accelerating ulcer healing. Exercise and physiotherapy can improve leg venous drainage supporting the venous pump function.

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Re-entry ways and perforators in venous disease of the lower extremity

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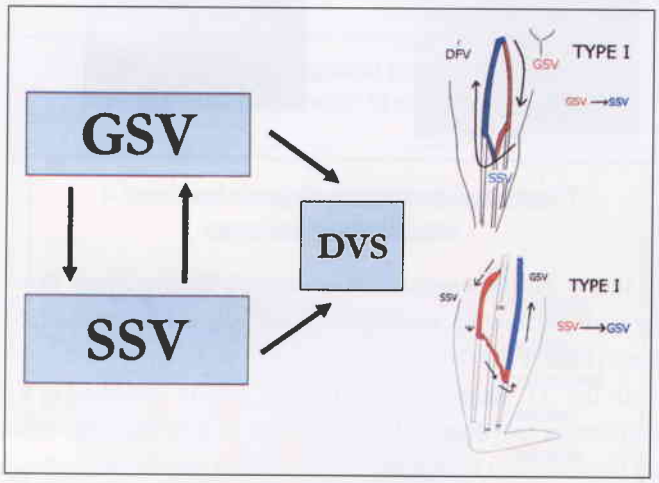

Figure 1. Type I of re-entry way.

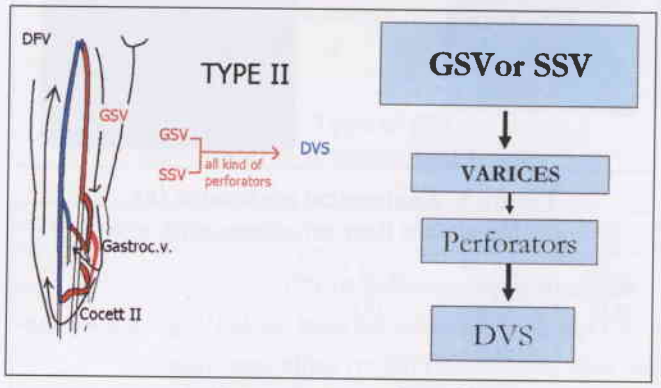

Figure 2. Type II of re-entry way.

Over 5 years (2000-2005) we performed 3350 operations because of varicose disease. All cases but four were operated on a 'one day surgery' basis. Every patient was examined with ultrasound in a standing position with a 7 MGHz probe and with colour Doppler option. In cases with diagnostic doubts PPG was added. Sometimes an examination after compression therapy was indicated. To classify the advancement of disease in everyday practice the 'C' (in *CEAP Classification*) proved to be useful. In C3 differential diagnosis should be kept in mind (cardiac, hormonal, orthopedic and drug-induced problems). To describe the extension of the varices we used the *Hach Classification,* although many patients only had partially developed GSV. Unfortunately, these descriptions do not explain the clinical picture. Trying to correlate this clinical picture with the dynamic stage of perforators, we introduced into our clinic our own classification.

Assuming that reflux can be detected in almost every patient with varicose disease, we distinguished typical ways of its propagation in the superficial venous system. In advantageous anatomical conditions a certain amount of back-moving blood can get into the deep venous system through other connections and ways than in the normal state. Patients with varices were examined in a vertical position during the examination by ultrasound with colour-doppler option. Three types of re-entry ways (RW) were defined:

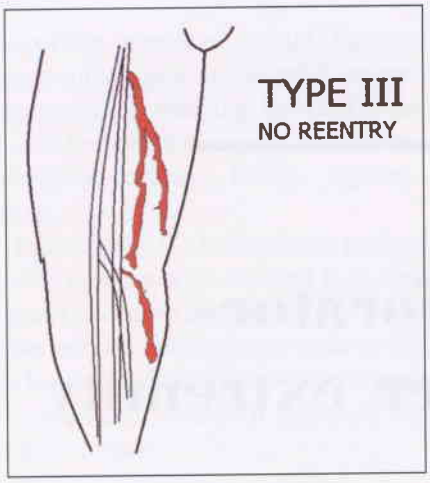

Figure 3. Type III of re-entry. No effective connection between insufficient superficial and deep system.

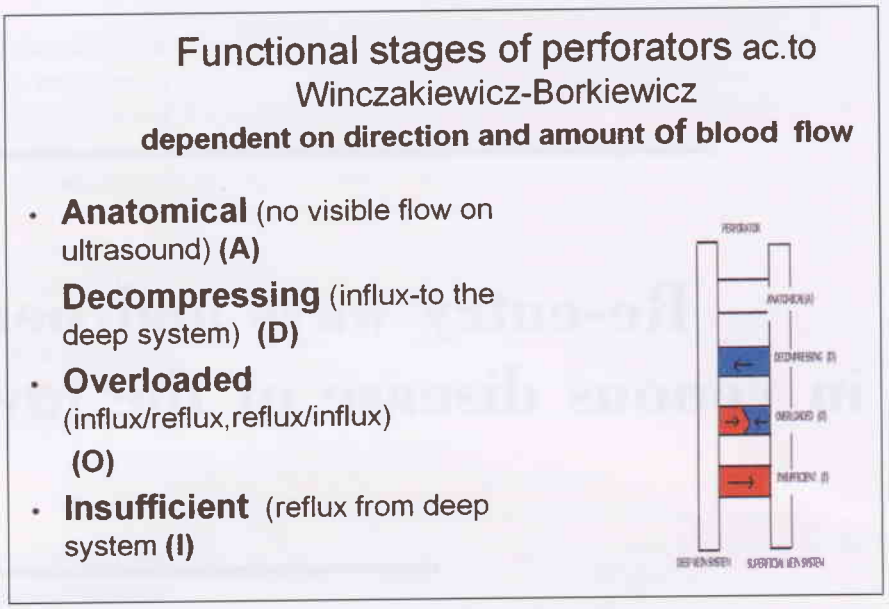

Figure 4. Functional stages of perforators.

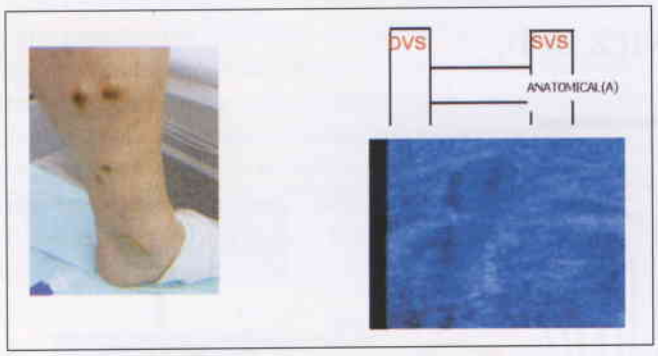

Figure 5. Anatomical perforator (A). No visible flow on ultrasound.

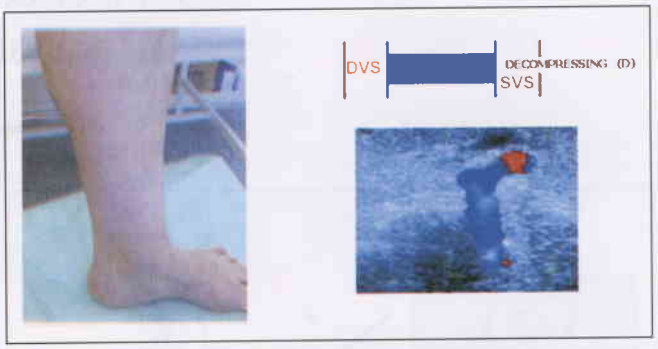

Figure 6. Decompressing perforator (D) in type II.

Re-entry ways according to PCC:

– Type I– connections between the GSV (greater saphenous vein) and the SSV (short saphenous vein).

– Type II – re-entry to the deep venous system (DVS) through perforators in various locations.

– Type III – no-connections with the DVS.

In type I re-entry ways develop inside the superficial system. Important tributaries connect the GSV and the SSV. **(Figure 1.)**

In type II back-moving blood in G-or SSV insufficiency gets in to the DVS alternatively through all kinds of perforators in various locations **(Figure 2.)** In type III no distinct connections with the DVS are detected ('blind' endings in subdermal tissue tributaries). **(Figure 3.)**

In type II, perforators (most often Cocett II. Boyd, middle-calf and perforator to gastrocnemius veins) were divided into four functional conditions (on ultrasound) – presented in **figure 4.**

In the 'A' stage we cannot distinguish distinct blood flow through perforators (during standard ultrasound examination). **(Figure 5.)**

In the 'D' stage blood is directed mainly into the DVS. Perforators are often wide in diameter. In next the stage blood flow starts to be bidirectional; in more overloaded perforators the backward component rises. **(Figure 6.)**

The last dynamic stage we called insufficient perforator: mainly one-directional blood flow from inside to outside is observed. But we wanted to stress, that insufficient perforators do not mean re-entry way insufficiency. We have patients with this kind of perforator but with an effective working re-entry way through other connections (for instance coexistence with type I). **(Figure 7., figure 8.)**

At this stage perforators are often very wide and one directional blood flow from inside to outside is observed.

