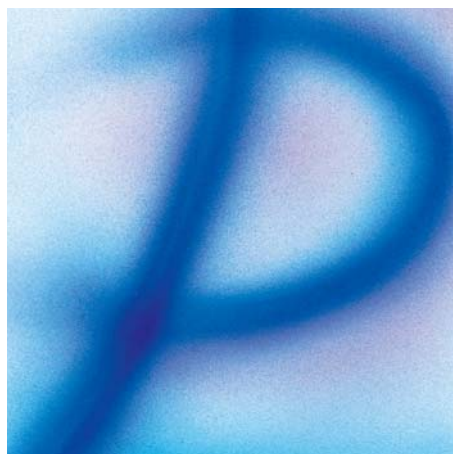


PHLEBOLOGY

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AIMS AND SCOPE

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

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

Phlebology is scientifically supported by a prestigious editorial board.

Phlebology has been published four times per year since 1994, and, thanks to its high scientific level, was included in the EMBASE and Elsevier BIOBASE databases.

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New!

**A look back:
four years of Phlebolympology
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Edema is one of the leading symptoms of acute and chronic venous diseases. As demonstrated in **Pascal Priollet's** contribution to this issue of Phlebology, many other disorders may also cause edema of the lower extremities. This can make differential diagnosis difficult, since a wide spectrum of various pathologies must be considered, sometimes occurring in addition to varicose veins or venous insufficiency.

It is not surprising, therefore, that leg edema is a frequent finding, even in the general population.

However, phlebologists, who are aware of the high incidence of varicose veins, may be surprised to learn that in a large population of more than 3000 individuals (not patients) leg edema was found nearly as frequently as varicose veins. In total, 13.4% of the population had manifest leg edema (CEAP C3) and 14.3% had large varicose veins (CEAP C2). These results are presented by **Eberhard Rabe and Felicitas Pannier** and summarize the highlights of their Bonn study. One of the strengths of this epidemiological study is the fact that a duplex examination was performed in every individual case and that, based on these examinations, the population was described and categorized according to the CEAP classification.

An interesting multicenter study from the Czech Republic shows that pain after conventional varicose vein surgery seems to depend on several technical details. **Lenka Veverková**, from Brno, and coworkers were able to demonstrate that the administration of two tablets of Daflon 500 mg may have reduced pain and bruising.

Foam sclerotherapy is currently one of the hottest topics in phlebology, stimulating the interest of an increasing number of colleagues. **George Geroulakos**, an academic vascular surgeon, gives a convincing overview of our present knowledge of this technique for treating varicose veins. In reading his article, it seems clear that this method is poised to present an increasingly challenging competition for classical varicose vein surgery. This is obviously especially true for patients with venous ulceration and vascular malformations, cases that are not very attractive to vascular surgeons, in general. However, more studies are needed, especially for the promising indication of abolishing long refluxes in the saphenous veins using foam in order to promote faster ulcer healing.

Last but not least, a true specialist in this field, **Marianne de Maeseneer**, from Antwerp, Belgium, gives an eloquent review of the different methods that have been used may to prevent neovascularization after varicose vein surgery. Endovenous procedures may be a promising alternative.

Enjoy your reading!

Hugo Partsch, MD



Venous edema of the lower limbs

Pascal PRIOLLET

*Vascular Medicine
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Chronic venous disorders of the lower limbs are manifest by many noticeable, but few specific, clinical signs. In France, some 18 million persons suffer from pain in the legs and 12 million may have varicose veins. Over 200 000 hospital admissions per year may involve venous disease, two-thirds of which require surgical management. Slightly more than 5% of cases of sick leave from work may be related to venous disease and the functional signs that accompany it, amounting to millions of lost workdays. Thus, without a doubt, venous disease is a problem of public health.

VENOUS EDEMA OF THE LOWER LIMBS – WHICH MECHANISM IS INVOLVED?

Edema is an accumulation of fluid in the extracellular compartment, which results in an increase in the volume of interstitial fluid. Physiologically, a balance exists between intravascular hydrostatic pressure and oncotic pressure on the one hand, and interstitial pressure on the other. Transcapillary hydrostatic pressure tends to drain fluid from blood vessels, whereas oncotic pressure, which is associated with protein concentrations, tends to produce fluid retention in blood vessels. A decrease in oncotic pressure (hypoalbuminemia) and/or an increase in hydrostatic pressure (heart failure) lead to an increase in salt and water in the interstitial compartment. Proteins pass through the wall of the blood vessel when venous and lymphatic microcirculation is impaired.¹

CAUSES OF LOWER-LIMB EDEMA

Generally, the causes of lower-limb edema are suggested by the clinical examination of the patient. The clinical interview should aim to identify a previous history of the condition, evaluate the acute or chronic feature of edema, and look for possible precipitating factors. Clinically, the examination should identify whether the edema is isolated or diffuse, painful or not painful, its consistency, the existence of urticaria-like lesions suggesting angioedema, the existence of a serous effusion (peritoneum, pleura), signs of thromboembolic disease, and clinical evidence of internal organ disease (heart, kidney, liver).^{1,2}

Diffuse edema

Keywords:

edema, lymphedema, venous insufficiency, phlebology.

In heart failure, increased ventricular filling pressure exists as well as increased pressure in the entire upstream plasma compartment. Furthermore, decreased cardiac output produces renal hypoperfusion, which worsens salt and water retention. Cardiac edema is related to right ventricu-

lar failure. The latter can complicate left ventricular failure, pulmonary disease, or pericardial disease. The first signs of salt and water retention are weight gain and oliguria. Edema subsequently occurs and, as a result of orthostatic posture, most often remains confined to the lower limbs. Edema may also be localized to the patient's back in the case of bed rest. Other signs of right ventricular failure are painful hepatomegaly with hepatojugular reflux and turgescient jugular veins.

In hepatic cirrhosis, the mechanism responsible for edema is multifactorial. The decreased oncotic pressure associated with hypoalbuminemia resulting from a lack of protein synthesis due to hepatocellular failure is the initial cause of salt and water retention. Its association with ascites related to portal hypertension amplifies the process by creating an obstacle to venous return. The existence of **kidney disease** also contributes to formation of edema. Clinically, this type of edema has the same features as cardiac edema and is associated with signs of hepatocellular failure and portal hypertension.

The primary causes of lower-limb edema related to kidney disease are *nephritic syndrome*, *nephritis*, and *chronic renal failure*.

- **Nephritic syndrome** is defined as proteinuria greater than 3 g/24 hr, hypoalbuminemia less than 30 g/L, and hypoproteinemia less than 60 g/L. Loss of albumin via the kidney is responsible for the decrease in oncotic pressure with salt and water retention. This form of edema involves the lower limbs, but also the upper limbs and face.
- **Nephritis** is characterized by a primary abnormality in the nephron, which causes fluid retention, and is mainly related to kidney disease. Increased intravascular hydrostatic pressure produces passage of fluid into the interstitial compartment. Generally, proteinuria remains moderate, and hematuria, hypertension, and organic renal failure may occur. This edema has the same features as nephritic syndrome-related edema.
- In the event of **chronic renal failure**, the existence of edema reflects a salt and water intake exceeding losses. It develops at a late stage in the course of renal failure.

Edema occurring in the context of **gastrointestinal disease** is associated with hypoalbuminemia, which

can be related to either inadequate protein intake as a result of malnutrition (Kwashiorkor, marasmus) or to excessive losses due to malabsorption (inflammatory bowel disease, surgical resection, exocrine pancreatic failure), or due to increased venous-lymphatic pressure in the setting of exudative enteropathy. In the case of malabsorption, hypoalbuminemia is associated with iron deficiency, hypocalcemia, and vitamin B, D, and K deficiencies. Useful laboratory tests include the measurement of steatorrhea, the d-xylose test, and the Schilling test. Increased clearance of α_1 -antitrypsin establishes the diagnosis of exudative enteropathy.

Idiopathic cyclic edema, an entity that affects young women of childbearing potential, produces edema in the face and upper extremities in the morning, and subsequently affects the lower limbs later in the day. The pathophysiology of this disorder has not been elucidated, but capillary hyperpermeability exists.

Hereditary angioneurotic edema, associated with C1-esterase inhibitor, manifests itself as more or less acute episodes of diffuse edema. Decreased titers of the C4 fraction of complement at the time of an acute episode should lead to a measurement of C1-esterase inhibitor.

Drugs can cause edema that is often moderate and remains limited to the lowermost, dependent anatomical areas. Certain drugs alter capillary permeability (calcium channel blockers, nitrates). Others produce salt and water retention of renal origin: nonsteroidal anti-inflammatory drugs (NSAIDs), steroids, and estrogen-progestin combinations. Finally, some drugs directly provide a sodium quantity (intravenous penicillin, oral alkalinizing agents, gastric mucosa protective agents, lithium).

Hypo- and hyperthyroidism, and increased plasma estrogen concentrations during the premenstrual syndrome (PMS) can also be accompanied by edema. Long-term intake of diuretics may affect the renin-angiotensin regulation and lead to resistant edema.

Edema limited to the lower limbs

An acute, swollen, red leg with fever, generally above 38.5°C (101.3°F), and laboratory data evidencing infection (leukocytes, inflammatory syndrome) suggest the

diagnosis of **erysipelas**. The causative organisms most commonly responsible are *Streptococcus* and *Staphylococcus aureus*. Necrotizing fasciitis is a very serious complication with signs of sepsis and local progression marked by the occurrence of blisters and skin necrosis.

Edema can be of venous origin as a result of **primary venous disease**, venous thrombosis, an extrinsic obstacle to venous return, or a syndrome with malformations such as Klippel-Trenaunay syndrome. The clinical examination supplemented by duplex ultrasonography confirms the suggested diagnosis. Measurement of d-dimers is useful when a venous thrombosis is suspected.

Lymphedema of the lower limbs, whether congenital, primary, or secondary, is a cause of increased limb size.³ Congenital lymphedema may be hereditary (Millroy's syndrome) and starts at birth. Primary lymphedema develops in childhood or adolescence (Lymphedema praecox), or after the age of 35 years (Lymphedema tardum). Hereditary lymphedema starting in puberty has been called Meige's syndrome. In some forms of lymphedema, genetic defects could be detected (eg, Turner's syndrome, yellow nails syndrome). Secondary lymphedema occurs following surgery (lymph node dissection, bypass grafting, venous surgery), radiotherapy, or due to tumor extension. It can also be related to compression of a structure or occur in the context of venous disease, whether advanced primary venous insufficiency or related to postthrombotic syndrome. Lastly, a specific context can guide the physician to the possible diagnosis of filariasis.

Other causes

In other cases, the recent history will guide the clinician, eg, a notion of pain and edema that occurred suddenly following exertion suggests a muscle strain, or tendon rupture, or a muscle compartment syndrome if an interval exists between the exertion and pain, and edema. In the absence of prior exertion, the possibility of a popliteal cyst rupture, a popliteal aneurysm rupture with signs of ischemia, or revascularization-related edema following late-stage elimination of ischemia should be considered.

Algoneurodystrophy, Lyme disease, periarteritis nodosa, bone tumors, muscle sarcomas, arthritis, and retroperitoneal fibrosis are other causes of lower-limb

edema. Charcot's blue edema associated with self-inflicted injury by placement of a tourniquet is a differential diagnosis.

