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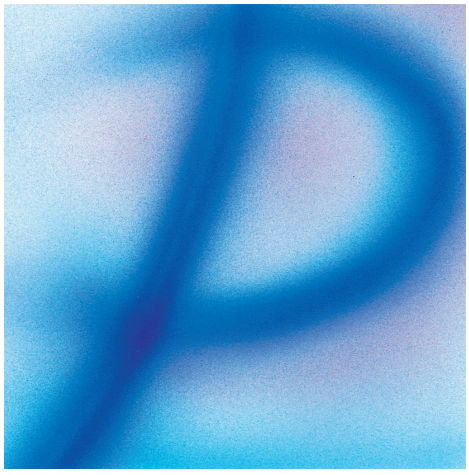

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## AIMS AND SCOPE

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

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

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

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

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

## CORRESPONDENCE

**Editorial Manager**
Françoise PITSCH
Servier International
50, rue Carnot
92284 Suresnes Cedex, France
Tel: +33 (1) 55 72 68 96
Fax: +33 (1) 55 72 56 86
E-mail: francoise.pitsch@fr.netgrs.com

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**Karel Roztocil**
**Prague, Czech Republic**

*Dear Readers,*

*This issue of* Phlebolymphology *once again brings topics of immediate interest to the fore—venous ulcers, varicose vein treatment, venous pelvic congestion syndrome, and superficial vein thrombosis. Allow me to comment on them briefly.*

*For years, chronic venous diseases have been neglected and considered to be less important than other cardiovascular diseases. At present such a view is definitely not acceptable, at least in patients with venous ulcers, which is the most serious condition associated with chronic venous diseases and the development of chronic venous insufficiency. The results of the recent* ***Vein Consult Program*** *have shown that the incidence of such advanced stages of chronic venous insufficiency is much higher than expected and that it represents a worldwide problem, which is not limited to developed countries. The socioeconomic impact is enormous due to longlasting treatments, their costs, and high work-incapacity levels, which exceed the yearly numbers obtained in patients with peripheral arterial disease, myocardial infarction, and other cardiovascular events. That is why in recent years some measures have been put in place to reduce this problem. One very good example is that of the ambitious program prepared by the American Venous Forum to reduce the incidence of venous ulcers in the population of the USA. The main measures include professional and public awareness of the problem, early and standardized diagnosis, choice of management, selection of scientific research topics, and organizational health care policy initiatives. No doubt both the contribution of* ***M. Perrin et al*** *and that of* ***S. Marinović Kulišić*** *and* ***J. Lipozenčić*** *are in keeping with these measures. The first article deals with ulcers of combined etiology, which occur in the presence of both advanced venous and arterial insufficiency, while the second article describes good clinical practice in dermatology for the management of patients with chronic leg ulcers.*

*The contribution of* ***A.O. Tonev et al*** *presents the experience of a Bulgarian vascular department and compares two methods used for the treatment of varicose veins. The results show rather clearly the advantages of the endovenous radiofrequency ablation technique over the classical surgical technique using saphenophemoral ligation and stripping. This is in keeping with the recent guidelines of the Society of Vascular Surgery and the American Venous Forum, which consider endovenous ablation as the preferred technique for the treatment of varicose veins. In this respect, one can wonder whether the better clinical results, less invasive approach, greater availability, and better patient compliance reported with the endovenous techniques will result in a reduction in the incidence of the terminal stages of venous insufficiency in the future.*

*Pelvic congestion syndrome is very often neglected or little known in general practice. Patients with this condition are sometimes very limited in their everyday activities and unsuccesfully visit different doctors. The review prepared by* ***J. Leal Monedero et al*** *is valuable and presents a diagnostic algorithm and the currently recommended treatments for this condition, where endovenous techniques have priority.*

*Superficial vein thrombosis has long been considered an insignificant and benign disease. In comparison with deep vein thrombosis, it was expected not to carry a risk of pulmonary embolism. However, in recent years we have witnessed a change of opinion about the management of these conditions, and the paper of* ***A. D. Giannoukas*** *is an excellent survey of the current opinions. It is clear that we now have to include and consider superficial vein thrombosis as one of the regular types of venous thromboembolism—together with deep vein thrombosis, postthrombotic syndrome, pulmory embolism and chronic thromboembolic pulmonary hypertension.*

*Have an enjoyable read!*

# Current management of superficial thrombophlebitis of the lower limb

Athanasios D. GIANNOUKAS

*Professor of Vascular Surgery, University of Thessalia Medical School Chairman of Vascular Surgery Department, University Hospital of Larissa, Larissa, Greece*

## ABSTRACT

Superficial thrombophlebitis is a manifestation of thrombosis that involves the superficial venous system of the lower limb. It is frequently underreported and is considered an insignificant entity. In some cases it may coexist with deep vein thrombosis, or may extend from the superficial system to the deep veins, increasing the risk of complications such as pulmonary embolism. Diagnosis by ultrasound scanning is essential to exclude deep venous thrombosis and confirm the extent of the superficial thrombophlebitis. When superficial thrombophlebitis coexists with deep vein thrombosis, or when the main trunk of the saphenous veins in the vicinity of the junctions is affected, treatment with low molecular weight heparins should be initiated.