In summary we imagine that the natural history of the perforator in varicose disease develops in the way presented in **figure 9.**

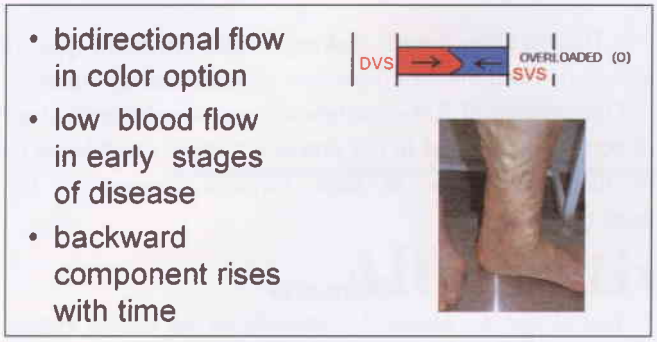

Figure 7. Overloaded perforator (O).

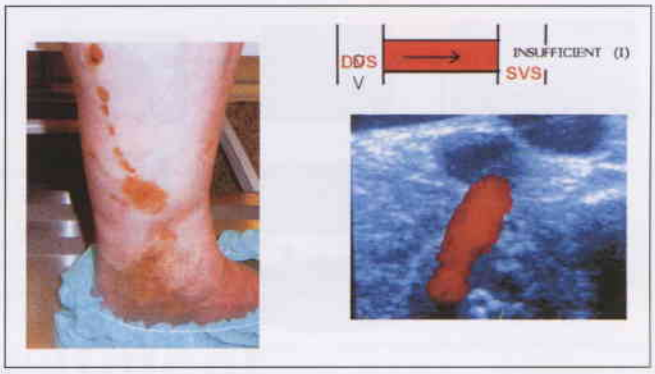

Figure 8. Insufficient perforator (I) in type II.

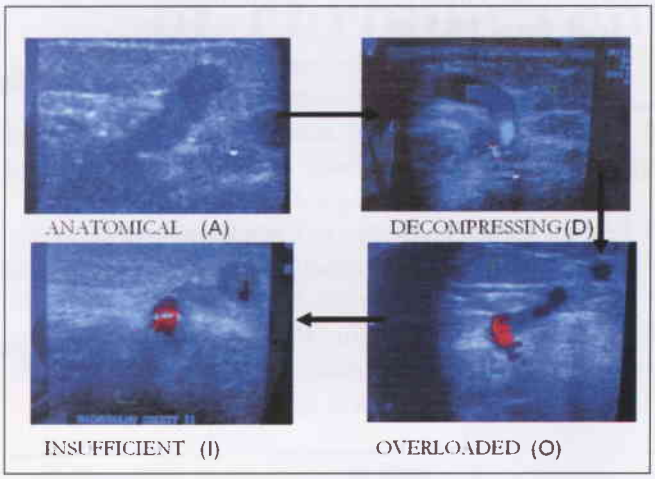

Figure 9. Stages of perforator.
History of the perforator in varicose disease.

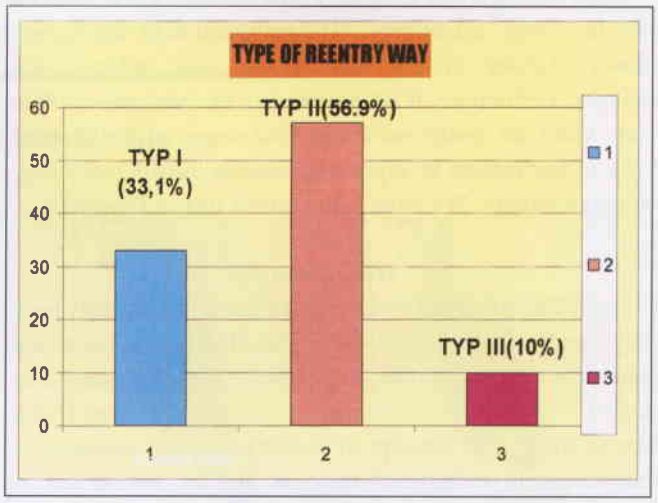

Table I. Type of RW
(according to predominant type).

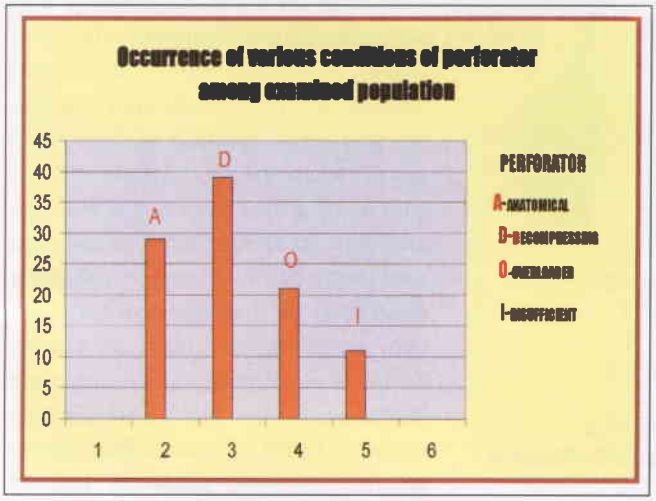

Table II. Condition
of perforators.

Type of re-entry ways	I	II	III
	22.12% (14)	70.1% (80)	65% (13)
		Decomp. –12%	
		O-loaded – 41%	
		Insuff. – 21%	

Table III. Occurrence of trophic change according to predominant type of re-entry way (hyperpigmentation, lipodermatosclerosis, ulcers).

We found in 200 consecutive patients, according to the most distinctive re-entry way, that most often type II. exists. (**Table I.**) But of course many patients have both types.

We also counted the number of perforators in the examined population according to their dynamic condition. (**Table II.**) Of course a single patient can have two or three perforators at various stages. What is important is that only about 10% of them are insufficient.

The correlation between trophic changes, type of RW and the condition of the perforator is illustrated in **table III.** The most important fact is that in our opinion trophic changes start to develop in RW insufficiency (which does not mean an insufficient perforator).

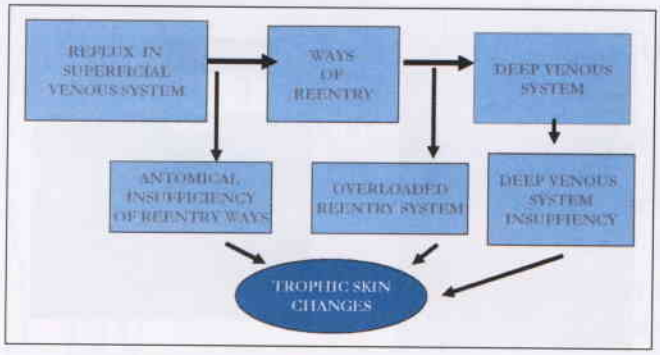

Figure 10. Re-entry concept of trophic changes.

Even large varices cause no skin changes if the re-entry system works effectively. The progression of the disease causes re-entry system insufficiency and induces skin changes. Perforators, if decompressive or overloaded (often very wide) are *beneficial* in the first stages of the disease. Lack of perforators in superficial venous insufficiency may be unfavourable. We have summarized this in **figure 10.**

Discussion

Hach Classification is descriptive but many patients have only a partially-developed GSV. This classification does not match the clinical picture very closely. We have patients at stage IV with minimal changes and patients at stage I with venous ulcer. The concept of re-entry ways in summary is this: in the first stages of varicose disease the amount of back-moving blood is minimal and is compensated by vein volume. In more advanced stages reflux tries to find connections with the deep vein system in an alternative way.

This concept assumes that the main factor initiating tro-phic changes in the skin is the widely understandable insufficiency of the re-entry system. It means that connections between the superficial and the deep vein system are not sufficient enough to transport the receding blood flow to the deep veins.

This insufficiency may be anatomical in character when:

1/ the patient has weakly developed connections between the GSV and SSV, or

2/ perforators are not incorporated in re-entry ways.

Perforators 'A' (anatomical) in this meaning are not a part of the re-entry system and are not a vital element of the pathophysiology of varicose disease.

The therapeutic implications are very important:

– Surgery on the superficial system is usually effective enough to stop varicose disease.

– It seems that perforators (in type II of re-entry) serve in the role of safety pistons for a long time, taking back the receding blood to the deep venous system.

– Perforator ligation is needed very rarely and indicated only in type II with insufficient perforator and re-entry way insufficiency.