Lipedema denotes a symmetrically increased lower-limb size associated with excessive adipose tissue extending from the hips to the ankles, but sparing the dorsal aspect of the foot. This condition is observed mostly in obese women, starting at puberty. It is a clinical entity different from lymphedema, but which can be confused with it. The dorsal aspect of the foot is not affected, at least in the early stage of development. The infiltrated area shows soft, nonpitting edema that is painful to the touch, which differentiates lipedema from lymphedema.⁴

Venous edema

Venous dysfunction is related to a primary defect in the venous valves of the superficial or deep veins, post-thrombotic deep vein valvular incompetence, incompetent distal perforator veins, deep vein valvular dysgenesis, dysfunctioning of the muscle pump, or compression that impedes venous return. Venous insufficiency generates venous stasis and increases ambulatory distal pressure, which is the cause of the vicious circle of events. Induced venous dilatation results in a defect in valvular coaptation. Increased venous pressure is the cause of microangiopathy, which is the source of skin trophic changes.^{5,6}

The patient with venous disease is evaluated by means of an interview, to look for factors precipitating the condition, and a clinical examination, with the patient erect, preferably on a platform, and alternating his or her weight on one foot, to examine the entire limb, the suprapubic area, and abdomen.

Edema of chronic venous disease, in particular, is sporadic, unilateral or bilateral, has no component of inflammation, is limited to the legs, but may also involve proximal parts of the lower extremity, is enhanced by prolonged orthostatic posture, and is improved by raising the legs.

Venous edema manifests itself as a "large cold leg" whose etiological diagnosis, guided by the clinical context in which the edema is progressing, can be extensively investigated with duplex ultrasonography. On examination, venous edema is variable in intensity,

tending to be soft. Increased warmth of the skin often exists, as well as a cyanotic presentation when the patient is in an orthostatic position. When edema becomes chronic, thickening of the skin and lymphedema may develop. The combination of edema and varicose veins, ankle telangiectasia, hyperpigmented dermatitis, white atrophy, cutaneous sclerosis, and eczema or venous ulcers on the lower leg, is a good indication of the venous origin of the edema.

Sequelae of deep vein thrombosis with destruction or alteration of valvular functioning—an obstacle to venous return due to occlusion, or more rarely, compression—generate venous-related edema. In **post-thrombotic disease**, edema is dependent on the degree of venous recanalization, the extent of valvular incompetence, and the development of a collateral circulation. The diagnosis is established relatively easily when the patient is known to have a documented past history of venous thrombosis. When thrombosis has gone unnoticed clinically or an episode of edema has not led to laboratory investigations, in some cases, duplex ultrasonography can identify sequelae of thrombosis and guide the diagnosis. **Valvular hypogenesis or agenesis** is a rare cause of edema. Postthrombotic disease is not the only possible cause of a “large cold leg” of venous origin. A compressive cause should also be sought, in particular, compression from a tumor, benign or malignant, located in the pelvis.

May-Thurner syndrome (venous spur, iliac compression syndrome), corresponds to compression of the left common iliac vein by the right common iliac artery. This anatomical abnormality is asymptomatic in most cases, or can manifest itself as unilateral edema of the left lower limb and can be enhanced by exertion. It is also responsible for the predominant occurrence of iliofemoral deep vein thrombosis on the left side.

Deep vein thrombosis is often responsible for unilateral edema of recent and rapid onset. It can be accompanied by a slight fever. Clinical signs, while nonspecific and not always present, can guide the clinician and include pain, collateral venous circulation, increased local warmth, loss of mobility, and cyanosis. Use of a clinical score allows the clinician to evaluate the probability of the diagnosis, but it is essential to confirm it with duplex ultrasonography within the first 36 hours, after initiating emergency anticoagulant therapy. A low clinical probability in combination with negative

d-dimers, determined by the enzyme-linked immunosorbent assay (ELISA) method, rules out the diagnosis of venous thrombosis as a result of the excellent negative predictive value of d-dimer.

The heavy legs syndrome

Heavy legs syndrome is one of the **most common manifestations of chronic venous disease**; it is a sensitive, but nonspecific symptom (*Table I*). It is described more often by women than men with a prevalence of 30% to 50%.^{7,8} It is not always associated with the existence of varicose veins, but sometimes with superficial venous reflux.⁹ This subjective impairment tends to affect young women. It can be constant, occur solely on exertion, or in orthostatic posture, particularly at the end of the day, and can be isolated or accompanied by edema and other signs of venous insufficiency. It invol-

With edema

- Primary superficial chronic venous disease
- Primary deep chronic venous disease
- Postthrombotic syndrome
- Constant venous compression
 - Lymph node affections
 - Tumors
 - Retroperitoneal fibrosis
 - Arterial aneurysm
- Sporadic venous compression
 - May-Thurner syndrome (Cockett's syndrome)
 - Pregnancy
- Lipodystrophy
- Primary or secondary lymphedema
- Lower-limb lymphedema of whatever cause
- Hypothyroidism
- Pretibial myxedema

With erythema

- Erysipelas
- Hypodermatitis
- Lyme disease
- Sarcoidosis

Occurring on exertion

- Peripheral arterial disease
- Narrow lumbar spinal canal
- Paraparesis and other neurological deficiencies

Table I. Primary causes of heaviness in the legs (based on ref. 11).

ves a sensation of heaviness or tiredness and swelling of the legs that is exacerbated at the end of the day, after prolonged standing, and pacing back and forth. Heavy legs are frequent symptoms in patients with occupations requiring prolonged sitting, or those who experience weight gain, a sudden reduction in muscular activity, or exposure to heat. Severe premenstrual syndrome, pregnancy, and estrogen-progestin combinations (the "pill") are factors that amplify such disorders.

The pathophysiology of heavy legs syndrome has not been elucidated with certainty. The circumstances of occurrence suggest a link with venous stasis, especially since symptoms are improved by a healthy lifestyle (not being overweight, regular physical activity, etc), methods of hydrotherapy, and venous tonic medicinal products. An epidemiological link exists with edema, independent of the severity of varicose veins and the existence of skin-trophic changes. Thus, in many cases, subclinical edema may exist, but also concomitant minimal functional lymphatic insufficiency, which can formally be demonstrated.¹⁰

All of the causes of venous edema mentioned in the above can be responsible for the sensation of heaviness in the legs: superficial or deep primary venous insufficiency, postthrombotic disease, and venous compression.¹¹

Lymphedema can also generate lower-limb heaviness. The mechanisms involved in the symptoms of chronic venous disease are poorly understood. In this field, epidemiology may detect several risk factors. This approach must be further improved by the use of methods that investigate venous physiology and microcirculation. In addition to good clinical evaluation and the use of ultrasonographic methods, when jointly applicable to a decision regarding treatment, management of chronic venous disease should include knowledge of the patient's socio-occupational context, as well as a documented approach to treatments, their usefulness, their mechanisms of action, long-term efficacy, and limits. Elastic compression therapy is useful whatever the clinical presentation of the disease and may be used in combination with measures to promote a healthy lifestyle and diet. Phlebotropic agents can be started as soon as symptoms occur.



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What have we learned from the Bonn Vein Study?

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ABSTRACT

Between November 2000 and March 2002, the German Society of Phlebology, in cooperation with the German Ministry of Health, performed the Bonn Vein Study in the city of Bonn and two rural townships. The participants were chosen from a simple randomized sample taken from the population registers. In total, 3072 (1722 women, 1350 men) participants between 18 and 79 years of age were investigated. Only 9.6% of the population (13.6% men, 6.4% women) showed no signs of venous disorders (C0) according to the CEAP classification, while 59.1% (58.4% men, 59.5% women) showed only telangiectasias or reticular veins (C1). In 14.3% (12.4% men, 15.8% women), varicose veins were present without edema or skin changes (C2), while 13.4% (11.6% men, 14.9% women) had pitting edema of the lower limbs at the time of the investigation (C3). Only 2.9% (3.1% men, 2.7% women) showed CEAP stage C4 with skin changes, like eczema, pigmentation, or lipodermatosclerosis. Even fewer, 0.6%, showed healed venous ulceration (C5) and active venous ulcers, 0.1% (C6). The frequency of more severe chronic venous signs, like eczema, pigmentation, lipodermatosclerosis, or venous ulceration has markedly decreased in the last two decades. This may be due to the fact that diagnostic and therapeutic options were applied more frequently within this period.

INTRODUCTION

Epidemiological evaluations of chronic venous disease were performed in many countries. Most of these were focused on varicose veins.¹⁻¹² In reviewing this data, some principal problems arose. Different definitions were used for either varicose veins or chronic venous insufficiency (CVI) in the studies.¹⁰ The investigated age groups also varied and different definitions were used. Only in very few cases was the investigated population based on a random sample of the general population. In many studies, only anamnestic data from questionnaires was used. In the earlier studies, the prevalence of varicose veins ranges from 1% to 73% in females, and 2% to 56% in males, while chronic venous insufficiency ranges from 1% to 40% in females, and from 1% to 17% in males.¹ Results vary by geographic region as well as by the methods used for evaluation. The incidence of varicose veins per year in the Framingham study was 2.6% in women and 1.9% in men.³

Keywords:

epidemiology, varicose veins, chronic venous insufficiency, general population, Bonn Vein Study.

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FORMER EPIDEMIOLOGICAL STUDIES

One of the larger studies of the late 70s was the Tübinger Study. The participants were between 20 and 75 years of age. The results were based on a standardized questionnaire and on standardized photographic documentation of the legs.⁷ For classification of the findings, the Widmer classification was used. In this study, only 14% of the population showed no venous changes while 51% had corona phlebectatica and slight venous changes (Widmer I), 40% had marked varicose veins with clinical relevance, and 13% had severe chronic venous insufficiency with skin changes up to venous ulceration. In this study, 76% of the women and 57% of the men had leg complaints thought to be typical of venous complaints (eg, heaviness). Finally, 2.7% had healed or active venous ulcerations.

In the 90s, the most representative population-based study concerning the prevalence of chronic venous disease came from Great Britain. The Edinburgh Vein Study examined a randomized sample of 1566 men and women taken from the registers of general practitioners in Edinburgh. The subjects, who were aged between 18 and 64 years, were asked to complete a standardized

questionnaire and were investigated clinically and by duplex sonography. Forty percent of the male and 32% of the female population had saphenous varicose veins. More than 80% had telangiectasias or reticular veins. Chronic venous insufficiency classified by the Widmer classification in stages II and III was found in 9% of the male and 7% of the female population. In agreement with the Tübinger study, the Edinburgh Vein Study showed a significant increase in prevalence of chronic venous disease with age.^{2,6,13}

In recent years, three studies have been published that are based on the CEAP (Clinical, Etiological, Anatomical, Pathophysiological) classification.¹³ However, their mode of recruitment of the study population, age range, and mode of investigation vary (*Table I*).¹⁴⁻¹⁶

In one study, 40 095 Polish adults were interviewed and clinically investigated by 803 participating primary care physicians (general practitioners, internists, gynecologists) in a cross-sectional multicenter study.¹⁵ C of CEAP (highest clinical severity) was used to classify the patients. CVI was diagnosed when any of the stages C1 to C6 was present. Leg complaints were reported in up to 81% of the varicose veins group and up to 35% of the varicose-free participants. C0 was found in 51.1% of the

	Polish Study ¹⁵	French Study ¹⁴
Design	Cross-sectional survey of consecutive patients from outpatient clinics	Cross-sectional survey of patients from telephone lists of primary care physicians
Investigators	Primary care physicians	Trained vascular medicine physicians
Participants	40 095	409
Males	6 404	277
Females	33 691	132
CVI definition	C1 – C6	Skin trophic changes
Classification	All	Men Women
	%	% %
C0	51.5	48.7 including C1
C1	16.5	
C2	21.8	23.7 46.3
C3	4.5	1.1 2.2
C4	4.6	4.0 2.1
C5	1.0	1.4 0.7
C6	0.5	0.0 0.0

Table I. Prevalence of C0 to C6 (CEAP) in the Polish study and the French study.

population, C1 in 16.5%, C2 in 21.8%, C3 in 4.5%, C4 in 4.6%, C5 in 1.0%, and C6 in 0.5%. Risk factors for CVI and varicose veins were similar among patients.