## EPIDEMIOLOGY, ETIOLOGY, CLINICAL PRESENTATION AND DIAGNOSTIC APPROACHES

The incidence of superficial thrombophlebitis (STP) in the general population ranges from 3% to 11%,[1-5] although this is considered to be an underestimate as only the more symptomatic cases seek medical attention. The mean age at STP presentation is 60 years[3,6-12] and the older the patient is the fewer the risk factors required for its development.[11,13] STP is more common (50%-70%) in women and prevalence increases with age.[3,6,7,11,12,14-21]

STP involves the greater saphenous system more often (60-80%) than the lesser saphenous system (10%-20%).[3,11,22,23] When STP develops in patients with varicose veins it is confined to the varicose tributaries rather than the saphenous trunks.[3,14] The prevalence of STP in patients with varicose veins ranges from 4%-59%;[3,11,14,15,23] bilateral SPT is reported in 5%-10% of patients.[3,6,11,23,24] Several factors including obesity,[3,25-31] age, and protein-S deficiency are associated with SPT in patients with varicose veins.[32]

The development of STP in the absence of varicose veins is relatively rare (5%-10% of all cases)[11,12,33] and various conditions have been implicated in its etiology including autoimmune disease (Behcet's, Buerger's, and Mondor's disease),[5,6,16] malignancy,[5,6,16,25,34-36] thrombophilia,[4-6,8,16,17,26,37-45] mechanical or chemical trauma or injury (venous infusion, catheter introduction),[16] radiation injury,[16] and bacterial or fungal infections.[16] Risk factors are the same as those for the development of deep vein thrombosis

**Keywords:**
elastic stockings, low molecular weight heparins, nonsteroidal anti-inflammatory drugs, saphenous veins, thrombosis, unfractionated heparin, varicose veins, vitamin K antagonists

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(DVT)[17,27] and include a history of thrombotic events,[46-48] pregnancy,[49,50] use of oral contraceptives and hormone replacement therapy, immobilization,[18,29,30,31,51] obesity, recent surgery[18,52] and trauma,[18,51] and sclerotherapy.[53,54]

As STP may coexist with DVT in 6%-53% of patients presenting with STP[5,9,11,14,15,19,23,55-66] it is important to perform a duplex scan to exclude DVT and to confirm the presence of STP and its extent. Thrombus extension from the superficial system into the deep veins may occur through the saphenofemoral and saphenopopliteal junctions and the perforating veins (*Figure 1*). Extension from the greater saphenous vein (GSV), particularly when the above knee segment is involved, into the femoral vein is the most common scenario[23] and occurs in 17%-19% of cases. When STP affects the below knee segment of the GSV (*Figure 2*) an association with DVT has been reported in only 4-5% of cases.[10,27,57] It should be noted that STP may be a risk factor for the development and recurrence of DVT.[3,5,11,22,67,68]

In the literature, pulmonary embolism in patients with STP has been reported at rates varying from 1.5% to 33%.[5,7,11,12,19,23,62,65,69,70] STP is also a risk factor for the recurrence of pulmonary embolism.[3,5,11,22,68] Pulmonary embolism is more common when thrombosis is confined to the GSV above the knee (18%) as compared with thrombosis confined to the short saphenous vein (4%).[23] However, it is unclear whether pulmonary embolism associated with STP results from a thrombus in the superficial veins, or after its progression to the deep venous system.[3]

STP may develop during pregnancy, but because the prevalence is very low (0.05-0.1%) it is unclear whether there is any etiological link.[3,17,49,50,71-73] However, the problem may be underestimated as the published literature only includes symptomatic patients.[49,50]

The typical clinical presentation of STP includes local pain, warmth, erythema, and swelling, with

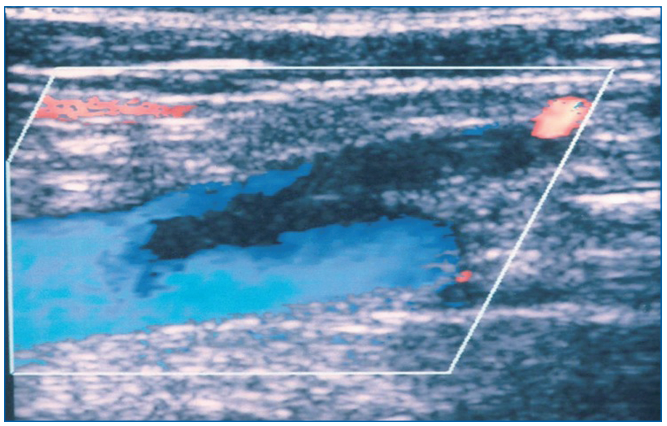

***Figure 1.*** *Thrombus in the greater saphenous vein extending to the common femoral vein through the saphenofemoral junction.*