– Despite skin changes looking for perforators in type III should be contraindicated because of unnecessary injury.

Our concept of RW-insufficiency and the dynamic stage of perforators is used in our practice routinely and helps us to understand how to treat varicose disease in the most effective way.

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Alternative methods in the treatment of chronic venous insufficiency

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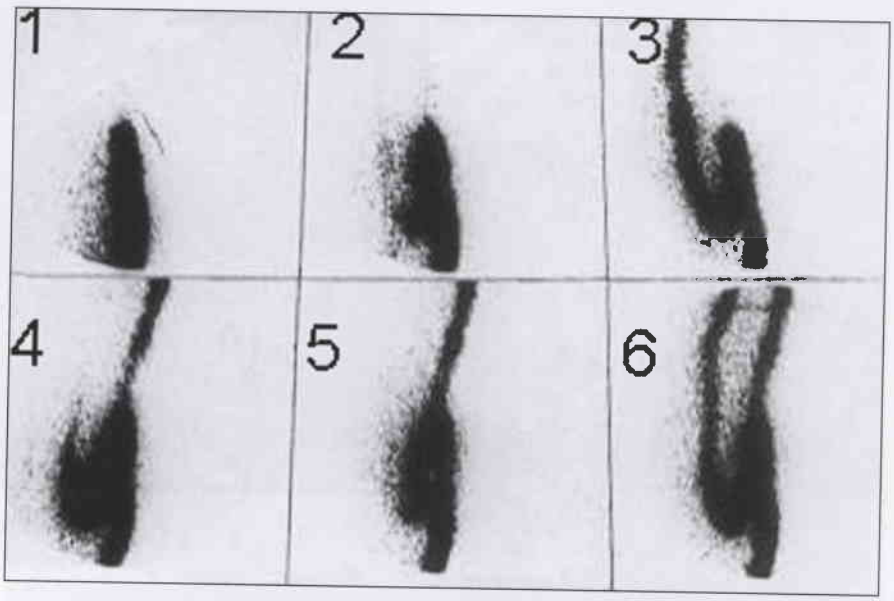

Figure 1. Isotope examination of a postthrombotic limb.
1. The isotope is introduced into a dorsal foot vein.
2. The material stops at the occluded deep vein.
3. Blood flow goes in superficial collateral channels.
4. There are some subfascial collaterals as well.
5. In this phase the subfascial collateral flow dominates.
6. Finally blood flow in the superficial and in the subfascial venous beds.

Varicectomy in deep vein occlusion

In varicosity blood does not flow toward the heart but to the ankle. This blood is a burden for the limb, therefore removal of varicose veins is a very effective therapy (5). For this reason one of our aims is to reduce possible contraindications of varicectomy even in occluded deep vein cases. The absence of deep venous drainage was a contraindication for a long time because the superficial veins are possible collateral pathways that drain the blood from the limb. In some cases there were severe complications after varicectomy. The question is, in which case the superficial veins are essential for the maintenance of blood circulation and in which ones the varicose veins are a burden for the limb.

Different clinical methods and more sophisticated devices are used to measure the venous function of the postthrombotic lower limb. *Rosfors* and *Noren* in their study stated that in many cases no reliable functional distinction could be made between limbs with patent and still occluded deep veins (10). Similar results were reported by *Rayu et al.* He recommends a reexamination of the traditional admonition against the removal of secondary varices (9). It seems that after deep vein thrombosis not only superficial veins will dilate, but *subfascial collaterals* will develop as well. In time these deep collaterals will be able to drain the venous blood from the whole limb. *In the pelvis* the internal iliac vein is a well-known collateral venous bed. *In the thigh* the most frequent anatomical subfascial collateral pathway is the deep femoral vein in the thigh muscles. Usually *in the leg* not every deep vein is occluded, or one or two of the gastrocnemius veins are patent and

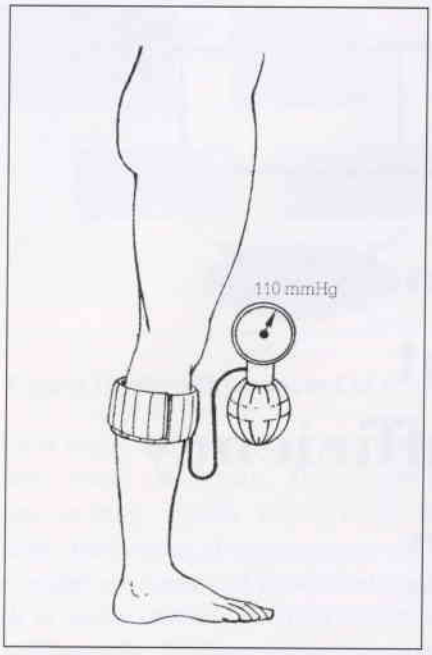

Figure 2. Subcutaneous varices are totally compressed by the tonometer cuff.

Figure 4. Phlebography: deep femoral vein branches as collateral pathways of the thigh.

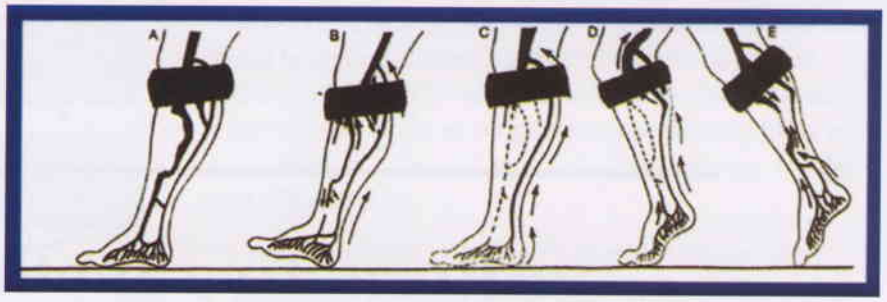

Figure 3. While walking blood circulation is higher and muscle-pump helps the subfascial collateral circulation so it gives a clear picture of venous function.

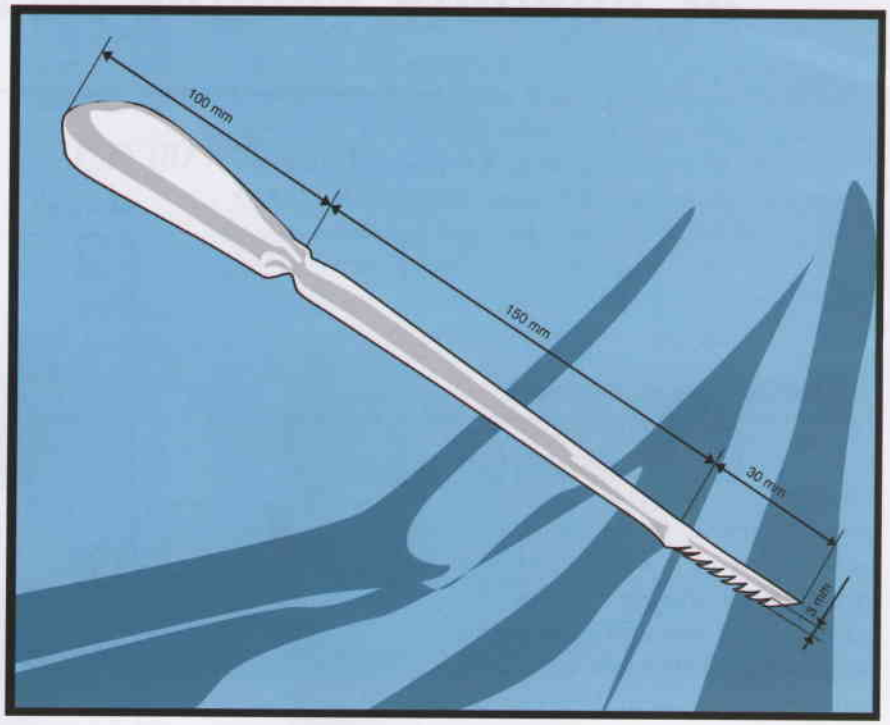

Figure 5. The saw-knife we use.

they can serve as a conduit for the venous blood. If there is not any preformed anatomically known venous channel, then small, unmarked veins will dilate. *The main problem* with them is that sometimes they are too small to be seen by picture-making diagnostic methods, like ultrasound, phlebography and isotope scintigraphy (**figure 1.**) examinations. The question is whether or not they are really suitable for the drainage of blood from the whole limb. In these cases functional tests such as plethysmography and pressure measurement can prove their presence and function. In our practice a new and simple diagnostic method proved to be reliable in deep vein occlusion and aplasia cases.