In a French cross-sectional study using a subpopulation of a survey of Raynaud phenomenon,¹⁴ 409 participants (277 males, 132 females) were investigated using a standardized questionnaire and clinical examinations performed by trained vascular medicine professionals. Of these, 48.7% had C0 or C1, while C2 was present in 23.7% of the males and 46.3% of the females. C3 was found in 1.1% and 2.2% of males and females, respectively, with C4 (skin changes) occurring in 4.0% of the men and 2.1% of the women. Healed ulcers were found in 1.4% of the males and in 0.7% of the females. No active ulcers were observed in this study.

Positive family history, advanced age, pregnancy and height in women, and exercise performed less than once a week in men were the main risk factors for varicose veins.

Bonn Vein Study¹⁶

Between November 2000 and March 2002, the German Society of Phlebology, in cooperation with the ministry of health, performed the Bonn Vein Study in the city of Bonn and two rural townships. The participants were chosen from a simple randomized sample taken from the population registers. In total, 3072 (1722 women, 1350 men) participants between 18 and 79 years of age were investigated.¹⁶ All participants answered a standardized questionnaire including the short-form health survey (36 items) (SF-36) quality of life questionnaire¹⁷ and standardized questions from the German health survey,¹⁸ and were investigated clinically

and by duplex sonography. The complete CEAP classification was used for classification of the findings. In the clinical classification, the participants were classified according to the most severe clinical findings. The participants were asked: have you had any of these symptoms (cramps, heaviness, etc) (*Table II*) in the last four weeks (day or night)? The results showed that 49.1% of the male and 62.1% of the female population had leg complaints related to the symptoms of venous diseases (eg, heaviness, sensation of swelling) (*Table II*). The prevalence increased with age (*Figure 1*).

Furthermore, 14.8% of the population, 7.9% of the men, and 20.2% of the women, had leg swelling in the last four weeks.

Concerning the CEAP classification, only 9.6% of the

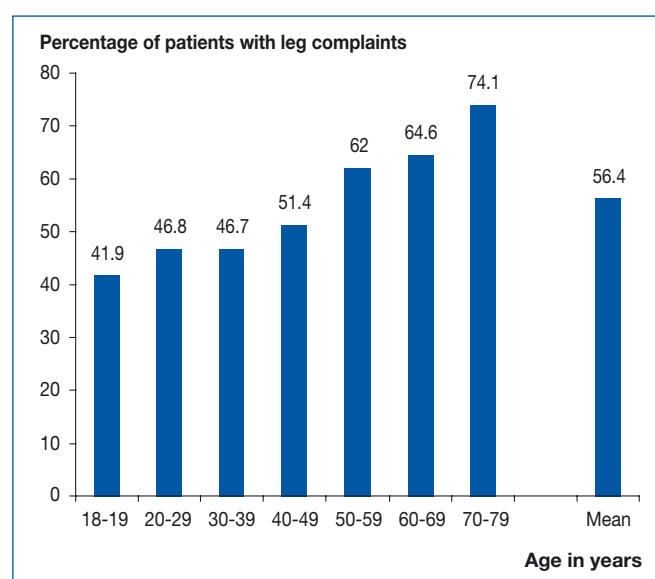


Figure 1. Increase in venous complaints in the last four weeks with age. Adapted from ref. 16.

	All		Men		Women	
	n	%	n	%	n	%
Heaviness	559	18.2	150	11.1	409	23.8
Tension	387	12.6	123	9.1	264	15.3
Sensation of swelling	8	0.3	5	0.4	3	0.2
Eczema	113	3.7	58	4.3	55	3.2
Pain while standing	611	19.9	195	14.4	416	24.2
Pain while walking	355	11.6	152	11.3	203	11.8
Cramps (foot or calf)	782	25.5	296	21.9	486	28.2
Itching	292	9.5	139	10.3	153	8.9
Restless legs	295	9.6	87	6.4	208	12.1

Table II. Prevalence of leg complaints in the last four weeks. Adapted from ref. 16.

population (13.6% men, 6.4% women) showed no signs of venous disorders (C0), while 59.1% (58.4% men, 59.5% women) showed only telangiectasias or reticular veins (C1) (Table III, Figure 2).

In 14.3% (12.4% men, 15.8% women), varicose veins were present without edema or skin changes (C2). Surprisingly, 13.4% (11.6% men, 14.9% women) had pitting edema of the lower legs at the time of the investigation (C3). Only 2.9% (3.1% men, 2.7% women) showed CEAP stage C4 with skin changes like eczema, pigmentation, or dermatoliposclerosis. Even fewer, 0.6%, showed healed venous ulceration (C5) and active venous ulcers, 0.1% (C6). Only for stages C2 and C3, was the prevalence significantly higher in the female population. The urban population showed a higher frequency of chronic venous insufficiency (C3 to C6) (Tables IV and V).

The prevalence of the stages C2 to C6 increased with age.

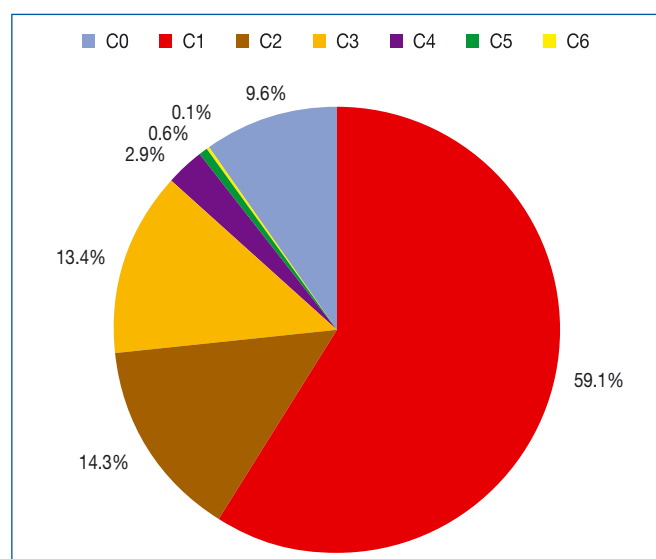


Figure 2. Distribution of C of CEAP classification in the Bonn Vein Study population.

	All		Men		Women	
	n	%	n	%	n	%
C0: no sign of venous disorders	294	9.6	184	13.6	110	6.4
C1: telangiectasias, reticular veins	1814	59.1	789	58.4	1025	59.5
C2: varicose veins	439	14.3	167	12.4	272	15.8
C3: edema	412	13.4	156	11.6	256	14.9
C4: skin changes	88	2.9	42	3.1	46	2.7
C5: healed venous ulceration	19	0.6	8	0.6	11	0.6
C6: active venous ulcer	3	0.1	2	0.1	1	0.1

Table III. Prevalence of C of CEAP classification in the Bonn Vein Study population.

C of CEAP (number/percentage)																		
		C0		C1		C2		C3		C4		C5		C6		Not determined		All
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n
Rural	Male	57	11.2	320	62.7	71	13.9	47	9.2	11	2.2	1	0.2	1	0.2	2	0.4	510
	Female	35	5.5	391	61.6	125	19.7	68	10.7	12	1.9	4	0.6		0.0		0.0	635
	All	92	8.0	711	62.1	196	17.1	115	10.0	23	2.0	5	0.4	1	0.1	2	0.2	1145
Urban	Male	127	15.1	469	55.8	96	11.4	109	13.0	31	3.7	7	0.8	1	0.1		0.0	840
	Female	75	6.9	634	58.3	147	13.5	188	17.3	34	3.1	7	0.6	1	0.1	1	0.1	1087
	All	202	10.5	1103	57.2	243	12.6	297	15.4	65	3.4	14	0.7	2	0.1	1	0.1	1927
All	Male	184	13.6	789	58.4	167	12.4	156	11.6	42	3.1	8	0.6	2	0.1	2	0.1	1350
	Female	110	6.4	1025	59.5	272	15.8	256	14.9	46	2.7	11	0.6	1	0.1	1	0.1	1722
	All	294	9.6	1814	59.0	439	14.3	412	13.4	88	2.9	19	0.6	3	0.1	3	0.1	3072

Table IVa. Prevalence of clinical stages (CEAP) of chronic venous disease, according to habitat and gender of the Bonn Vein Study population.

Age	C of CEAP (number/percentage)														Total n
	C0		C1		C2		C3		C4		C5		C6		Non determined
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	
18-19	31	50.0	31	50.0		0.0		0.0		0.0		0.0		0.0	62
20-29	102	28.4	228	63.5	18	5.0	9	2.5	2	0.6		0.0		0.0	359
30-39	78	12.7	433	70.6	63	10.3	36	5.9	1	0.2	1	0.2	1	0.2	613
40-49	34	5.5	429	69.3	70	11.3	80	12.9	5	0.8	1	0.2		0.0	619
50-59	32	6.0	297	55.9	94	17.7	85	16.0	18	3.4	3	0.6	1	0.2	531
60-69	13	2.3	273	48.8	114	20.4	118	21.1	34	6.1	6	1.1		0.0	560
70-79	4	1.2	123	37.5	80	24.4	84	25.6	28	8.5	8	2.4	1	0.3	328
Total	294	9.6	1814	59.0	439	14.3	412	13.4	88	2.9	19	0.6	3	0.1	3072

Table IVb. Age distribution of the Bonn Vein Study population, according to clinical stages of chronic venous disease (CEAP).

	All		Men		Women	
	n	%	n	%	n	%
Surgery	212	6.9	61	4.5	151	8.8
Sclerotherapy	168	5.5	23	1.7	145	8.4
Compression bandages	180	5.9	38	2.8	142	8.2
Compression stockings	450	14.6	101	7.5	349	20.3
Oral venous drugs	212	6.9	45	3.3	167	9.7
Local venous drugs (creams)	230	7.5	52	3.9	178	10.3

Table V. Frequency of treatment of chronic venous disease in the Bonn Vein Study population.

Of the general population, 22.9% had had therapeutic procedures on their veins in the past, 12.7% of the men and 31.0% of the women (Table V). The most frequent therapy was compression stockings followed by venous surgery and drug treatment.

DISCUSSION

The high prevalence of chronic venous disease in the general population is known from many studies.^{1,5,12} The comparability of the results from recent studies, in which the participants were properly investigated by clinical investigation, duplex sonography, and classified by CEAP, with older studies, in which only questionnaires and photography were used, is questionable. Due to the fact that the prevalence of chronic venous disease is age- and gender-dependent in most of the studies, all of the data has to be adjusted for these parameters at least. In addition, different classification systems were used. In the Tübinger Study,⁷ and in the Edinburgh Vein Study,^{2,6,10} the Widmer classification was used,¹¹ while in the Bonn Vein,¹⁶ Polish,¹⁵ and French studies,¹⁴ the CEAP

classification was used. Nevertheless, the results are comparable in some aspects.

The prevalence of telangiectasias and reticular veins was 58% in the Tübinger Study, 59% in the Bonn Vein Study, and 80% in the Edinburgh Vein Study. If the patients of the Bonn Vein study in stages C2 to C6 (those having telangiectasias and reticular veins in addition to more severe findings) had been included, the prevalence of telangiectasias and reticular veins would have reached 80% as well.