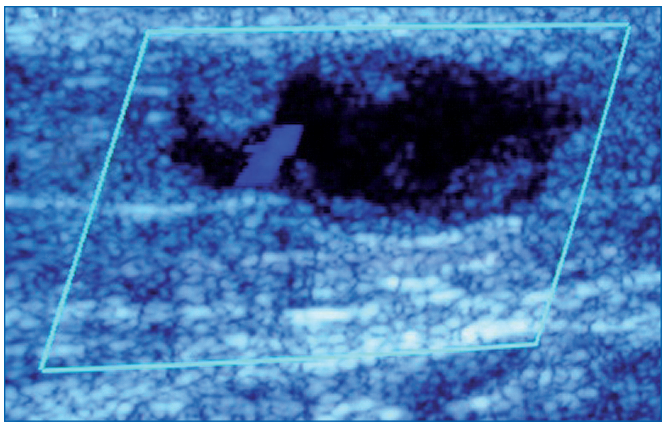

***Figure 2.*** *Thrombosed varicosity in the calf.*

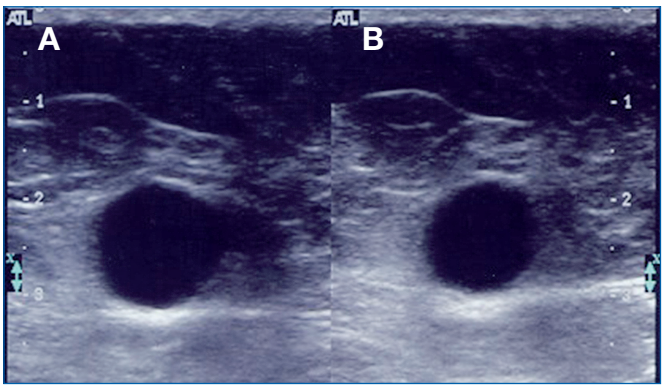


***Figure 3.*** *Thrombosed greater saphenous trunk at the thigh: A. without compression, B. with compression. The vein is incompressible and dilated containing echolucent material (fresh thrombus).*

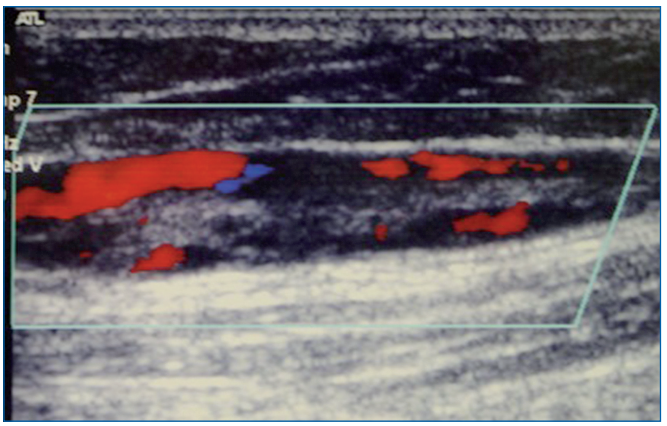

***Figure 4.*** *Greater saphenous vein with an old thrombus as characterized by the presence of recanalization and echogenic material inside its lumen.*

the superficial vein becoming solid like a cord.[3,6,33,74] It is important to reiterate here the value of Duplex ultrasound for the confirmation of STP, estimation of thrombus extent (*Figures 3 and 4*), exclusion of DVT and for follow-up.[5,6,9,10,20,23,35,55,58-63,75]

## TREATMENT

The treatment of STP varies greatly in clinical practice. Among 634 patients in the POST study, a prospective epidemiologic study conducted in France, treatments included anticoagulation in therapeutic or prophylactic doses, vitamin K antagonists, elastic stockings, topical or oral use of nonsteroidal anti-inflammatory drugs (NSAIDs) and surgery.[11]

In a randomized study of 562 patients, unfractionated heparin, low-molecular-weight heparin (LMWH) and vitamin K antagonists were found to have equal efficacy and were superior to elastic compression or flush ligation combined with elastic compression in terms of STP extension at 3 months.[16]

A randomized, double-blind trial of 427 patients[52] that compared LMWH (enoxaparin 40 mg and 1.5 mg/kg) with an NSAID (tenoxicam) or elastic stockings alone for 10 days showed that the prophylactic dose of LMWH (enoxaparin 40 mg) was the most effective treatment. Similar findings were reported in another open randomized trial involving 117 patients.[76]

The use of high doses of unfractionated heparin twice daily seems to be superior to prophylactic doses, but is inferior to LMWH in prophylactic or therapeutic doses.[77-79] A systematic review has shown that both LMWH and NSAIDs significantly reduced the incidence of extension or recurrence of STP by approximately 70% compared with placebo, and both had similar efficacy and safety.[80]