This is a modification of the Perthes test. Instead of a rubber strip tourniquet, *a tensiometer cuff is placed on the limb* just below or above the knee. The cuff is inflated to 110 mmHg (**figure 2.**) and the patients are asked to walk quickly for 5 minutes (**figure 3.**). In this case superficial veins are compressed, deep veins are occluded, only the subfascial collaterals can drain the venous blood from the limb. *In positive cases,* the limb became livid and the patient complained of heavy pain within 1 or 2 minutes. This meant that there were no or not well-developed subfascial, intramuscular collaterals. *In negative cases,* when collateral channels in the subfascial space were sufficient in number and diameter to drain the venous blood from the leg, the

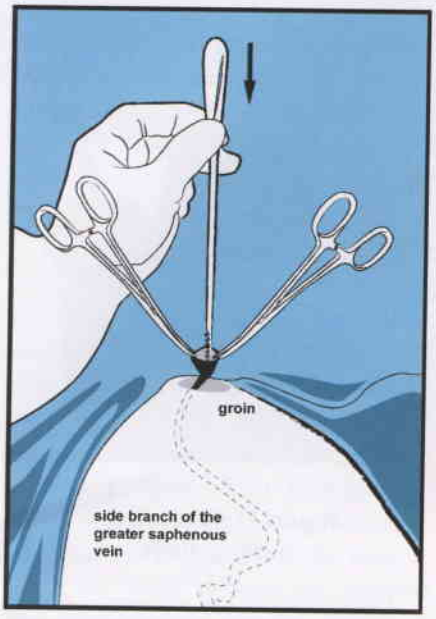

Figure 6. The saw-knife is suitable for the removal of dilated side branches of the greater saphenous vein in the thigh.

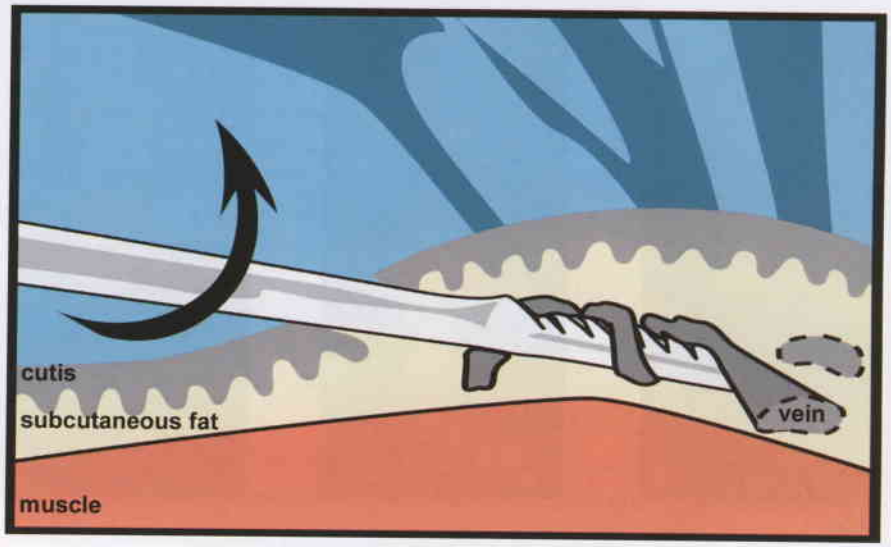

Figure 7. Extra-luminar usage of the saw-knife.

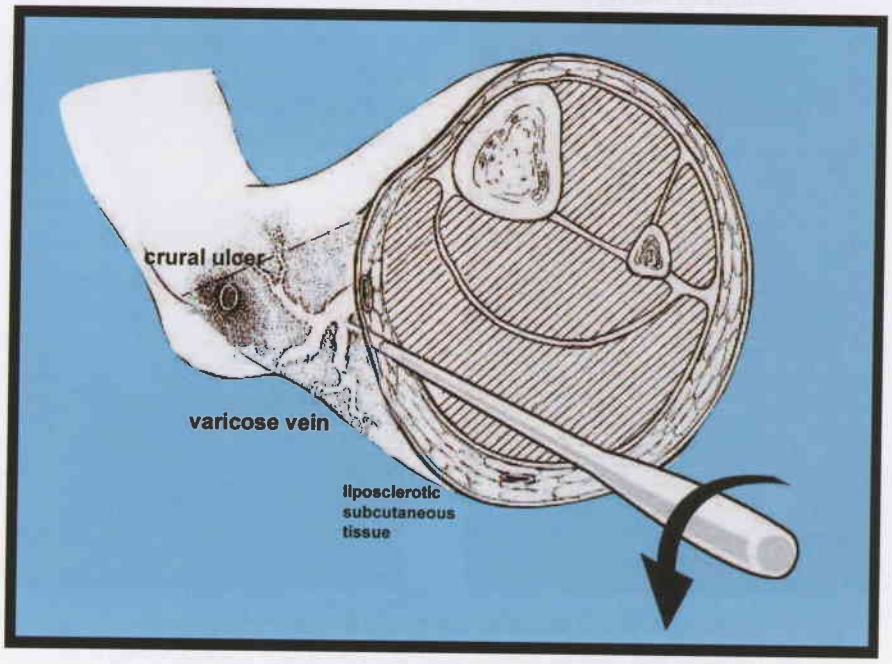

Figure 8. Usage of saw-knife in liposclerotic tissue under a crural ulcer.

patient informed us that his leg felt better. In this case varicose, superficial veins can be removed (2, 3).

In 69 occluded deep vein (**figure 4.**) and in 6 deep vein aplasia and hypoplasia cases radical varicectomy was performed by us according to this indication without any circulatory complication (2, 3).

Saw-knife phlebectomy

The saw-knife has been used by me and my colleagues since 1974 (1, 11).

Altogether 3000 varicose veined limbs were operated on using the following methods:

– *crossectomy*,

– *stripping* of the greater saphenous vein (usually the thigh part),

– removal of tributaries and tearing of perforator veins with a *saw-knife*.

Regarding crossectomy and stripping we refer to other publications (5, 6, 7, 13) but the saw-knife is not so widely known therefore we would like to show our instrument, methods and long-term results.

Our saw-knife is 28 cm long. It consists of a handle (10 cm), a shaft (15 cm) and a blade (3 cm). The latter has teeth like a saw (**figure 5.**). For the removal of varicose veins in chronic venous insufficiency limbs it is much better than in cosmetic varicose vein cases.

The technique is very different from other instruments and therefore needs a tutor at the beginning to provide some experience in its use. This knife is suitable for the removal of very dilated varicose side branches and non-sondable saphenous trunks in a post-thrombotic, post-phlebitic and lipodermatosclerotic limb. This instrument is also excellent for recurrent varicosities after surgery or sclerotherapy.

Three methods have been developed for its use:

1. *Intravascular method* for the removal of the femoral part of the greater saphenous stem or side branches on the thigh if a sonde cannot be introduced (**figure 6.**).

2. *Extravascular method:* the knife is introduced from a separate incision

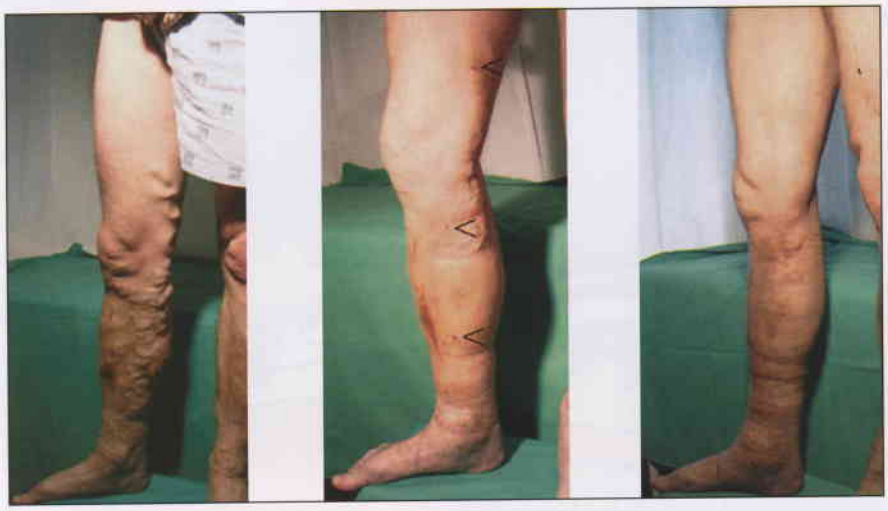

Figure 9. a/ Greater saphenous vein stem varicosity with a crural ulcer on the tibial edge. b/ Early postoperative picture showing stab wounds of the operation. c/ Two months after varicectomy.

Figure 10. a/ Greater saphenous vein varicosity. b/ Three months after ultrasound-guided foam sclerotherapy.

and pushed forward into or adjacent to the vein. The teeth of the knife anchor the vein, then it is reeled up and can be pulled out with the knife (**figure 7.**).