In the Tübinger Study, 15% had clinically relevant varicose veins, while in the Bonn Vein Study, 14.3% had C2-stage without additional signs of chronic venous insufficiency. The overall prevalence of varicose veins, including those participants in stages CEAP C3 to C6, was 23%. The prevalence in the Edinburgh Vein Study was slightly higher with 40% of the men and 30.2% of the women having varicose veins. In the Polish study, the prevalence of C2 was 21.8%, and in the French study it was 23.7% for men and 46.3% for women.

The method by which pitting edema was verified was only mentioned in the Bonn Vein Study. This, and principal problems associated with the definition of this stage, may have caused differences in the prevalence of C3, which varied between 1.1% and 14.9%.

The prevalence of severe chronic venous disease (Widmer stages II and III, CEAP classification C4-C6) has decreased in the last 20 years. In the Tübinger Study, Widmer II and III were present in 13% of the population. In the Edinburgh Vein Study, the prevalence was only 1.8%, and in the Bonn Vein Study, 3.6%. The lower value in the Edinburgh Vein Study might be due to the fact that the study population was between 18 and 64 years of age, compared with the Bonn Vein Study, between 18 and 79 years. The prevalence of C4-C6 in the Polish study reached 6.1% and in the French study, 5.4% for men and 2.8% for women.

The prevalence of healed and active venous ulcers decreased from 2.7% in the Tübinger Study to 0.7% in the Bonn Vein Study, and 1.5% and 1.4% in men and 0.7% in women in the Polish and French studies respectively.

The prevalence of specific venous treatment is very high in the population of the Bonn Vein Study.

SUMMARY

Chronic venous diseases like varicose veins and chronic venous insufficiency are among the most frequent diseases in Western populations.^{5,8} As a result, venous symptoms like heaviness of the legs and sensations of swelling and pain while standing are frequent complaints in the general population. The frequency of more severe chronic venous signs like eczema, pigmentation, dermatoliposclerosis or venous ulceration has markedly decreased in the last two decades. This might be due to the fact that diagnostic and therapeutic possibilities have been used more frequently in the last 20 years.



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Analysis of the various procedures used in great saphenous vein surgery in the Czech Republic and benefit of Daflon 500 mg to postoperative symptoms

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SUMMARY

The aim of this clinical study was to compare the intensity of postoperative pain using a 10-cm Visual Analog Scale (VAS), a quality-of-life questionnaire (CIVIQ), and a patient diary between two groups of patients, consisting of:

- a treatment group: patients who underwent a stripping procedure of the great saphenous vein (GSV), and were treated with Daflon 500 mg^{®*} 14 days before and 14 days after the operation, 2 tablets 500 mg/day;
- a control group: patients who underwent stripping of the GSV, but were not treated with Daflon 500 mg[®].

In addition, the two groups were also compared for the size of postoperative hematoma, analgesic consumption, and for the incidence of other symptoms associated with chronic venous disease (edema, tired and heavy legs, cramps, sensation of itching), using the VAS scale. Lastly, overall efficacy of the treatment was assessed.

The present trial included 181 patients from 15 medical centers throughout the Czech Republic. High ligation and partial stripping of the GSV in one lower limb was performed in all patients (short stripping from groin to knee). Patients were randomly assigned either to the treatment group (92 patients) or to the control group (89 patients). The degree of pain and the patient's condition were evaluated by the physician 14 days prior to the surgery (D-14), then 7 days (D7) and 14 days (D14) after surgery. Results indicated that Daflon 500 mg reduced the intensity of postoperative pain, which resulted in decreased consumption of analgesics. The size of postoperative hematoma was significantly smaller in the treatment group compared with the control group ($P < 0.001$), and associated symptoms of CVD and quality of life were significantly better in this group.

Effective phlebotropic drugs, like Daflon 500 mg, administered to patients 14 days before and 14 days after stripping surgery may improve postoperative morbidity.

Keywords:

chronic venous disease, great saphenous vein, pain, quality of life, micronized purified flavonoid fraction, surgery.

INTRODUCTION

Chronic venous disease of the lower limbs is a common disorder.^{1,2} Results of an epidemiologic survey in the Czech Republic show that 18.6% of the general population suffers from at least 3 of the symptoms attributed to chronic venous disease (CVD): pain, heaviness in the legs, and a sensation of swelling.³ Most of the CVD patients in this trial were untreated.³ Varicose veins (VV) are a frequent manifestation of this disease. Their prevalence in a recent epidemiological survey performed in Europe and using the clinical, etiological, anatomical, and pathophysiological (CEAP) classification,⁴ amounted to 40% in women and 20% in men.⁵

Until now, stripping surgery has been the procedure most often used for removing VV. Stripping surgery aims to eliminate venous reflux in the superficial venous system whilst the patient is in the standing position⁶ by eradication of the refluxing part of the superficial veins. Thus, a brief preoperative Doppler investigation is usually performed in order to locate the section affected by valvular incompetence. Despite excellent postoperative results of stripping surgery and very low complication rates, morbidity due to hematoma in the thigh and postoperative pain and edema are reported.⁷

The anti-inflammatory effect of Daflon 500 mg has been demonstrated in a number of studies.⁸ Therefore, Daflon 500 mg may improve major symptoms seen after surgery, particularly pain, and traumatic signs such as hematoma.

AIM OF THE STUDY

The primary objective of the study was the evaluation of postoperative symptoms and signs in two groups of patients undergoing varicose vein stripping of the great saphenous vein (GSV): a treatment group receiving 1 month of treatment with Daflon 500 mg, and a control group with no Daflon 500 mg treatment.

The secondary objective of the study was to report on methods of stripping used for the resection of varicose veins and analyze their possible impact on postoperative morbidity.

STUDY DESIGN

This study was an open-label, multicenter, prospective, randomized trial conducted by 15 vascular surgeons in

the Czech Republic. One hundred eighty-one patients were evaluated (92 in the treatment group, 89 in the control group) who needed to undergo surgical treatment (stripping), regardless of their participation in this study.

Duration of therapy with Daflon 500 mg in the treatment group was 1 month (14 days prior to and 14 days after surgery), at a dosage of 2 tablets of Daflon 500 mg a day.

Assessment visits were performed as follows: 14 days prior to surgery (D-14), 7 days (D7) and 14 days (D14) after surgery.

INCLUSION CRITERIA

Patients had to be between 18 and 60 years of age, scheduled to undergo GSV partial stripping as follows: high ligation + a short stripping from groin-to-knee, procedure to be performed on one lower limb without sclerotherapy and without ligation of perforating veins. One of the following procedures could be used: conventional stripping (using the Babcock stripper), invagination stripping, cryostripping, phlebectomy.

Postsurgical compression:

- Compression stockings and bandages were allowed post-surgery.

Additional conditions:

- Treatment with any other phlebotropic drug during the 4 weeks prior to inclusion was unauthorized;
- Existence of primary VV associated with venous reflux had to be confirmed by duplex ultrasonography.

Statistics:

- At baseline, the comparison between groups was tested using the Student's t-test; and Mann-Whitney's U Tests were performed for comparison between the control and treatment groups of quantitative variables. A value of $P < 0.05$ was considered significant.

INVESTIGATION AND EVALUATION

A 10-cm visual analog scale (VAS) was used to evaluate pain and symptoms in patients with CVD in visits to the physician at D-14, D7, and D14.

CIVIQ, a 20-question quality-of-life questionnaire dedicated to CVD, was filled in at D-14 and D14.

Patient's diary: the pain dimension of the CIVIQ (4 questions concerning pain, see *Table I*), 10-cm visual analog scale (VAS), and consumption of analgesics were self-assessed by patients on a daily basis.

The physician evaluated the size of the hematoma at D7 and D14 visits using transparent adhesive tape to outline the hematoma and measure it (a computerized – Hematoma Analyser was used for the hematoma assessment).

1. To what extent did the patient experience any limitations at work or in any other daily activities?
2. Did the patient have any sleep-related difficulties on the previous night?
3. To what extent did the patient feel somewhat limited in remaining in a standing position?
4. Did the patient feel any pain currently in the ankles or legs, and, if so, how intense was the pain?

Table I. Four questions related to pain in the CIVIQ (pain dimension).

RESULTS

1) Pain

In both the treatment and control groups, patients reported relief from the pain they complained of prior to surgery. In the treatment group, better pain relief was reported, namely during the first 7 post-surgical days, with a decrease in pain intensity by almost half (43%).

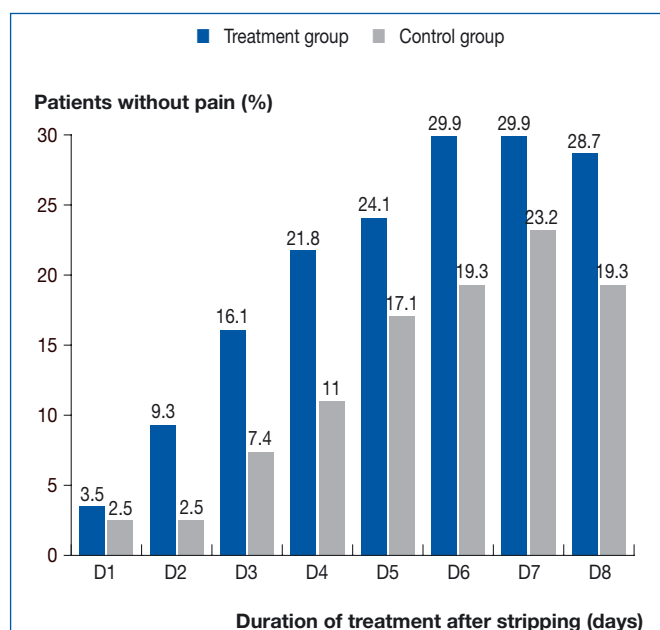


Figure 1. Complete resolution of pain after surgery.

Moreover, a daily greater improvement trend and complete pain relief were seen in the treatment group, compared with the control group (*Figure 1*).

Slower regression of postoperative pain in control patients was also manifest by a higher consumption of analgesics. A significant difference was observed between the two groups in terms of analgesic use from D4 since 4-times as many control patients required analgesics (*Figure 2*).

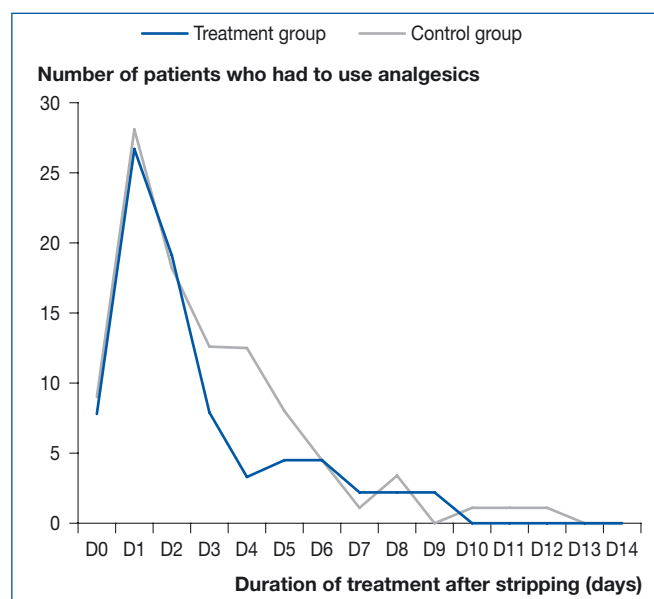


Figure 2. Decrease in the consumption of analgesics.