The CALISTO trial was an international, randomized, double-blind, placebo-controlled trial of 3,002 patients[12] that compared subcutaneous fondaparinux 2.5 mg once daily for 45 days with placebo. Participants included hospitalized or nonhospitalized patients 18 years or older, with acute, symptomatic lower limb STP, at least 5 cm long, as confirmed by compression ultrasonography. Exclusion criteria were an interval between the onset of symptoms and planned randomization of more than 3 weeks; treatment for cancer within the previous 6 months; presence of symptomatic or asymptomatic DVT; symptomatic documented pulmonary embolism; STP associated with sclerotherapy or placement of an intravenous catheter; STP located within 3 cm of the saphenofemoral junction; and DVT or pulmonary embolism within the previous 6 months. Patients were also excluded if they had received an antithrombotic agent (other than aspirin at a dose of ≤325 mg per day) for more than 48 hours or a NSAID for more than 72 hours as treatment for the current episode; if in the investigator's opinion a saphenofemoral junction ligation was required; if they had had major surgery within the previous 3 months; if there were conditions that could confer predisposition to bleeding including creatinin clearance <30 ml/min, platelet count <100,000/mm$^3$; and any women that were pregnant.

The primary efficacy outcome (a composite of death from any cause or symptomatic pulmonary embolism, symptomatic DVT, or symptomatic extension to the saphenofemoral junction or symptomatic recurrence of superficial vein thrombosis at day 47) occurred in 0.9% of patients in the fondaparinux group and 5.9% in the placebo group ($P$<0.001). The rate of pulmonary embolism or DVT was 85% lower in the fondaparinux group. Similar risk reductions were observed at day 77. No difference was observed in major bleeding between the two groups. However, several concerns were expressed in relation to this trial, especially when applying such treatment to any STP, because of the high cost of the therapy.[81]

Surgical treatment combined with elastic stockings is associated with a lower rate of venous thromboembolism and progression of STP compared with elastic stockings alone.[80] Another review in which surgical therapy was compared with anticoagulation therapy showed similar rates of STP progression, but the incidence of venous thromboembolism and complications were higher with surgery.[82] In another study, no difference was observed between surgery and 4 weeks of enoxaparin therapy.[83]

The role of antibiotics is of no benefit in the management of STP[33,84] unless the cause of thrombosis is secondary to an indwelling intravenous catheter.

Hirudoids and some topical agents (piroxicam cream, piroxicam patch) improve local symptoms, alleviating pain and local inflammatory signs, but there is no information on progression to DVT.[80,85-87] Local

application of heparin was reported to have effects on symptoms comparable to LMWH.[88] If tolerated, elastic stockings are traditionally used as an adjunctive treatment together with anticoagulation[6,16,33,52,89]

In summary, all patients with STP should have bilateral duplex scanning to exclude DVT. As far as treatment is concerned, LMWH in intermediate doses for at least 1 month or fondaparinux 2.5 mg daily for at least 4 weeks are effective therapies. Surgery is no more effective than LMWH, but when the thrombus is close to the saphenofemoral or saphenopopliteal junctions, both are acceptable options depending on the patient's characteristics and the treating physician's preference. For isolated STP at the below knee segment confined to varicosities, local application of heparinoids, NSAIDs and elastic stockings form an acceptable treatment option.

**Corresponding author**
Athanasios D. GIANNOUKAS, MD, MSc, PhD, EBSQvasc
Professor of Vascular Surgery
Faculty of Medicine, University of Thessaly
Chairman, Dept. of Vascular Surgery
University Hospital of Larissa
Mezourlo, 41 110 Larissa, Greece

E-mail: giannouk@med.uth.gr

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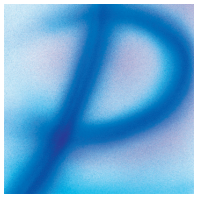

# Management of mixed arterial and venous lower leg ulcers

Michel PERRIN,[1]
Marzia LUGLI,[2]
Oscar MALETI[2]

*1 Vascular and Endovascular Surgery department Jean Kunlin Lyon, France.*
*2 Hospital Hesperia, Modena, Italy*

## ABSTRACT

Vascular mixed ulcers are identified in about 10% of lower leg ulcers, but their prevalence is underestimated. A combination of anatomical and physiopathological venous and arterial anomalies makes their management difficult. Both must be investigated in detail to allow optimal treatment. There is consensus that when the ankle brachial index is less than 0.6, the first step should be revascularization for ulcer healing and to prevent recurrence. Conversely, when the ankle brachial index is above 0.6 there is no consensus on the treatment sequence and procedures that should be followed. If initial treatment is successful, close follow-up is strongly recommended as recurrence of vascular mixed ulcers due to revascularization failure is frequently difficult to manage.

## INTRODUCTION

The origin of mixed etiology leg ulcers is primarily due to chronic venous insufficiency and the ability of mixed ulcer to heal is determined mainly by the severity of the coexisting arterial insufficiency. These ulcers cause considerable pain and distress for patients and pose a difficult wound-management problem for health care professionals. Accurate diagnosis of mixed arterial and venous leg ulcers is essential as compression bandages may not be suitable if there is significant arterial disease. This paper reviews the literature on the management of patients with mixed arterial and venous leg ulcers and suggests recommendations for treatment.

## DEFINITION

There is no precise definition of mixed arterial and venous leg ulcers (MAVLU), also known as combined arterial and venous insufficiency ulcers.[1,2] Nevertheless, there is consensus that patients presenting with MAVLU combine chronic venous insufficiency (CVI) and peripheral arterial occlusive disease (PAOD).