3. The saw-knife can be used *under a crural ulcer in the lipodermatosclerotic tissue.*

The same manoeuvre is performed as descriped above, but the veins are firmly attached to the surrounding tissue therefore they can be usually destroyed, less frequently removed (**figure 8.**).

After the operation the bleeding is treated with bandages. The number of these stab-incisions is between 1-5, usually 2 or 3 (**figure 9/a-b-c**).

The benefits of the saw-knife technique are:

– Varicose veins are removed even after phlebitis or sclerotherapy and in CVI complicated with lipodermatosclerosis.

– With the removal of varicose veins the perforator veins are torn as well.

– In these difficult cases the duration of the operation is no longer than in simple aesthetic cases (less than 1 hour).

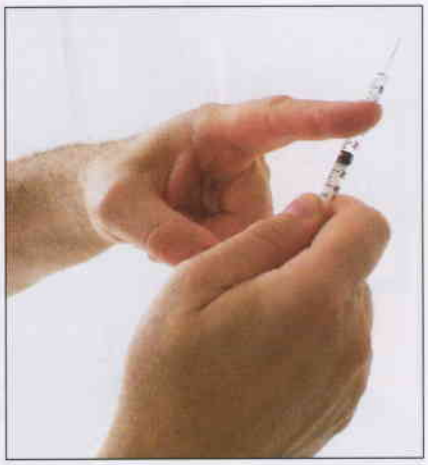

Figure 11. Method for making froth.

Drawbacks of the saw-knife are:

– Not really suitable on the hand and foot.

– More experience is necessary for its use than for other phlebectomy instruments.

– More suffusion than with hooks.

A long-term control check-up of the varicectomy of 141 primary greater saphenous vein varicosity cases was performed (**table I.**). After 12 years there was recurrent varicosity in 28.4% of primary CVI limbs. This seems to be good compared to the international literature, where the accepted postoperative recurrency rate in general is 20% in 5 years (8). There were 11 crural ulcer cases in this series and none of them had recurrent ulcers even if varicosity recurred.

Foam sclerotherapy

In recent years foam sclerotherapy has been introduced into phlebological practice. Foam is more effective than the usually used liquid because the bubbles press out the blood from the vein which means that blood will not dilute the sclerosing agent. A further benefit of foam is that ultrasound equipment can easily follow its flow in the vein and even around the junctions. Its effectiveness seems to be equal to surgery (4, 15, 16).

Our standard method: For the preoperative physical and ultrasound

examination the patient is standing. We measure the diameter of the saphenous stem and detect the amount of reflux in that. The reflux is evoked with the aid of vein compression and the Valsalva maneouvre.

If there is reflux it means that sclerotherapy is indicated; if the diameter is less than 15 mm the vein is suitable for foam sclerotherapy. The patient lies down, her limb is horizontal or can be raised to 20 degrees. For the treatment foam is made from liquid sclerosing agent. Two syringes are used, one containing 2 ml polidocanol or tetradecyl sulphate and the other 4 ml of air. These syringes are attached to a three-way tap, and the solution is pressed 15 times out of one syringe into the other. This produces a relatively good, long-lasting (10 minutes) thick foam. This foam is given into the greater saphenous vein by 1-5 direct punctures. After the treatment the patient stays in the lying position for 3 minutes, to slow down the inflow of foam into the circulation of the body. The whole limb is bandaged and the patient is asked to walk a lot (4, 12, 15). In many cases foam is used by us in the treatment of side branches as well. *For side branch varicosity another technique is used.* It seems to be indicated if the side branch is very wide and so the liquid sclerosing agent is not effective. In these cases there is no need to make such a thick and long-lasting foam (**figure 12**). The syringe is tapped about 10 times which makes a froth.

Results: The results of the greater saphenous vein treatment can be checked by ultrasound. If the vein is not compressible, and some echodens material is seen in the lumen, this means there is clot in the vein and the treatment was successful. In some cases there is no clot at all or only half the lumen is filled with this echodens material and reflux can be evoked. In these cases sclerotherapy was not successful and further treatment is necessary.

Years	Number of limbs	Recurrencies / year	All recurrencies	%
1	141	1	1	0.7
2	139	2	3	2.1
3	135	3	6	4.2
4	130	5	11	7.8
5	121	9	20	14.2
6	118	3	23	19.1
7	114	4	27	23.9
8	111	3	30	21.3
9	109	2	32	22.7
10	104	5	37	26.2
11	102	2	39	27.6
12	100	1	40	28.4

Table I. Recurrency in the 12 year follow-up study.

The results of treatment in *side branch varicosity* are usually excellent. The disappearance and hardening of big varicose veins can be observed at that first visit.

Regular mid-term and late control check-ups are recommended after successful treatment, once or twice a year. If there is some recurrence, it means that a part of the greater saphenous vein is patent and then the therapy can easily be repeated. At the beginning the aim is the closure by clot and later by scar of the entire greater saphenous vein distally from the first tributaries in the groin.

Indications: this treatment is indicated not only in the varicosity of the greater saphenous vein but also in the lesser one as well. It has a very good effect on the healing of crural ulcers, therefore an open leg is not a contraindication but an indication (14).

Contraindications: are the same as for liquid sclerotherapy. If the patient has migraine then this treatment can provoke some headache or temporary visual disturbances. Giving more than 10 ml of foam in one session is not recommended to avoid complications.

Using this technique almost every type of big stem varicosity can be solved. Although we do not have long-term results yet, it is known from

Figure 12. Froth sclerotherapy of very dilated side branches.

colleagues that in many cases it is similar to the operative treatment.

Alternative methods mentioned in this article are not widely used but have proved to be useful in our practice. Therefore we recommend them for every phlebologist who treats severe varicosities.

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Surgical options for chronic venous insufficiency

GÁBOR MENYHEI M. D., PhD.

Introduction

The management of chronic venous insufficiency has relied on compression treatment with adjunctive venoactive drugs and surgical interventions for many years. With the advent of minimally invasive procedures like endoscopic perforator surgery (SEPS) there have been considerable advances in the surgical treatment of incompetent perforators over the past 10-15 years (1). At the same time, there have been no dramatic changes seen in the field of deep venous reconstruction, although endovascular technique (for example stenting chronic stenosis of iliac veins) seems to be a promising option (2). The objective of this paper is to give a short review of surgical treatment in chronic venous disease of the lower extremity and to analyse the results of surgical interventions that have been used at the author's institute over the past decade.

Patient selection and preoperative evaluation

Patients with severe symptoms (skin changes, leg ulcer, CEAP class. 4-6) are the main candidates for surgical treatment. The main objective in the preoperative evaluation is to assess whether patients can be candidates for successful surgical repair. For this reason, both morphologic tests and functional assessments are needed. The morphologic test should focus on revealing the location and extent of valve incompetence or venous obstruction. Apart from detailed history and thorough physical examination, the Duplex scan has become the basic tool in the diagnosis of chronic venous disease, although contrast venography still has some role in the evaluation (for instance prior to deep venous reconstruction and SEPS) (3). Some noninvasive tests, like plethysmography and radionuclide venography, appeared to be very useful in certain studies (4, 6). It should be noted, however, that the decision to operate should be based on the clinical status of the patient rather than on the diagnostic findings.

Surgery in superficial venous insufficiency

It is important to emphasize that pure primary superficial incompetence can lead to severe venous symptoms if not treated properly in time. Careful preoperative evaluation is mandatory with Duplex scan to assess the extent of superficial incompetence and to check deep veins. High ligation and stripping of the long or short saphenous vein is the treatment of choice. This is one of the most rewarding operations in vascular surgery: the patient with severe symptoms (such as a leg ulcer) will benefit a lot from a relatively simple procedure. If there is a postthrombotic incompetence of deep veins in conjunction with superficial insufficiency, abolishing superficial reflux alone may result in significant improvement of chronic venous symptoms. **(Figure 1.)**

Surgical treatment in perforator insufficiency

Perforating vein incompetence can be demonstrated as a causative factor in many cases of chronic venous insufficiency. Compression therapy, the Linton procedure and paratibial fasciotomy have been the most favoured treatments for many years. All have their disadvantages. In 1985, *Hauer* reported a minimally invasive technique of perforating vein dissection using an endoscope. Subfascial endoscopic perforator surgery (SEPS) has become an accepted method

Figure 1. Chronic venous insufficiency caused by pure superficial reflux.