2) Hematoma

On D7, control patients showed a larger hematoma (131 cm² on average) than the treated ones (110 cm², $P<0.001$) (*Figure 3*).

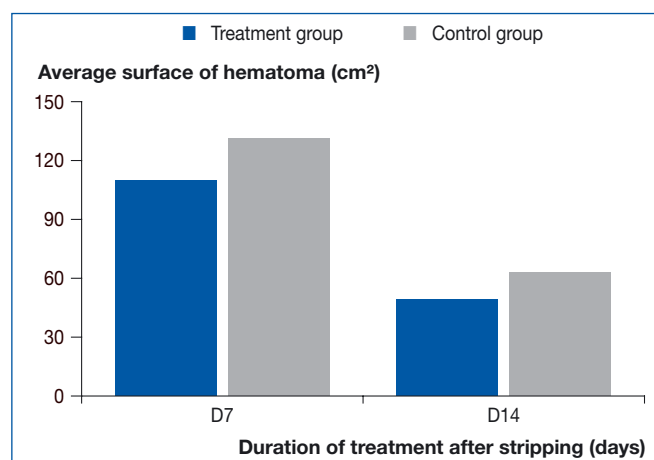


Figure 3. Decrease in the area of hematoma.

3) Quality of life

Regarding daily quality of life on the shortened CIVIQ (pain dimension only), a better improvement in each of the 4 items was reported in the treatment group compared with the control group (Figure 4).

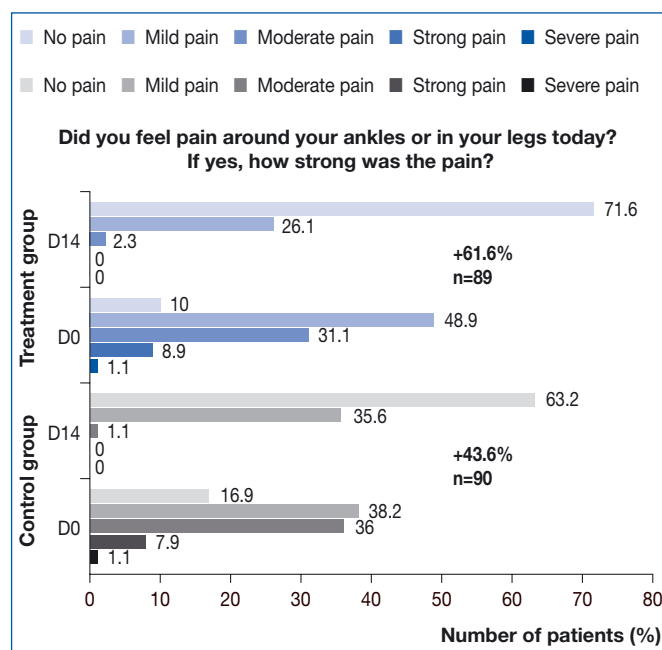


Figure 4. Evaluation of daily quality of life related to pain.

By the end of the study (D14), quality of life on the 20-item CIVIQ was rated as better by 21% of patients in the treatment group versus only 3% of patients in the control group.

4) Other symptoms related to chronic venous disease (CVD)

Patients in the treatment group also reported improvement in other symptoms of CVD: lower-limb edema decreased in 84%, sensation of heaviness in the

legs in 89%, and itching in 92% of patients in this group. In this last group, patients reported early relief from lower-limb fatigue and cramps, starting on the first postoperative day. Improvement in all symptoms and signs was significantly better in the treatment group compared with the control group ($P < 0.001$).

5) Multifactorial analysis of surgical procedures

A total of 181 patients underwent surgery, 28 of whom were in the hospital outpatient department. One hundred fifty-three patients were hospitalized, representing 85% of all included patients. Average hospital stay was 2 days (range: 1-6 days). Surgery was performed under general anesthesia in 139 patients. Other types of anesthesia used were local anesthesia in 3, epidural in 9, and spinal anesthesia in 33 patients. Based on records from the patients' diary, the type of anesthesia did not have any effect on total pain in both groups of patients.

Table II shows that the majority of the patients were over 40 years of age (60.9%) and consequently at risk for thrombotic complications. Data on this type of complication in the postoperative period after stripping, as well as in the long term, are lacking in the Czech Republic. Such complications in predisposed patients are known to increase the costs of treatment in the absence of preventive management, even in case of a minimally invasive procedure (Table III). Because a substantial percentage of the study population (34.3%) was considered at risk for thrombotic complications (over 40 years of age, receiving hormonal therapy, presenting with VV, undergoing surgery, etc), low-molecular-weight heparins (LMWH) were administered to them, although use of such LMWH is very low in standard practice. Administration of LMWH did not increase the size of the post-surgical hematoma.

Age (years)	Number	Percentage
18 – 30	n=21	11.6%
31 – 40	n=50	27.6%
41 – 50	n=62	34.3%
51 – 60	n=47	26.0%
>60	n=1	0.6%
Total	n=181	100.0%

Table II. Classification of patients by age.

Patients at risk of thrombogenic complications	Number of patients Total number=181	Percentage of patients
With hormonal therapy	n=24	13.3%
Low-molecular-weight heparins administered in postoperative period	n=62	34.3%

Table III. Administration of low-molecular-weight heparins.

In accordance with the study protocol, the following resection procedures had to be recorded by the investigator: high ligation associated with partial trunk stripping just below the knee and single leg resection procedure excluding any associated sclerotherapy, and excluding perforator vein ligation. The techniques that could be used for this surgery were the following: conventional stripping (with Babcock's stripper), stripping by invagination, pin-stripping, cryostripping, and phlebectomy, by means of either exoluminal or endoluminal stripper, with the stripper pulled back in one of these two possible directions: from groin to knee

or from knee to groin. Whether tributary stab avulsion was performed or not had to be reported by investigators. If tributary stab avulsion was performed, the location of stab avulsion (thigh, calf, medial side, lateral side) as well as the type of device used (hook, Trivex®, needle, mosquito forceps, other) and the time of stab avulsion (before or after the vein stripping) had to be recorded. All surgical techniques used in the present study are listed in *Tables IV, V, VI*. The invagination stripping technique was used the most often (70.2%). Only 28.7% of patients underwent the conventional stripping procedure.

Invagination stripping	n=127	70.2%
Conventional stripping	n=52	28.7%
Cryostripping	n=2	1.1%
Phlebectomy	n=77	42.5%
Total population	n=181	100.0%

Table IV. Type of surgery performed in the present study in the Czech Republic.

Direction of insertion and removal of branches	Number of patients Total number=181	Percentage of patients
From the groin down to the knee	n=133	73.5%
From the knee up to the groin	n=48	26.5%
Stab avulsion prior to stripping	n=112	61.9%
Stab avulsion after stripping	n=61	33.7%

Table V. Effect on pain according to various directional insertions of the stripper.

Instrument	Number of patients Total number=181	Percentage of patients
Mosquito forceps	n=109	60.2%
Smetana's knife	n=75	41.4%
Small hook	n=34	18.8%
Other than Varixset scalpel	n=29	16.0%
Needle	n=2	1.1%

Table VI. Type of instrument used.

Statistically less pain and smaller hematoma size were reported by patients who had their VV stripped by invagination.

Of the 127 patients who underwent stripping by invagination, only 67 (48.2%) needed to take analgesics at D1 (all patients took analgesics at D0, just after being operated on) versus 68% of those stripped with other procedures. Direction of pulling stripper and time of stab avulsion are described in *Table V*. Among the other resection procedures used, the mosquito forceps caused fewer traumas than Smetana's knife (*Table VI*).

Patients who underwent stab avulsion before the stripping experienced less postoperative pain than those with stab avulsion after stripping. Similarly, patients in the treatment group reported significantly less pain after surgery than patients in the control group (treatment effect, $P < 0.05$).

Compression therapy is an integral component of postoperative management. Compression stockings and compression bandages are commonly used in post-stripping. In this study, the medium-compression bandages were used in a majority of patients, ie, a total of 132 (73%), and elastic stockings were used in only 49 patients (27%). Short-compression bandages can be indicated after this type of surgery. However, due to their cost, they were only used in a small percentage of patients in the present study. Hematoma size proved to be significantly smaller in those patients who received compression stockings postoperatively, rather than bandages.

DISCUSSION

Varicose veins in the lower extremities should not remain untreated in the long term since the venous reflux they induce is known to damage adjacent tissues. This can result in further complications such as skin pigmentation, dermatitis, and lastly, the most advanced stage represented by crural venous ulcers.⁹⁻¹¹ Phlebotropic drugs are of benefit to symptoms in all stages of CVD insofar as they decrease pain generated by endothelium-mediated activation due to venous stasis.¹² Whenever VV appear, they should be treated by surgery⁶ in combination with pharmacotherapy. As early as the year 500, BC Hippocrates recommended making multiple punctures in varicose veins. In the 2nd century, AD Galen

defended the removal of varicose veins using a small hook. In the 16th century, Amboise Paré recommended ligation and excision of varicose veins. In 1884, Madelung performed a long incision on the inner aspect of the leg and removal of the entire GSV. In 1905, Keller attempted to perform venous stripping by inserting a curved wire through the venous lumen. In 1906, Charles May used an extraluminal stripper to loop the vein. In 1907, Babcock described a rod-like stripper with a cylinder pin at one end. The development of the surgical technique has progressed very rapidly up to the present-day concept, which stipulates the removal only of the functionally incompetent vein and is associated with the best cosmetic result. Although the stripping procedure produces very good postsurgical results with few complications⁷ (postoperative hematoma in the thigh, edema, and pain). It appears that an effective phlebotropic agent can help to decrease this morbidity. Despite the recommendations by many scientific societies, prevention of thrombogenic complications is not considered in all cases. The reasons for this might be the additional costs such prevention can imply, and concern about the large postsurgical hematoma that LMWH can cause. The results of the present study demonstrated that the prevention of thrombogenic complications by LMWH does not increase the size of postoperative hematoma.

Regarding the different stripping procedures used, it appears that hematoma size was smaller after use of a mosquito forceps, removal of venous branches prior to stripping, and use of compression stockings. Patients reported less pain following the invagination stripping procedure compared with other procedures.

Patients in the Daflon 500 mg treatment group had smaller hematoma and a lower consumption of analgesics. These patients also experienced a significant improvement in symptoms of CVD as well as in quality-of-life parameters. The findings of this study show that better results were obtained by administering Daflon 500 mg 14 days prior to surgery and 14 days postsurgery. The administration of a phlebotropic agent, such as Daflon 500 mg, can be helpful in mitigating postoperative pain and hematoma after stripping of the GSV.

Results of this study were first presented at the Phlebology Congress held in Hradec Králové, from 21 to 22 October, 2004.

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Foam sclerotherapy for the management of varicose veins: a critical reappraisal

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SUMMARY

Foam sclerotherapy is often presented as a new method for the management of varicose veins. However, several reports established most of its principles approximately 50 years ago. Minor modifications in the way foam is produced, as well as the use of ultrasound to guide it to all of the sites of venous reflux, have resulted in a renewed interest in this technique. Recently, we have progressed from observational studies that established the efficacy and safety of this technique to the first randomized controlled trials. We need long-term follow-up in properly controlled randomized studies before we can claim that ultrasound-guided foam sclerotherapy has reached maturity and can be performed with the fully informed consent of our patients.