**Keywords:**
mixed arterial and venous ulcer, chronic venous disease, peripheral arterial occlusive disease

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## PREVALENCE

Chronic leg ulceration affects 1%-2% of the population. It is a major cause of prolonged morbidity and is commonly associated with delayed healing and multiple recurrences. Significant venous disease exists in over 70% of ulcerated limbs, but a variety of other etiologies have been identified.[3,4] Arterial disease may coexist with venous dysfunction, but the precise prevalence of MAVLU is difficult to establish and is probably underestimated.[4-6] If an ankle brachial index (ABI) < 0.8 is used as the criteria to determine MAVLU prevalence, the rate is 15% according to Marston.[7] In the series reported by Bohannon et al, patients with MAVLU represented 0.08% of all discharges at two large tertiary care hospitals over a 10-year period.[8] Correct and precise determination of each vascular abnormality is crucial as it allows a logical approach to MAVLU management.

## PATHOPHYSIOLOGY

The pathophysiology of MAVLU can be attributed to a combination of venous hypertension, primary or post-thrombotic venous reflux and/or obstruction, and a reduction in blood inflow due to peripheral arterial occlusive disease of various anatomical locations. The mechanism of tissue damage involves a low oxygen partial pressure and the activation of inflammatory pathways. The difficulty in determining which component is predominant in venous and arterial anomalies affects MAVLU management.

## PHYSICAL EXAMINATION

Ulcer diagnosis is clinically obvious, but does not provide reliable information on etiology and physiopathology. Nevertheless, some relevant information can be obtained from reviewing the patient's family and personal medical history, as well as by performing a physical examination to determine the ulcer features and localisation, presence of varices or venous skin changes, and absence of femoral, popliteal, or tibial pulses (*Figures 1A and 1B*).

## INVESTIGATIONS

When MAVLU is suspected the patient should be examined according to the algorithm presented in *Figure 2*. The level of assessment may vary according to the intention to treat.

## OPERATIVE TREATMENT METHODS

The term "operative treatment" refers to open surgery and endovascular procedures and can address peripheral arterial occlusive disease, chronic venous disease (including that of the superficial, perforator, and deep venous systems), and sometimes both arterial and venous anomalies. The aim of MAVLU treatment is twofold: first, to achieve ulcer healing, and second, to prevent recurrence. When an operative or conservative treatment leads to ulcer healing, this does not necessarily imply recurrence prevention. Treatments may address the venous and/or arterial aspects of the disease depending on the outcome of clinical and physical examination findings.

### MAVLU healing

When peripheral arterial occlusive disease is detected, the options for treating the arterial disease are open surgery or endovascular procedures, as recommended by the Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II).[9] In this specific group of patients, the indication for a distal bypass using an autologous vein may be limited by the availability of a functioning saphenous vein (due to varicose vein pathology and/or previous saphenous ablation).

The management of venous disease is controversial in patients with peripheral arterial occlusive disease. Two randomized controlled trials have demonstrated that surgery combined with compression therapy had no advantage over isolated compression on venous ulcer healing,[10,11] but the application of compression therapy is still a matter of debate in patients with MAVLU.[7,12,13]

Both compression therapy and superficial vein ablation have been performed with or without arterial procedures, but there are no data concerning deep venous surgery, either for obstruction or reflux.

### Prevention of MAVLU recurrence

Arterial disease plays a major role in the recurrence of MAVLU. Recurrence may be associated with failure of revascularization as well as progression of peripheral arterial occlusive disease. Monitoring and treatment of risk factors for atherosclerotic disease, as well as optimizing pharmacological therapy for atherosclerosis, may play a decisive role in preventing MAVLU recurrence.