Figure 3. Subfascial dissection during SEPS.

in the treatment of perforating vein surgery over the past decade (1). However, what the haemodynamic consequences of perforating vein interruption are is not clear. 61 SEPS procedures were carried out for severe chronic venous disease (predominantly on leg ulcer patients) at our department in the past 6 years. With the follow-up of 51 patients,

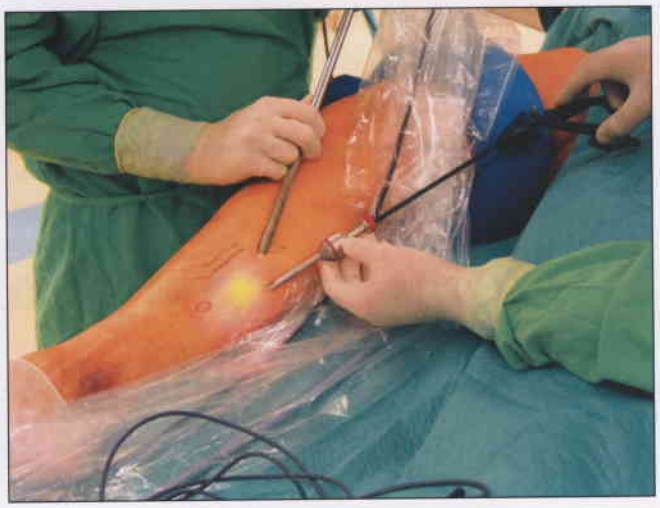

Figure 2. SEPS procedure. Two-port technique.

CEAP grade	Healed / Improved	Un-changed	Ulcer recurred
C_6 n = 40	25 (62%)	7 (18%)	8 (20%)
C_{4-5} n = 11	8	2	1
Total n = 51	33 (64%)	9 (18%)	9 (18%)

Table I. Mid-term clinical outcome after subfascial endoscopic perforator surgery. C_4: skin changes, C_5: healed ulcer, C_6: active ulcer.

a prospective clinical trial was carried out to assess mid-term clinical outcome and to analyse changes in calf muscle pump function with photoplethysmography (5). Clinical symptoms improved and proved to be durable in 33 (68%) of the 51 patients during the mean follow-up of 29 months (**table I.**). The clinical outcome appeared to be much more favourable in patients without postthrombotic incompetence of deep veins. The average venous refilling time of 33 patients who underwent photo-plethysmography increased significantly from 12.5 sec to 14.6 sec after SEPS confirming the beneficial effect on venous haemodynamics (**table II.**), (**figure 2., 3.**).

Deep venous reconstruction

Chronic obstruction

Chronic venous obstruction as a predominant cause of venous disease is rare. The majority of these cases result from the absence of recanalisation after deep venous thrombosis, mainly in the iliofemoral segment. The most commonly used diagnostic tests are contrast venography, Duplex scan, plethysmography and venous pressure measurement. It is important to evaluate the pressure gradient between the two femoral regions before planning a bypass operation. In our institute, dynamic radionuclide venography is used as a standard diagnostic procedure to assess morphology and haemodynamics prior to iliac vein reconstruction (6).

	Patients	VRT before SEPS (SD)	VRT after SEPS (SD)	P-value
Deep and perforator reflux	22	10.8 (3.8)	11.3 (3.4)	p = 0.17 NS
Superficial and perforator reflux	11	15.2 (4.3)	19.8 (5.2)	p < 0.001
Total	33	12.5 (4.5)	14.6 (5.9)	p < 0.05

Table II. Photoplethysmography results before and after SEPS.
VRT: Venous Refilling Time, SEPS: Subfascial Endoscopic Perforator Surgery, SD: Standard Deviation.

Phlebography findings	Improved	Unchanged	Total
Iliac vein occlusion and intact deep veins below	10 (83%)	2 (17%)	12
Iliac vein occlusion and postthrombotic deep veins below	14 (47%)	16 (53%)	30
Total	24 (57%)	18 (43%)	42

Table III. Long-term results of Palma operation according to phlebography findings.

Figure 4. Palma operation on a scheme and in the operation theatre.

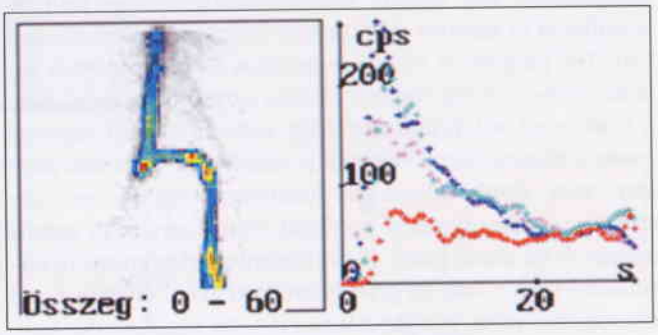

Figure 5. Dynamic radionuclide venography after Palma operation. Open Palma graft with good haemodynamics (steep time-activity curve).

Femoro-femoral crossover saphena bypass (Palma operation)

This is the most frequently performed procedure for chronic obstructive venous disease. Several authors have confirmed its efficacy in segmental chronic iliac vein occlusion (7). Over the past 15 years, more than 60 Palma operations were performed at our unit. The indication almost exclusively was postthrombotic occlusion of iliac veins. During the operation meticulous surgical technique and endvenectomy was used if the latter was necessary. A temporary arteriovenous shunt was not applied routinely.

A retrospective study of 42 patients was carried out to evaluate the long-term outcome (8). All patients had undergone the intervention for postthrombotic iliac vein occlusion. The mean follow-up time was 5.8 years. At the follow-up visit the patients were assessed by physical examination and radionuclide venography to check saphenous graft patency. It was also evaluated how distal (femoro-popliteal) postthrombotic damage observed at the time of the Palma procedure influenced the long-term outcome and graft patency. Our results confirmed that favourable clinical outcome and good long-term patency can be achieved after the Palma operation (69% at 6 years). Distal postthrombotic changes did not affect patency but the clinical outcome was significantly worse in these cases (**table III.**). Radionuclide venography has proved to be a valuable tool in the preoperative evaluation and postoperative follow-up. (**Figure 4., 5.**)

Surgical repair of incompetent venous valves

Surgical correction of the deep venous system should only be considered for these patients who have persistent, severe manifestations contrary to optimal compression treatment. Commonly, these patients undergo some type of superficial venous surgery prior to deep venous reconstruction. Assessment of clinical status should start with noninvasive tests, like Duplex ultrasonography and plethysmography. Prior to the operation, patients should undergo ascending and descending venography, which can distinguish between primary and secondary valve damage.

For primary deep venous reflux, *internal and external valvuloplasty* have proved to be durable surgical options. *Angioscopic assisted valvuloplasty and external banding* are new techniques with promising results (9).

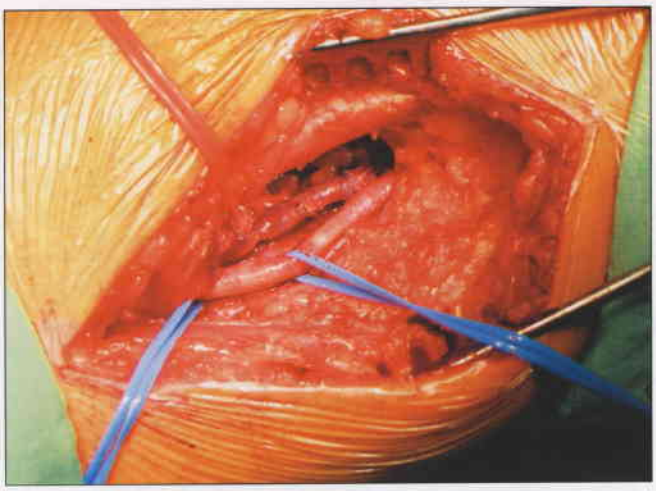

Figure 6. Axillo-popliteal venous segment transplantation.

For secondary (postthrombotic) deep venous reflux, vein transposition and venous segment transplantation can be considered in patients with severe symptoms (class C5 and C6). The purpose of *vein transposition* is to transpose a venous segment (long saphenous vein or profunda vein) with a competent valve into the deep vein. In *venous segment transplantation,* the donor site is usually the proximal axillary vein (with at least one functioning valve), and the recipient is the diseased popliteal vein. Long-term results appear to be much better if the transplanted segment is surrounded with a Dacron graft in order to avoid dilatation and consequent valve incompetence (10). At our vascular unit, we have also had some limited experience with the latter technique with a favourable outcome **(figure 6.)**.

Summary

Over the past decade, there has been a remarkable advance in the diagnosis and surgical treatment of chronic venous insufficiency. New, noninvasive diagnostic methods like Duplex scanning and minimally invasive surgical techniques like SEPS have become universally accepted and have proved their efficacy. In the meantime, many special vascular centres like ours have carried out different types of deep venous reconstruction in carefully selected patients with favourable clinical results. At the same time, there are still a lot of questions to answer. Large, multicentre, randomised trials are needed to compare the outcome of surgical procedures and optimal medical treatment.