HISTORICAL OVERVIEW

For the last few years, there has been a revival of foam sclerotherapy as a treatment for varicose veins. However, this technique is not new. It was first described in 1939 by S. McAusland.¹ He injected froth, produced by shaking a rubber-capped bottle filled with sodium morrhuate, into spider veins. A few years later Robert Rowden Foote produced foam by shaking 1 mL of ethanolamine oleate in a 2-mL syringe. He reported that this soapy froth was the best injection fluid for the management of spider veins.² In 1949, Sigg was the first to report that the injection of foam into a vein was beneficial because it washed away less rapidly, thus introducing the concept that increased viscosity foam has advantages over other contemporary sclerotherapy techniques.³ The following year, Orbach compared the efficacy of sodium tetradecyl sulfate (STS) foam with that of an injection of an equal amount of STS in liquid form. The end point was established as the length of thrombus generated by injecting the tail vein of mice. He found that the STS foam had 3.5 to 4 times the thrombogenic property of the solution.⁴ In 1953, the Norwegian doctor Arve Ree injected pure etamolin foam into varicose veins and reported excellent results in a series of 50 patients. The foam was produced by vigorously shaking a bottle of sclerosant solution and aspirating the bubbles into a syringe.⁵ The amount of foam injected varied from 2 to 7 mL according to the size of the varix. In 1956, Peter Fluckiger was the first to notice that the foam could be directed into regions other than the site of injection by manual manipulation.⁶ This concept is now widely practiced with ultrasound-guided foam sclerotherapy.

Keywords:

sclerotherapy, varicose veins, ultrasound.

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In the 1990s, there was some refinement of the techniques that produced foam and this led to a revitalized interest in treating varicose veins using this method. Juan Cabrera used a rotating brush to produce microfoam with CO₂ as a carrier gas.⁷ The advantage of CO₂ is the faster foam degradation that is achieved if used instead of air. The details of this method were not published although the results were good. Alain Monfreux produced foam by generating negative pressure. He did so by drawing back the plunger of a glass syringe containing liquid sclerosing solution whose outlet was tightly closed with a plastic cap.⁸ This technique produces relatively large-diameter bubbles, but it cannot be standardized and, as a result, the quality of the foam that is produced varies when equal proportions of air and liquid are mixed.

Lorenzo Tessari's Tourbillon technique is the most frequently reported in the English literature. Two plastic disposable syringes are connected by a three-way stopcock. The foam is formed by mixing the liquid sclerosant with 4 or 5 parts of air, through 20 passes between the two syringes with the hub at a 30° rotation. This rotation narrows the stopcock passage generating high turbulence, which produces a high quality microfoam⁹ (Figure 1).



Figure 1. Foam (6 mL) was produced with a double syringe and a three-way stopcock (Tessari's Tourbillon technique).

DEFINITIONS AND PROPERTIES OF THE SCLEROSING FOAM

Sclerosing foam is a mixture of gas bubbles in a liquid solution that contains surface-active molecules. The gas

must be well tolerated by patients, physiologic, and the bubble size should be, preferably, under 100 μ . According to the bubble diameter, foams can be classified as froth, macrofoam, minifoam, and microfoam.

If the relative volume fraction of liquid is less than 5%, the foam is classified as dry, whereas if it is more than 5%, it is classified as wet. Wet foam (eg, Tessari's foam) has the maximum stability.¹⁰ Uniform bubble diameter also provides more stability because smaller bubbles empty into larger bubbles. This can be explained by Laplace law, which states that the distending pressure in a bubble is inversely proportional to its radius. Frullini was likely the first to emphasize that silicon, which is present in catheters and syringes, interferes with the structure of the sclerosing foam by breaking the links of polar macromolecules thus reducing the half-life of the foam. He concluded that the shorter the contact of such molecules with silicon the better the quality and duration of the foam.¹⁰

Foam holds several advantages over traditional liquid sclerotherapy. Once a liquid is injected, it mixes with blood in the vein and dilutes the concentration of the sclerosant. Foam, on the other hand, displaces the blood allowing direct contact of the sclerosant with the endothelium. As a result, the efficacy of the sclerosant is increased hence a lower concentration can be given to treat varicose veins. In addition, a given volume of liquid can be used to produce four or five times its volume in foam, depending on the foaming method. This allows the use of a smaller total dose of sclerosant to achieve the desired effect. Moreover, extravasated foam is much better tolerated than extravasated liquid. Probably the most significant advantage of foam is that it is echogenic, which dramatically increases the accuracy with which individual varicose veins can be treated.¹¹

Most authors cited have injected the foam directly into the great saphenous vein or the small saphenous vein under ultrasound control. During this process, the leg is elevated resulting in the reduction of the diameter of the vein. A survey has revealed that a majority of experts inject 2 to 10 mL of foam into the great saphenous vein and 1 to 4 mL into the small saphenous vein.¹²

CLINICAL STUDIES

The clinical effectiveness of ultrasound-guided foam sclerotherapy was reported in a series of 500 patients

with varicose veins by Cabrera et al.¹³ All patients had an incompetent saphenofemoral junction with an initial diameter of between 9 and 32 mm. After 3 years, 81% of the patients had a fibrosed great saphenous vein, while in 96.5% of the patients, all superficial branches had disappeared. From this study, it is not clear what percentage of the originally recruited patients were followed up for 3 years. Further studies did not subsequently confirm the very high incidence rate of disappearance of superficial branches. The authors reported no serious complications, such as deep vein thrombosis (DVT), however, it appears from the methodology that they did not specifically look for DVT with duplex ultrasonography in the follow-up visits at 7 days and 1 month.

In another study, 177 patients with varicose veins, who were recruited from 3 different practices in Italy, were used to assess the efficacy and safety of ultrasound-guided foam sclerotherapy. Complete obliteration of the injected vein or antegrade flow within the treated vessel was observed in 161 (91%) patients at 1 month. This percentage was reduced to 67% among 66 patients who had a second follow-up visit at 138 (mean) days. An improved outcome was observed at 30 days for patients with CEAP (Clinical, Etiological, Anatomical, Pathophysiological) clinical class 2 than for CEAP clinical classes 3 to 6. The authors do not appear to have tested for the statistical significance of this difference.⁹

Bhowmick et al, in a series involving 35 legs with great saphenous varicose veins treated with polidocanol microfoam, reported that 2 patients developed deep vein thrombosis in the distal calf veins. In addition, 7 legs had symptoms resembling superficial thrombophlebitis. In this study, 15 to 20 mL of microfoam was injected.¹⁴ Two years following the publication of this study, in the European consensus meeting on foam sclerotherapy, the majority of the participants stated that a volume of 6 to 8 mL should be administered per session for the management of great saphenous varices and no more than 3 mL for the management of the small saphenous vein.¹² Hopefully, adherence to this recommendation will decrease further incidences of this complication.

There is a single case report of stroke that developed following foam sclerotherapy for the management of varicose veins.¹⁵ In total, 20 mL of foam was injected. A carotid duplex-ultrasonography performed immediately following this event showed normal arteries with rapidly

moving echogenic particles within the carotid lumen. A transesophageal echocardiogram confirmed the presence of a large (18 mm) patent foramen ovale (PFO). The patient had a good recovery, but the authors have since changed their practice and now inject less than 10 mL of foam per session. A restricted amount of foam was recommended at the European consensus meeting for PFO patients.¹²

Van Neer, in an elegant case report, presented a patient with varicose veins secondary to an incompetent thigh perforator that was successfully treated with ultrasound-guided foam sclerotherapy.¹⁶ More studies are needed to investigate the effectiveness and safety profile of this technique in the management of incompetent perforating veins.

There is limited information on the effectiveness of ultrasound-guided foam sclerotherapy in the management of recurrent varicose veins. My group has recently reported our experience with this technique in a series of 38 patients who had symptomatic recurrent varicose veins in 45 legs. A single sclerotherapy session was adequate in 26 (58%) of all legs. Only 5 legs (11%) needed 3 or more sessions. In 87% of all legs, complete elimination of both varicose veins and all reflux points had been achieved at the end of treatment. A positive association between the amount of injected foam and CEAP class ($r=0.45$, $P=0.002$) and venous clinical severity score (VCSS) ($r=0.45$, $P=0.012$) was found. There were no instances of DVT, but self-limiting superficial thrombophlebitis occurred in 6 (8.2%) of the 73- injection sessions.¹⁷

RANDOMIZED CONTROLLED TRIALS

A randomized prospective multicenter trial was conducted to evaluate the efficacy of foam sclerotherapy compared with liquid sclerotherapy in the great saphenous vein. Forty-five patients were randomized to receive foam sclerotherapy and 43 to receive liquid sclerotherapy. Immediate spasm was observed in 29 cases after foam treatment versus 12 with liquid. Elimination of reflux after 3 weeks was observed in 84% (38/45) of the foam group and in only 40% (17/43) of the liquid group. These results were maintained at the 1-year follow-up. The authors concluded that sclerosing foam is more effective than liquid sclerotherapy.¹⁸ These results were confirmed by another study in Japan that

compared liquid sclerotherapy with ultrasound-guided foam sclerotherapy in the treatment of isolated great saphenous vein incompetence. Duplex scanning demonstrated complete occlusion of the great saphenous vein in 67.6% (25/37) of the limbs in the foam group; this was significantly higher than that observed, 17.5% (7/40) of the limbs, in the group that received liquid sclerotherapy.¹⁹ At one year, recurrent varicose veins were found in 3 patients in the foam group and 10 in the liquid sclerotherapy group ($P=0.048$).

My group has prospectively compared, in a randomized study, ultrasound-guided foam sclerotherapy with saphenofemoral ligation ($n=30$) with surgical treatment of varicose veins along the distribution of the great saphenous vein system ($n=30$). All patients were suitable for day-case surgery. Surgical treatment included saphenofemoral ligation, stripping of the great saphenous vein, and multiple phlebectomies. Median time to return to normal activities was significantly reduced in the foam sclerotherapy group (2 days) compared with the surgical group (8 days) ($P<0.001$, Mann-Whitney). The Aberdeen Vein Questionnaire score was significantly reduced at 3 months, by 46% in the sclerotherapy group and by 40% in the conventional surgery group ($P<0.001$, Mann-Whitney). The cost of the procedure in the sclerotherapy group was 672.97 pounds sterling—significantly less than conventional surgery (1120.64 pounds sterling). In the foam group, at 3 months, four patients had a recanalized vein that needed a further session of sclerotherapy, which resulted in a short-term closure rate of 87%.²⁰

Alos et al performed a controlled clinical trial to assess the safety and efficacy of sclerotherapy using polidocanol foam compared with liquid polidocanol.²¹ The foam group received a 50% lower concentration of sclerosant than the liquid sclerosant group. Pain, inflammation, and pigmentation appeared more often with foam sclerotherapy. Interestingly, at one year the incidence of pigmentation was 6.3% in the liquid group and 33% in the foam group. The authors attributed the higher

incidence of pigmentation to the use of elastic compression for only 48 hours following sclerotherapy. The longer the compression the less the incidence of pigmentation.²²

CONCLUSIONS

Foam sclerotherapy was first described in 1939. Several reports in the 40s and early 50s established most of the principles of this technique. More recently, well-documented observational studies have demonstrated a good safety profile and satisfactory short and intermediate results with foam sclerotherapy. A couple of randomized trials have clearly shown the superiority of this technique versus liquid sclerotherapy in eliminating the sites of reflux along the great saphenous vein system. The long-term results of ultrasound-guided foam sclerotherapy have not been compared with the traditional surgical treatment for varicose veins. In addition, this technique has not yet been compared with other minimally invasive techniques such as radiofrequency or laser ablation of the saphenous vein. These types of studies are urgently needed and will help us provide our patients with the information required to give a truly informed consent.