*Figure 1. 1A and 1B. Mixed arterial and venous ulcers*

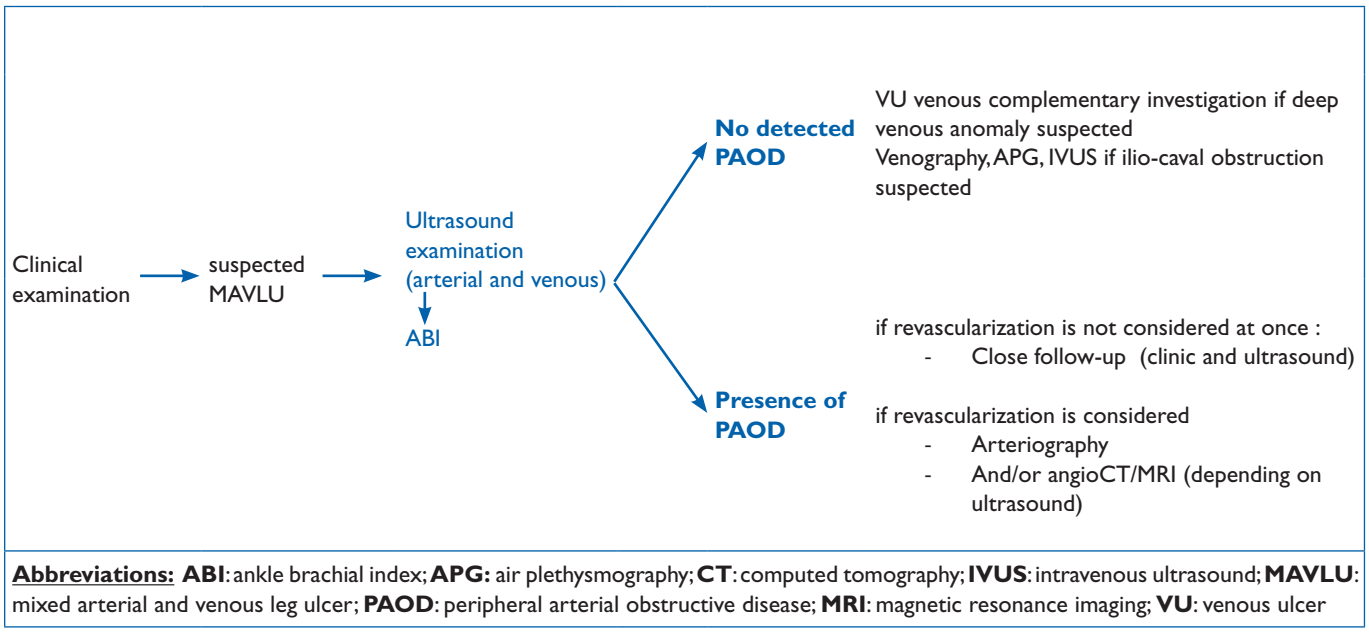


*Figure 2. Diagnostic algorithm*

## TREATMENT RESULTS

Treatment results are difficult to interpret as the decision to perform conservative and operative treatments is determined by different ABI values, and is based on the tendency of the ulcer to heal in response to conservative treatment. Some outcomes in patients with MAVLU are listed in *Table 1*.[1,2,6,8,13-15]

## TREATMENT INDICATIONS

The first decision concerns whether or not to perform revascularization, and this is based on clinical signs, ABI, and anatomical arterial lesions. ABI is widely used to measure arterial impairment, but other parameters must also be taken into account when assessing the severity of arterial disease. These include pain at rest, tissue damage, and anatomical patterns associated with peripheral arterial occlusive disease. If ABI is below 0.6, most studies recommend revascularization as first-line treatment using either an open or endovascular procedure, depending on TASC lesion distribution and technical feasability.[2,15] For ABI values between 0.6 and 0.8, data are insufficient to indicate whether revascularization should be performed before or after supervised compression therapy and/or superficial venous ablation.

Superficial axial reflux should be corrected alone or in association with other procedures. Endovascular ablation should be the first-line treatment as it is minimally aggressive.

| Author (ref) | Year | Number of extremities | Selected criteria for inclusion or / and treatment | | Follow-up months | Results |
|---|---|---|---|---|---|---|
| Ghauri [1] | 1998 | Group 1=33 | Group 1➔ ABI 0.85-0.5+ SVI or/and DVI | SMC failure (12/33) è ARS (5/12) + 5 SVS | | 33 limbs<br>21 limbs. Healing 64% with SMC<br>12 limbs. No healing 36% with SMC<br>5 successful ARS. Healing in 80% |
| | | Group 2=13 | Group 2➔ ABI <0.5 +SVI or/and DVI | ARS (8/13) + 2 SVS | 9 | 13 limbs<br>3 limbs. Healing 23% with SMC<br>2 limbs. No ARS<br>8 limbs. Successful ARS. Healing 60% |
| Treiman [2] | 2001 | Group 1=22<br>Group 2= 7<br>Group 3=22<br>Group 4= 8 | Group 1➔ ABI (mean 0.52) PAOD+SVI<br>Group 2➔ ABI (mean 0.56) PAOD+SVI+ DVI<br>Group 3➔ ABI (mean 0.36) PAOD+ PTS<br>Group 4➔ ABI (mean 0.34) PAOD+ 4 SVI +4PTS | 22 ARS successful + 19 SVS<br>7 ARS successful + 2 SVS+ compression<br>19 ARS successful + compression<br>3 primary amputation (ARS unsuccessful) | 19.8<br>26<br>23<br>19.5 | 22 limbs. Healing 95%<br>7 limbs. Healing 57%<br>22 limbs. Healing 41%<br>8 limbs. Healing 0% |
| Bohannon [8] | 2002 | 15 | ABI 0.1-0.78 (mean 0.46) + SVI or/and DVI | 12 ARS (9 successful)<br>2 primary amputation<br>1 sympathectomy | 33.6 | 13 limbs. Healing 3 limbs 23%<br>Ulcer Recurrence 2 limbs<br>At last follow-up 10% healing |
| Karkos [14] | 2005 | 9 | ABI<0.8 PAOD + SVI | 9 subintimal angioplasty + 7 SFJL or/and SPJL | 32 | 9 limbs.<br>Healing 100%<br>Median 32 months, Extremes 4- 82<br>1 ulcer recurrence at 36 months |
| Humphreys [6] | 2007 | Group 1=193 | Group 1➔ ABI 0.85-0.5 +SVI or/and DVI | SMC failure at 3 months ARS (17/193) | 9 | 193 limbs. Healing 67.6% |
| | | Group 2= 31 | Group 2➔ ABI <0.5 +SVI or/and DVI | ARS (15/31) | | 31 limbs. Healing 53% |
| Obermeyer [13] | 2008 | 28 | ABI>0.8 + SVI | SVS + shaving and skin graft | 38.4 | 28 limbs<br>Healing 68%<br>Nonhealed 21%<br>Ulcer recurrence 11% |
| Lantis [15] | 2011 | 27 | ABI 0.55 (+/- 0.21) + SVI or PTS | PAR + postoperative compression | Mean 18 (6-36) | 27 limbs<br>Healing 100% at 5.5 months<br>4 ulcer recurrences,<br>3 related to arterial reocclusion |