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Diagnostic and minisurgical treatment of chronic venous insufficiency

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In the treatment of chronic venous insufficiency (CVI) it is very important to make an appropriate diagnosis, to measure and localise the haemodynamic failure before starting treatment. We do not want to mention all the diagnostic procedures, just the Phlebodynamometry and the Functional Doppler test.

To achieve good therapeutic results it is not always necessary to use difficult and expensive diagnostic and therapeutic procedures. Is is more important, especially among patients with CVI, to have a method which is as atraumatic as possible. These patients have vulnerable tissue and edemas, so a radical procedure could damage the tissue and as a result the edema will be worse than before.

Diagnostic

Phlebodynamometry according to Várady

Varicose veins are not only an anatomical problem but also a haemodynamical one. With the patient in a standing position large varicose veins are visible which disappear when the leg is elevated because the venous pressure drops.

This method makes possible a judgement about the haemodynamic situation, the transporting capability of the according veins and of the valve function.

Measured are the hydrostatic pressure P_1, then the pressure under maximal strain P_2, the pressure under strain and occlusion $P2_{Occl}$ and finally the time for regain of the filling of the veins t_0.

As is well-known the most important parameter here is the pressure drop $\Delta P = P_1 - P_2$ which can be determined very accurately (**figure 1**).

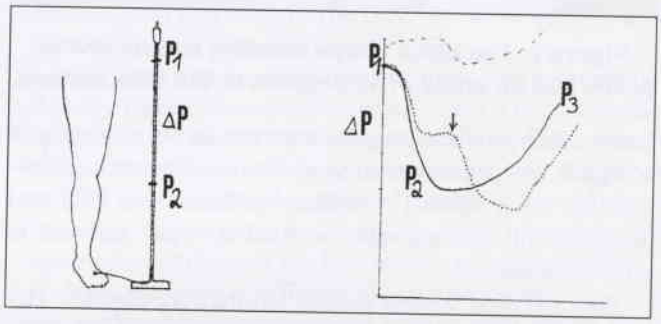

Figure 1. The most important parameter is the pressure drop. $\Delta P = P_1 - P_2$.

The regain of the filling of the veins is also important but it comes only in second place behind the pressure drop.

The functional Doppler test with flat probe

For many years phlebologic diagnosis has been unthinkable of without the Doppler probe. Generally the pen probe is used which is permanently installed on most devices. The test is performed on the resting patient. With this method among others the insufficiency of the venous valves is demonstrated, perforating veins are localised and a deep venous thrombosis is diagnosed with more or less certainty. For these applications the pen probe is sufficient, which is placed upon the skin in at an angle of 45^0 while the patient is lying down or standing upright. If the patient moves then the probe cannot be held in the correct position and so valid results are not achieved unless it is a static test.

Especially in recent years functional testing methods have become more important, primarily blood phlebodynamo-

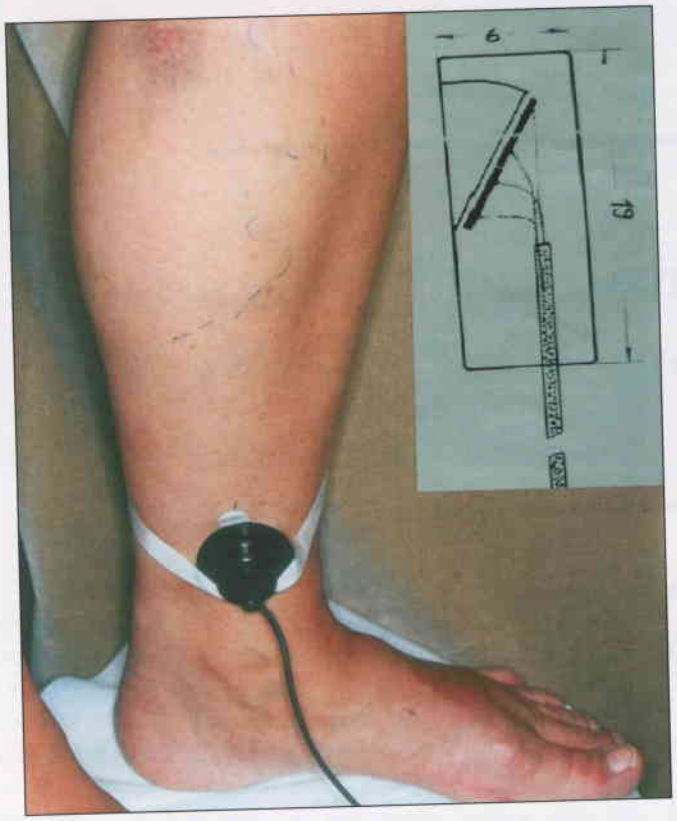

Figure 2. The block shape sending and receiving probe has an angle of 45 degrees to the skin surface.

metry which produces very accurate results but was not well accepted by patients because of the inconvenience. Therefore by using several bloodless methods like PPG and occlusion plethysmography it tried to find answers to different questions.

Thus the tests are less precise but they are painless. However before purchasing expensive instruments it should be considered whether testing can be extended using the instruments already available.

Description of the probe: the probe has a block shape. The sending and receiving unit is located inside at an angle of 45 degrees to the skin surface (**figure 2**).

What are the answers the test can give?

On one side there is the formulation of the question of PPG and on other side that of phlebodynamometry. An answer to both is given by the dynamic Doppler test because it combines the method of the ordinary Doppler probe with the results of phlebodynamometry an exercise programme.

Phlebodynamometry is mentioned here as far as comparison with the Doppler test makes it necessary. It gives the same results but with a bloodless technique: with phlebodynamometry the pressure is determined, based on the flow velocity.

The procedure is similar to the bloody venous pressure test: the first measurement is made on the motionless patient. Then the patient bends his knees several times until the pressure does not drop any further, i.e. the curve does not change any more. Now the occlusion test follows where the

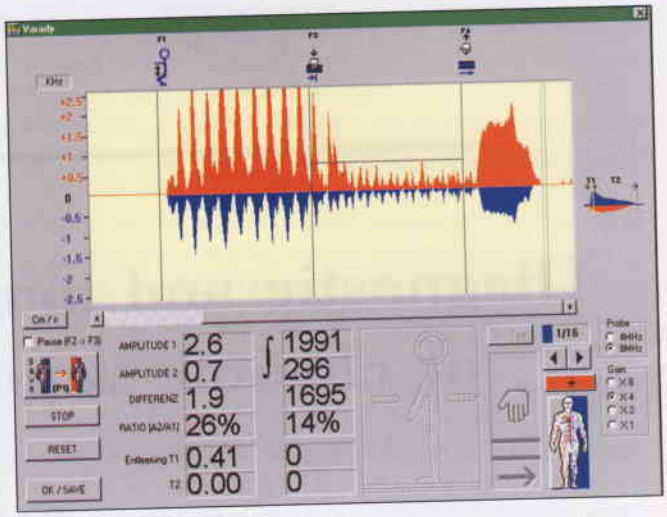

Figure 3. Functional Doppler curve of extensive varicosis with valve insufficiency.

vein is shut off by finger pressure or with a special cuff. This gives P_{2Occl} (pressure under maximum strain and occlusion). After this the filling regain curve is drawn with the patient standing still. This makes the same conclusions possible as with PPG + phlebodynamometry as well as giving more information.

The result is the following: you get more information than with PPG and phlebodynamometry but with a bloodness test. For the last few years we have been using a computer programme which gives more information and makes calculations automatically.

The description and interpretation of a sample curve: extensive varicosis with valve insufficiency (**figure 3**).

Phase 1. The curve shows respiration-synchronous movement of the blood with low velocity caused by large calibre veins with valve insufficiency producing a counter-pressure.

Phase 2. It can be observed how through the effect of the muscular pump the stasis is reduced, indicated by a large increase in the flow velocity. The substantial amplitude indicates a large amount of regurgitated bloodflow.

Phase 3. This shows the situation during the occlusion test: the blood is drained through the deep venous system. Because the v. saphena magna and the varicose veins are shut off the amount of regurgigated bloodflow has diminished substantially (low amplitude).

Phase 4. The last part of the test can be observed: while the patient is standing still the blood flows back into the varicose veins at high velocity, which shows that these were extensively emptied before. If the patient is standing and the occlusion persists the perforating venous valves can be tested.

Basic parameters

Pumping performance. Amount of blood (ml) over a period of time (integral of blood velocity over period of time = area under the curve).

Figure 4. The Phlebextractor has two ends: one is a hook and the other one is spatula.

Pumping power. Amount of decrease of drained blood volume (the ascending curve = changing of the blood velocity).

Healthy leg. Normal blood volume, which is drained quickly. Refilling minor and slow (small amplitude and minor slope of the curve).

Large caliber varicose veins with free deep vein. Large blood volume with little change during strain. Indication of oscillating blood.