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Strategies to minimize the effect of neovascularization at the saphenofemoral junction after great saphenous vein surgery: an overview

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ABSTRACT

The recurrence rate remains high after great saphenous vein (GSV) surgery. One of the major contributing factors is neovascularization at the level of the ligated GSV stump. To mitigate the effect of neovascularization, several approaches are possible, which are reviewed in this article.

Some surgical strategies directly focus on the saphenofemoral junction (SFJ). Instead of simple ligation of the GSV stump, modified techniques have been tested: complete elimination of the GSV stump, hiding (inverting) the GSV stump, increasing the spatial separation between the stump and surrounding superficial veins, adding the construction of a prosthetic or anatomical barrier to the classical ligation, or even completely abandoning SFJ ligation. The recently developed endovenous techniques to obliterate the GSV also aim at limiting neovascularization in the groin by omitting a surgical intervention at this level.

Although some results are promising, more studies will be needed to investigate the effectiveness of all of these techniques to minimize varicose vein recurrence.

INTRODUCTION

The problem of recurrent varicose veins remains incompletely resolved. Some obvious solutions have been proposed to prevent the important causes of recurrence from happening, such as a better understanding of venous anatomy and hemodynamics, adequate preoperative assessment, and most importantly, correct and carefully performed surgery. Although remarkable progress has been made in all the above-mentioned fields, surgical treatment of varicose veins continues to be marred by the development of recurrent reflux, most commonly in the area of the saphenofemoral junction (SFJ), causing recurrent varicose veins from the thigh downwards in the entire leg

Keywords:

great saphenous vein, saphenofemoral junction, surgery, recurrence, neovascularization, barrier methods, patch saphenoplasty, endovenous laser treatment, radiofrequency ablation, foam sclerotherapy.

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(Figure 1).¹ The recurrence rate remains high, even after “correct” surgery including comprehensive SFJ ligation, above knee stripping of the great saphenous vein (GSV), and ligation of all incompetent perforating veins, and appears to increase with additional years of follow-up.² Clinical, ultrasonographic, surgical, and histopathological studies have illustrated the existence of a phenomenon called neovascularization (formation of new veins) as a possible explanation for recurrence after correctly performed previous operations (Figure 2).³⁻⁵ Such stump-related neovascularization might originate from hypoxia-induced activation of endothelial cells distal to the SFJ stump ligation, which could be mediated by growth factors. As neovascularization is part of the normal healing process, it cannot be inhibited completely. However, we can at least try to mitigate the effect of neovascularization. This may be achieved by several approaches.



Figure 1. A 33-year-old baker came to the venous clinic because of stubborn recurrent varicose veins (C5s; Ep; As,p; Pr) after having been declared “incurable” by 3 surgeon-colleagues. He had already been operated on for varicose veins in another hospital at the age of 25 years and 29 years, each time including surgery at the saphenofemoral junction.



Figure 2. A 59-year-old woman had bilateral varicose vein surgery 8 years ago. She underwent a duplex ultrasound at 2 months, which showed a perfect postoperative situation in the groin. At a one-year follow-up, according to a duplex scan, a new vein had developed on the anterior side of the common femoral vein in the groin of both legs (classified as “grade 2” neovascularization, connecting with some tiny, clinically not yet visible, tortuous veins on the thigh). After 8 years, she presented with typical recurrent varicose veins (C3s; Ep; As; Pr) from the groin downwards, encompassing the entire leg, and had to be reoperated on.

1) Efforts to reduce neovascularization at the SFJ

a. Elimination of the GSV stump

The axiom “no stump, no neovascularization” is one of the important starting points when trying to reduce the incidence of neovascularization. Complete elimination of the stump can theoretically be accomplished by placing a vascular side clamp on the SFJ and dividing the GSV at its junction with the common femoral vein, leaving a short venotomy that can be closed with a two-layer running suture (with a 5.0 or 6.0 monofilament suture). The immediate result is a completely covered intima, a much smaller foreign body burden than an external ligature, and an intact common femoral vein lumen. However the incidence of recurrent reflux in the above-described technique in the long term has not yet been reported. Up to now, preliminary results have only been published in congress proceedings.

b. Hiding or destroying the stump endothelium

Based on the idea of hiding the stump endothelium, Frings et al⁶ published satisfying preliminary results of a study in which they ligated the stump with a nonresorbable suture and then buried the stump with a

running polypropylene suture. Recently, the same authors reported the results of color duplex venous imaging two years after operation in 152 of 500 initially included limbs.⁷ They could show that recurrent reflux in the groin was reduced by oversewing the ligated SFJ with a running polypropylene suture (3% versus 11% in limbs without endothelial closure). However, in a prospective randomized study with follow-up up to 5 years after surgery, Haas et al⁸ could not confirm any beneficial effect of such inverting suture of the stump endothelium. On duplex ultrasound control, they still found neovascular vessels in 9% of 279 limbs operated on with this technique. Also, other investigators have chosen to focus only on the stump endothelium, destroying it with chemical or heat cauterization, or in some instances reducing the amount of endothelium exposed by placing a second ligature near the free end of the GSV stump, all without conclusive results.^{9,10}

c. Spatial separation of the stump

It also seems important to achieve greater spatial separation between the deep veins underlying the fossa ovalis and the superficial venous system, by careful ligation of all tributaries in the groin beyond their junction and routinely stripping the thigh portion of the GSV.¹¹⁻¹³ Hence, the rationale for stripping the above-knee GSV lies not only in the fact that thigh perforators are disconnected, but also that the most important conduit for recurrent reflux is eliminated by stripping. Some authors have even suggested that stripping of the anterior (and/or posterior) accessory great saphenous vein should be performed as far distally as possible.¹⁴ This additional maneuver further reduces the potential conduits for reflux originating in newly formed refluxing veins in the groin, in the case of postoperative neovascularization. The importance of adding this to the classical surgical strategy should be confirmed in future prospective studies.

d. Barrier techniques

Interposition of a physical barrier (prosthetic or anatomical) between the ligated GSV stump on the common femoral vein (CFV) and the surrounding superficial veins can prevent tiny neovascular veins developing at the stump from connecting with superficial veins in the groin and thigh. Various barrier techniques have recently been studied in primary as well as in recurrent varicose veins. Glass¹⁵ was the first to report apparently good results on clinical follow-up 4 years after patch implantation and closure at the SFJ.

Earnshaw et al¹⁶ studied the results of a comparable barrier technique using a polytetrafluoroethylene (PTFE) patch (small patch, 1 x 2 cm), not only on clinical examination, but also with duplex ultrasound scanning after one year. This study indicated that patch saphenoplasty was safe, but did not abolish neovascularization after one year. In another study at our center, we compared two groups of limbs with and without a silicone implant (2 x 3 cm) and closure of the cribriform fascia one year after the operation with duplex scanning (Figures 3a,b,c).¹⁷ Silicone patch saphenoplasty significantly lowered the incidence of neovascularization (Figure 4).

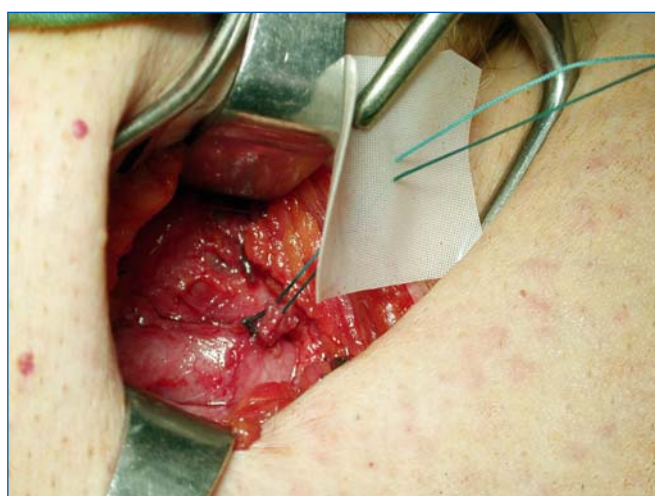


Figure 3a. Silicone patch saphenoplasty at the saphenofemoral junction: (a) the saphenous stump has been ligated with a nonresorbable suture and a silicone patch is fixed to the ligated stump.

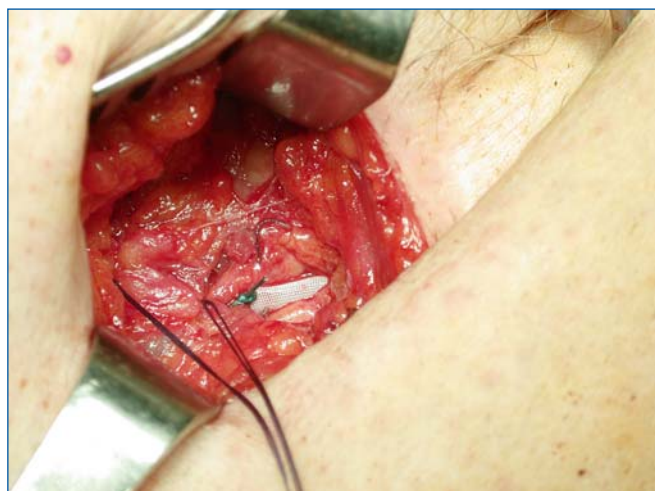


Figure 3b. after the patch has been tucked under the cribriform fascia, covering in this way the anterior half of the common femoral vein, the cribriform fascia is closed with separate stitches.

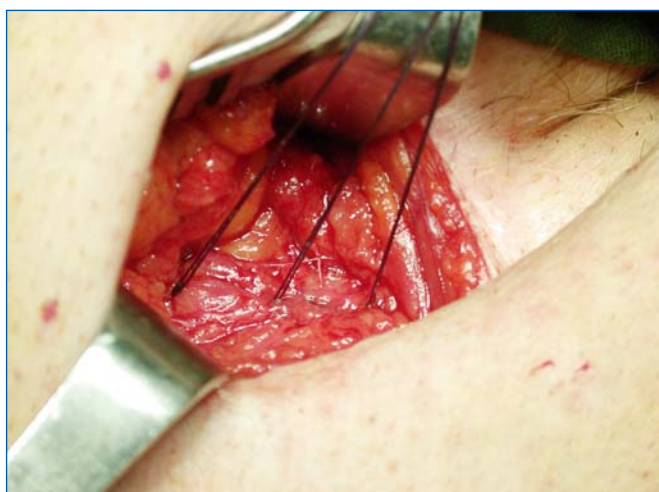


Figure 3c. situation before closing Scarpa's fascia: the saphenous stump is not visible anymore as it has been covered with a prosthetic and anatomical barrier.

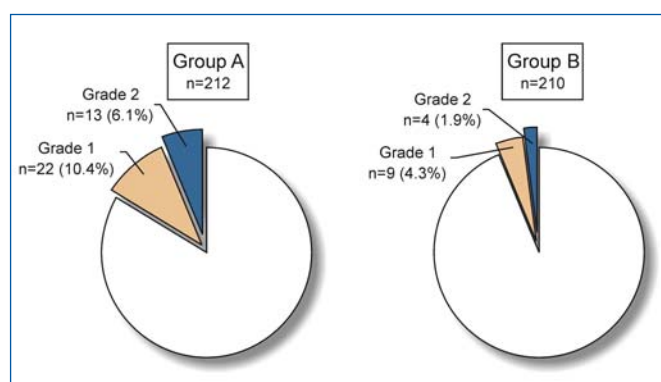


Figure 4. Incidence of the different degrees of neovascularization on duplex examination in group A (without silicone patch) and group B (with silicone patch) 12 months postoperatively. Grade 1: tiny new vein(s) < 4 mm at the previously ligated saphenofemoral junction; Grade 2: tortuous new communicating vein(s) with a diameter > 4 mm and with pathological reflux.