**Abbreviations: ABI**: ankle brachial index; **ARS**: arterial reconstructive surgery; **DVI**: deep venous insufficiency; **PAOD** peripheral arterial occlusive disease; **PAR**: percutaneous arterial revascularization; **PTS**: postthrombotic syndrome; **SFJL**: saphenofemoral junction ligation; **SMC**: supervised modified compression; **SPJL**: saphenopopliteal junction ligation; **SVI**: superficial venous insuficiency; **SVS**: superficial venous surgery.

***Table I.*** *Outcome in mixed arterial and venous ulcers according to treatment.*

The indication for deep venous surgery is determined by etiology (postthrombotic or not) and anatomical and physiopathological lesion distribution. However, given its complexity, surgery to correct deep venous reflux can rarely be performed in such patients. Conversely, surgical endovascular correction of ilio-caval obstruction should be considered.

Follow-up assessments should be scheduled to identify any possible deterioration in the reconstructive arterial surgery in patients presenting with MAVLU. Early detection is essential to prevent revascularization failure and the requirement for repeat revascularization, which is more complicated than primary revascularization.

If MAVLU recurs, a full diagnostic reassessment is mandatory before any new treatment is started. In most cases, progression of an arterial disease anomaly is the cause and repeat revascularization is the mandatory first step to achieve MAVLU healing and relieve patient symptomatology. When arterial revascularisation is not successful, amputation is often the only option to relieve pain.

Exceptionally, the cause of ulcer recurrence is a previously underscored venous anomaly, which in the majority of cases is related to a severe deep venous insufficiency, usually postthrombotic. In the presence of supra-inguinal obstruction, stenting should be considered, while endovascular ablation is recommended for superficial reflux as previously mentionned.

## CONCLUSIONS

MAVLU is a challenging condition to treat and its optimal management has not been precisely established. Nevertheless, there is consensus that if ABI is less than 0.6, revascularization should be performed if possible. In daily practice, the management of MAVLU is mainly determined by individual factors.

**Corresponding author**
Michel PERRIN, MD
Vascular Surgery
26 Chemin de Decines
F-69680 Chassieu
France

Email m.perrin.chir.vasc@wanadoo.fr

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# The Essentials from the XVIIth World Meeting of the Union Internationale de Phlébologie, 7-14 September 2013, Boston, USA

## VENOUS SYMPTOMS AND CHRONIC VENOUS DISEASE

Whether venous symptoms form part of chronic venous disease (CVD) was the first question asked in the Daflon 500 mg symposium organized under the framework of the 'Union Internationale de Phlébologie' (UIP) in Boston. This remains a controversial question. For some patients, lower limb pain is poorly related to the presence of varicose veins,[1-3] C-class of the Clinical, Etiological, Anatomical, Pathophysiological (CEAP) classification, [4] degree of reflux,[5] or to the presence of inflammatory markers.[6] In contrast, other patients may have a significant correlation between lower limb pain/symptoms and worsening clinical signs of CVD or CEAP clinical classes.[7-12]

In the recent Vein Consult Program (VCP), which was performed in 22 countries and gathered information on 95 000 subjects screened by general practitioners (GPs) for CVD, positive correlations between increasing CEAP clinical classes and the presence of pain were observed *(Figure 1)*. When adjusted for age, gender and body mass index, the multivariate analysis in the VCP showed that the occurrence of venous symptoms was clearly linked