Occlusion test: drain through the deep vein.

a/ Fast drop of the amplitude.

b/ Small area under the curve.

Refilling quick with large blood volume.

Acute deep venous thrombosis clinically typical. The leg is swollen, there is only a little blood present which is not drained during movement, thus venous pressure is even increased.

Therapy

Besides the basic compression therapy it is necessary to remove insufficient varicose veins to decrease the hemodynamic failure.

The majority of patients suffering from varicose veins are women, and this implies that not only medical but also cosmetic aspects have to be considered in therapy. Often stripping is combined with fairly large and numerous cuts to extract branches. In many cases scars after traditional surgery are more annoying for the patient than the varicose veins before. Besides this many develop edema because of the destruction of lymphatic vessels. Therefore it is of the greatest importance to have a method in mind which includes both aspects.

Many had throught of removing varicose veins through micro-incisions. Using more or less appropriate small hooks they tried to extract varicose veins without considering that veins are fixed in their surrounding tissue. Therefore neither the technique nor the instruments used were suitable to get any further with this problem. About twenty years ago I developed a method for which the German company Aesculap provides the necessary instrumentation. It is the first method based on surgical principles together with matching surgical instruments, the Phlebextractor and the Phlebodissector, by which modern minisurgery of varicose veins could be established.

Figure 5. Long varicose vein section can be removed from a tiny incision.

Materials and methods

Instruments **(figure 4).** The Phlebextractor has two ends: one is a hook and the other is a spatula. This is really two instruments in one with different functions, so it is not necessary to switch very often. The spatula is firm, arced and not flexible. We use different Phlebextractors for all kinds of situations, as there are large calibre varicose veins, reticular veins and spider veins.

The Phlebodissector has spatulas on both ends which are flexible, thin and longer. The firm spatula is used first and the flexible one thereafter.

The big difference from other methods and instruments is that my Phlebextractor does not have just a hook but also a spatula, and with this new concept or method it is possible to prepare varicose veins over a long range and it is not necessary to make a large number of incisions. So, besides the specially shaped hook the spatula is most important. With these new instruments the best results will be achieved.

Method of surgery **(figure 5).** Tiny incisions 3 to 5 mm) are made with a special micro scalpel with which no big cuts can be made accidently. By using the spatula-end of the Phlebextractor veins are loosened in each direction. After this the instrument is turned around, and with the other end (the hook) the vein is pulled out. With your fingers you can imprint the skin in order to find and feel the vein more easily. The hook is pressed against the fingertip, locating the vein between them. So the vein is found easily and no nerve can be hurt because this would be noticed instantly.

The loosened vein is grasped with the mini-Mosquito forceps. Under continuous pulling with the mini-Mosquito the vein is prepared further with the help of the spatula. The tip of the spatula must point towards the skin. You must be able to feel the tip, in order not to hurt anything. Having pulled out the vein a second incision is made 5 to 15 cm from the first incision. The location depends on how far the vein can be prepared. This consideration distinguishes minisurgery from other methods. Now the other end of the vein is loosened and the whole vein section can be removed. A cutaneous suture is rarely necessary.

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Chronic venous insufficiency in congenital vascular malformations

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Introduction

The blood vessels of the extremities develop in the 5-10th week of embryonic life, in three stages: capillary, retiform and truncular (5, 6, 10).

Extratruncular venous malformations and arterio-venous (a-v) shunts in disturbances of the retiform phase come into existence because of disontogenic influences.

In the truncular phase the great blood vessels develop. In the middle of the extremity bud the artery develops and from it both the marginal veins develop. The neighbouring deep veins appear later in the 12-14th week. After birth the marginal veins largely regress: from the fibular group there remains only the vena saphena parva, and from the dorsal group the ischiadic vein (the connection of the femoral-ischiadic veins). Later in the 12-15th week dysontogenetic effect may cause *the persistence of the marginal veins, aplasia, hypoplasia, stenosis, dilatation of the truncular veins* (3).

In the Hamburg Classification the malformation is first classified by the predominant component of vascular defect (e.g., arterial, venous, arteriovenous [AV] shunting, combined or lymphatic): then it is further classified according to truncular or extratruncular form, depending on the embryonic stage at which developmental arrest occurs and remaines through (1).

The inborn errors may be influence with age changing the circulation of the extremity to a high degree.

Material and methods

We have seen the change of venous pressure according to age, the change of LDH activity in the venous blood of the extremity, and we have made blood-gas analysis according to age. These parameters were seen in the cases of vascular malformations of the extremities (9).

Results

In the case of venous malformations the following changes occur, owing to reduced circulation:

– total blood flow of the extremity decreases,

– LDH activity decreases in the tissues,

– oxygen consumption increases (pO_2 decreases),

– venous pressure increases or decreases,

– stagnatic hypoxia in the tissues,

– hypotrophy of the extremity.

Consequences of this chronic venous insufficiency are the angio-osteohypotrophic or angio-osteohypertrophic syndromes.

Angio-osteohypotrophic syndrome is:

– in the hypoplasia of the artery and vein,

– in diffuse deep and superficial phlebectasias,

– in numerous deep extratruncular infiltrating malformations.

Case 1.
Diffuse deep and superficial phlebectasias, dilatation of veins

Nevus, varicosity and hypotrophy of the extremity (**figure 1**).

Treatment: after step-by-step resection of the marginal vein, and formation of valvulas, the progression was reduced.

Figure 1. Nevus, varicosity and hypotrophy of the extremity.

Figure 4. 2 month-old infant: naevus and varicosity.

Case 2.

Numerous deep extratruncular infiltrating venous malformations

Phlebectasias, hypotrophy of the extremity and osteoporosis, focal osteolysis (**figure 2, 3**).

Angio-osteohypertrophic syndrome is:

– in the AFV truncular,

– in the aplasia of the deep vein, (+AVF),

Figure 2., 3. Phlebectasias, hypotrophy of the extremity and osteoporosis, focal osteolysis.

Figure 5. Phlebography of the same child.

– in the aplasia of the deep vein with embryonic vein (+AVF),

– in the hypoplasia of the deep vein with marginal vein (+AVF),

– in diffuse infiltrating venous defect and intact deep vein.

Figure 6. At the age of 15 expressed varicosity, trophic disturbances on the leg and bone hypertrophy.

Case 3.

Aplasia of the deep vein

2 month-old infant: Nevus, varicosity (**figure 4, 5**).

At the age of 8 mild bone hypertrophy, venous pressure, pO_2 increased

– because of the A-V shunt. At the age of 15 expressed varicosity, trophic disturbances, bone hypertrophy, increased pO_2 in the vein (**figure 6**).

In this case and at the arteriovenous shunt:

– the total blood flow of the extremity increases,

– LDH activity increases,

– oxygen consumption decreases (high pO_2),

– venous pressure grows,

– circulatory (hypoxic) hypoxia in the tissues,

– hypertrophy of the extremity because of parasitic circulation.

Treatment: skeletonisation of the embryonic vein or resection of superficial truncular a-v communications together with efferent phlebectasias.

It is important to note that in cases of venous malformation in childhood, bone hypertrophy is noticeable only in association with a-v fistulas. The opening of the shunt in cases of venous malformations is mostly noticeable at the age of 6-10 years. To a certain extent the outcomes are milder if the persistent marginal vein is accompanied by the hypoplasia of the deep vein.

Case 4.
Hypoplasia of the deep vein, persistent marginal vein

2 year-old boy – nevus, varicosity, hypoplastic deep vein and marginal vein (**figure 7**).

At the age of 12 mild hypertrophy of the extremity, increased pO_2 in the vein.

Treatment: step-by-step resection of marginal vein – to re-route the venous flow from the superficial dilated veins to the hypoplastic venous trunk.

Discussion

Vascular malformations have a great influence on the haemodynamics and metabolism of the extremity.

In cases of venous malformations reduced circulation, decreased or delayed blood flow and stagnation hypoxy – chronic venous insufficiency – cause the hypotrophy of tubular bones (4).

In some forms of venous malformations reduced circulation (aplasia, hypoplasia, stenosis of deep veins) bone hypertrophy is noticeable, in association with a-v fistulas. The pathogenetic connection between decompensated venous reduction and the opening of short circuits was indisputably proved by the experiments of *Soltész* (7). According to my experience in cases of venous malformations there is no hypertrophy and shunt immediately after birth. The opening of the shunt and bone hypertrophy is mostly noticeable at the age of 6-10 years (8, 10).

By early adequate planned treatment at the age of 3-8 years we can prevent serious consequences of vascular defects from decompensated venous reduction and the opening of the shunts.

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Figure 7. Phlebography of a 2 year-old boy who has nevus and varicosity. Margial vein and hypoplastic deep vein can be seen.

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