In particular, in groins being reoperated on for recurrent SFJ reflux, patch saphenoplasty appears to be a valuable adjunctive measure to reduce the incidence of recurrence.¹⁸⁻²⁰ In a recent study at our center, we found that patch saphenoplasty significantly improved the clinical and duplex ultrasound results five years after repeat surgery.²⁰ Recurrent thigh varicosities were observed in 58% of limbs in the group without a patch and in 26% of those with a patch. Duplex scans revealed important neovascular vessels in 45% versus 9% of limbs. In redo procedures, it is of particular importance to fix the patch well to the CFV, as there is usually no cribriform fascia left to cover the patch and keep it where

it should stay (covering the saphenous stump in close apposition to the CFV). Only by maintaining the patch at the right location, can it act as an efficacious barrier to contain neovascularization. Of course, the obvious disadvantage of the use of a prosthetic implant in the groin is the risk of infection. This may appear as an acute infection in the immediate postoperative course or even many years after the initial procedure due to a sudden exacerbation of a “silent” infection. In very obese patients (BMI > 35), often with preexisting mycotic infection in the groin, it is therefore wiser to refrain from implantation of such a prosthetic patch. Postoperative symptomatic stenosis of the common femoral vein due to excessive scar tissue formation around the patch has also been observed after silicone patch saphenoplasty in exceptional cases (unpublished observation).

To contain neovascularization and hence prevent recurrence in the groin, the use of an anatomical barrier to cover the ligated saphenous stump has also been proposed.^{15,21,22} The easiest approach to construct such an anatomical barrier consists of simply suturing the opening in the cribriform fascia, once the SFJ has been ligated. At our center, the results of duplex ultrasound scanning one year after closure of the cribriform fascia in GSV surgery (first varicose vein operations) were comparable with those obtained after silicone patch saphenoplasty (unpublished observation). A more complex barrier technique, first described by Sheppard²¹ consists of the use of a flap of pectineus fascia at the SFJ. In a randomized controlled trial, Gibbs et al²² could not confirm the previously suggested benefit of this particular technique. Further critical evaluation of the effects of a simplified barrier technique without the use of foreign material is mandatory.

e. Abandoning SFJ ligation?

Finally, what about comprehensive SFJ ligation, the “sacred cow”? Although we have always been taught that an accurate groin dissection with detachment of all tributaries is the ideal method to prevent recurrence in the groin, in fact, the reverse could become true during the forthcoming years. On one hand, the usefulness of stripping the GSV (above knee) rests on clear-cut experimental clinical evidence.^{12,13,23-27} On the other hand, the importance of ligating all tributaries of the GSV in the groin has always been assumed since the introduction of “high ligation” in the groin, but never really proved. Chandler et al²⁸ tried to define the role of extended SFJ ligation, while studying radiofrequency

ablation of the GSV (VNUS®). They compared no ligation of the SFJ in the groin with extended SFJ ligation in combination with radiofrequency obliteration.²⁸ They found no notable differences between both groups. These results questioned the axiom stating that SFJ ligation with ligation of all tributaries is an essential component of the treatment of GSV insufficiency. Perhaps complete (endovenous) exclusion of the thigh portion of the GSV from the superficial venous system could be sufficient to achieve equal therapeutic benefits in cases of a refluxing main GSV trunk. The quite revolutionary idea of abandoning SFJ ligation in the management of primary varicose veins associated with GSV reflux will certainly have to be further examined. Prospective randomized long-term follow-up studies will have to clarify this important issue.

2) Alternative treatment methods without SFJ ligation

a. Endovenous radiofrequency obliteration

The recently developed endovenous treatment methods do not seem to be associated with neovascularization in the groin and could, therefore, become the future method of choice for treatment of primary varicose veins. A prospective multicenter randomized trial showed significant early advantages to endovenous radiofrequency GSV obliteration with the VNUS® closure method compared with conventional high ligation and stripping.²⁹ An earlier return to work and routine daily activities, and a significantly better quality of life early after the intervention (and maybe a lower incidence of recurrence) could provide advantages in the form of reduced indirect costs of the procedure. However, the direct costs of endovenous obliteration remain more than twice that of surgery.³⁰ The recently reported results of GSV radiofrequency obliteration after 3 and 5 years continue to be promising, and duplex ultrasound findings confirm the absence of neovascular veins in the groin.³¹⁻³³

b. Endovenous laser treatment

This is another endovascular technique to treat saphenous vein incompetence. The endovenous laser (810 nm / 940 nm diode laser) causes endothelial and vein wall damage by intraluminal delivery of laser energy, ultimately resulting in fibrosis of the vein. It has been successfully applied in GSV and small saphenous vein insufficiency.^{34,35} Duplex scans showing occlusion of the vein one year after the procedure, also showed that

the vein remained occluded at further controls up to 3 years after treatment.³⁶ Potential advantages of the endovenous laser are the small diameter and flexibility of the laser fiber and the faster withdrawal rates, which result in less heat-related damage to adjacent nontarget perivenous tissue compared with radiofrequency.

c. Ultrasound-guided foam sclerotherapy

Foam sclerotherapy under duplex ultrasound guidance was introduced as a third alternative treatment method.³⁷ The increased efficacy of foam, in comparison with classical sclerotherapy with liquid sclerosants, is attributed to its displacement of blood from the treated vein and its increased contact time between the sclerosant and the vein. The foam is clearly imaged by duplex ultrasound so that precise filling of an incompetent vein can be assured. Foam sclerotherapy, therefore, enables treatment of varicose veins with larger diameter and even main superficial trunks.³⁸ Promising results have also been obtained in patients with recurrent varicose veins. Minor complications are similar to conventional liquid sclerotherapy. The advantage of foam sclerotherapy is that it requires no general or regional anesthesia to perform and takes much less time than other current techniques. The most significant concern with this technique has been deep vein thrombosis.

d. External valvuloplasty of the SFJ

Repair of the terminal valve of the GSV, hence reconstituting competence of the main trunk seems to be an attractive physiological alternative to high ligation of the SFJ and stripping. Lane et al³⁹ recently reported promising results after external valvular stenting of the SFJ by means of Venocuff implantation. This technique has the potential advantage in that the GSV is not transected in the groin, which might reduce the stimulus for postoperative neovascularization.

CONCLUSION

During the past decades, our knowledge about the causes of recurrent varicose veins after surgery has grown considerably. In particular, surgeons have become more aware of neovascularization at the ligated GSV stump being one of the important phenomena potentially leading to recurrence. Important efforts have been made to try to find the optimal method to avoid recurrence, focusing on either the SFJ or the main trunk of the GSV.

However, the final solution has not yet been found. At the level of the SFJ, simple closure of the opening in the cribriform fascia might be the easiest way to cover (and isolate) the ligated stump in a first GSV operation. In groins being operated on for recurrent SFJ reflux, covering the stump with a prosthetic barrier might be preferred. At the level of the main trunk of the GSV, results of alternative treatment techniques are promising, but remain inconclusive. Critical investigation using well-established criteria and long-term follow-up periods (of at least 5 years) are, therefore, needed to evaluate the effectiveness of the above-mentioned (and other) procedures.



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Congress and conference calendar

■ SOCIÉTÉ FRANÇAISE DE MÉDECINE VASCULAIRE

This congress will be held in Versailles (France) from September 21 to 23, 2006.

• *For further information, please contact:*

Congress President: J-P. Laroche

Organizing secretariat:
Alexandra Leclerc - Elisabeth Negre
Palais des Congrès
10, rue de la Chancellerie
78000 Versailles, France

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E-mail: congres@nex-com.com

Web site: www.palaisdescongres-versailles.com

■ Xth ANNUAL MEETING EUROPEAN SOCIETY FOR VASCULAR SURGERY

This congress will be held in Prague (Czech Republic) from September 21 to 24, 2006.

• *For further information, please contact:*

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Secretary General
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■ XLVIIIth ANNUAL CONGRESS OF THE GERMAN SOCIETY OF PHLEBOLOGY

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• *For further information, please contact:*

President: Prof Michael Jünger

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■ XIIth NATIONAL SURGICAL CONGRESS

This congress will be held in Sofia (Bulgaria) from October 5 to 8, 2006.

• *For further information, please contact:*

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■ **VIIIth INTERNATIONAL CONGRESS OF
PHLEBOLOGY – SCLEROTHERAPY 2006**

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■ **XXVIIIth SIAPAV NATIONAL CONGRESS**

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• *For further information, please contact:*

Congress President: Prof F. A. Allaert

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LETTER TO THE EDITOR

Letters that raise new or controversial issues of interest to readers, or posing a question or challenge to an article published in Phlebology will be considered for publication. The Editor may send the letter to the authors of the original paper so their comments may be published simultaneously.



Four years of Phlebology.

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Thromboembolic disease	2004;43	Ogawa T	Epidemiology of pulmonary embolism in Japan
Venous malformations	2004;43	Lee BB	Current concepts of venous malformations
	2004;47	Lee BB	Lymphedema-angiodysplasia syndrome: a prodigal form of lymphatic malformation

Topic	Phlebology, Year; N° or Vol (issue)	First author	Title
Varicose vein (surgery)	2006;13(4)	Veverková L	Analysis of surgical procedures on the great saphenous vein in the Czech Republic and effect of Daflon 500 mg after stripping
	2006;13(4)	De Maeseneer MG	Strategies to minimize the effect of neovascularization at the saphenofemoral junction after great saphenous vein surgery: an overview
Varicose vein (endovenous treatment)	2004;45	Fassiadis N	The evolution of endovenous radiofrequency ablation (VNUS Closure) of varicose veins
	2005;48	Perrin M	Endovenous treatment of lower-limb varices by laser and radiofrequency
	2006;13(4)	De Maeseneer MG	Strategies to minimize the effect of neovascularization at the saphenofemoral junction after great saphenous vein surgery: an overview
Varicose vein (sclerotherapy)	2003;40	Frullini A	Foam sclerotherapy: a review
	2006;13(4)	Geroulakos G	Foam sclerotherapy for the management of varicose veins. A critical reappraisal
Venous anatomy and pathology	2004;47	Corcos L	Histopathology of great saphenous vein valves in primary venous insufficiency
	2005;48	Creton D	Saphenopopliteal junctions are significantly lower when incompetent. Embryological hypothesis and surgical implications
	2006;13(1)	Uhl JF	Relationship between the small saphenous vein and nerves: implications for the management of chronic venous disease
Venous aneurysms	2006;13(3)	Perrin M	Venous aneurysms
Venous ulcer	2003;41	Eliska O	Morphological changes in lymphatic vessels from edema to venous leg ulcer
	2004;44	Herouy Y	The role of matrix metalloproteinases (MMPs) and their inhibitors in venous leg ulcer healing
	2004;45	Perrin M	Rationale of surgery in the treatment of venous ulcer of the leg
	2004;47	Humbert P	Wound healing assessment
	2005;48	Fassiadis N	Patient compliance with venous leg ulcer treatment
Venous physiology	2006;13(1)	Lurie F	A new concept of the mechanism of venous valve closure and role of valves in circulation

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