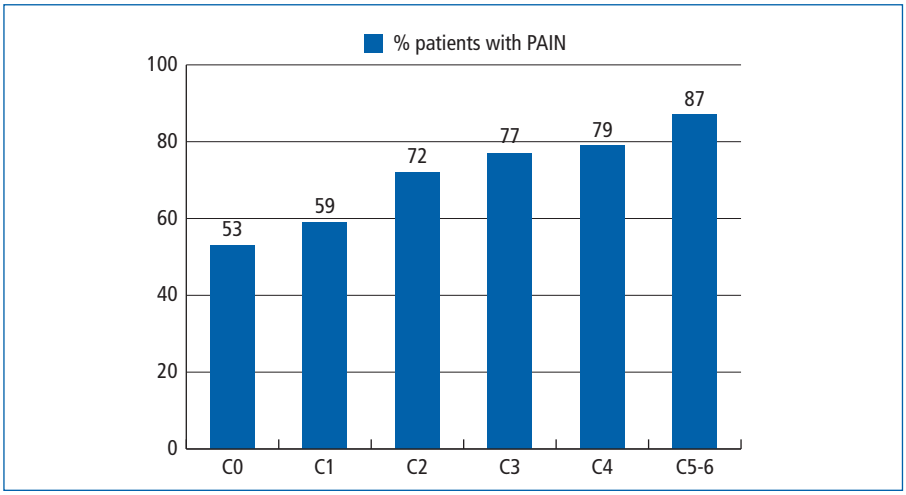


***Figure 1.*** *Frequency of venous pain in subjects participating in the Vein Consult Program according to clinical class of the CEAP classification.*[13]

**Keywords:**
chronic venous disorder, cost, epidemiology, pain, quality of life, venoactive drug

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| C of the CEAP | Adjusted odds ratio (95% Confidence Interval) |
|---|---|
| **C0 (N=26 810)** | **Reference** |
| **C1 (N=16 254)** | **5.63** (5.30 - 5.97) |
| **C2 (N=13 395)** | **9.19** (8.46 - 9.98) |
| **C3 to C6 (N=18 271)** | **16.71** (15.18 - 18.38) |

***Table I.*** *Independent risk factors for venous symptom occurrence in the multivariate analysis of the Vein Consult Program (VCP)*

to clinical CEAP class *(Table I)*. The risk for developing symptoms increased significantly with disease severity. Individuals with a chronic venous insufficiency (CVI) classification C3-C6 were 16-fold more likely to be symptomatic than individuals in C0. When considering individual symptoms according to CEAP clinical class, 'heaviness' and 'sensation of swelling' appeared more related to the C3 class (edema), while itching was related to skin changes *(Table II)*. The prevalence of

| CEAP class | Total N=77505 | C0s N=15290 | C1 - C3 N=41838 | C4 - C6 N=7421 |
|---|---|---|---|---|
| Mean number of symptoms | | **2.3±1.5** | **3.4±1.7** | **4.7±1.8** |
| % Symptomatic patients | 80.4 | **100** | **94.7** | **96.8** |
| Heavy legs | 72.4 | **58.1** | **75.0** | **81.1** |
| Pain in the legs | 67.7 | **52.8** | **68.3** | **81.1** |
| Sensation of swelling | 52.7 | **29.3** | **56.9** | **75.3** |
| Night cramps | 44.3 | **32.6** | **43.4** | **59.6** |
| Sensation of 'pins and needles' in legs | 37.0 | **27.4** | **36.6** | **50.3** |
| Sensation of burning | 29.0 | **15.8** | **29.6** | **52.3** |
| Itching | 23.6 | **15.3** | **22.3** | **42.5** |

***Table II.*** *Distribution of the prevalence of CVD symptoms according to CEAP class*

symptoms in the VCP was high in all geographical areas studied. Moreover, distribution of symptom prevalence (by decreasing frequency: heavy legs, pain, sensation of swelling, night cramps, etc) was similar whatever the area considered. This suggests that perception of pain is similar in all countries studied and is likely to be disconnected from any cultural phenomenon *(Table III)*.

In the literature, the presence of symptoms attributed to venous pain correlates with worse quality of life (QOL).[4]

| Symptom % patients (rank) | World N=67186 | Western Europe N=23944 | Eastern Europe N=25869 | Latin America N=9700 | Middle East N=2612 | Far East N=7112 |
|---|---|---|---|---|---|---|
| **Heaviness** | **72.4 (1)** | 79.0 (1) | 76.4 (1) | 52.3 (2) | 54.7 (2) | 67.7 (1) |
| **Pain** | **67.7 (2)** | 66.8 (2) | 67.3 (2) | 72.0 (1) | 77.1 (1) | 60.5 (2) |
| **Sensation of swelling** | **52.7 (3)** | 55.2 (3) | 56.6 (3) | 50.1 (3) | 36.0 (4) | 34.9 (4) |
| **Cramps** | **44.3 (4)** | 39.6 (4) | 47.3 (4) | 47.9 (4) | 45.1 (3) | 44.2 (3) |
| **Pins and needles** | **37.0 (5)** | 35.9 (5) | 38.3 (5) | 39.5 (5) | 26.6 (5) | 36.7 (5) |
| **Sensation of burning** | **29.0 (6)** | 24.0 (7) | 33.7 (6) | 37.3 (6) | 25.0 (6) | 15.0 (7) |
| **Itching** | **23.6 (7)** | 26.1 (6) | 20.0 (7) | 29.7 (7) | 19.4 (7) | 20.3 (6) |

***Table III.*** *Frequency of venous symptoms according to geographical areas surveyed in the Vein Consult Program.*

This was also found in subjects participating in the VCP and individuals with venous symptoms had a lower global index score (GIS) than those without symptoms, indicating a worse QOL for patients complaining of pain in their lower limbs *(Figure 2)*.

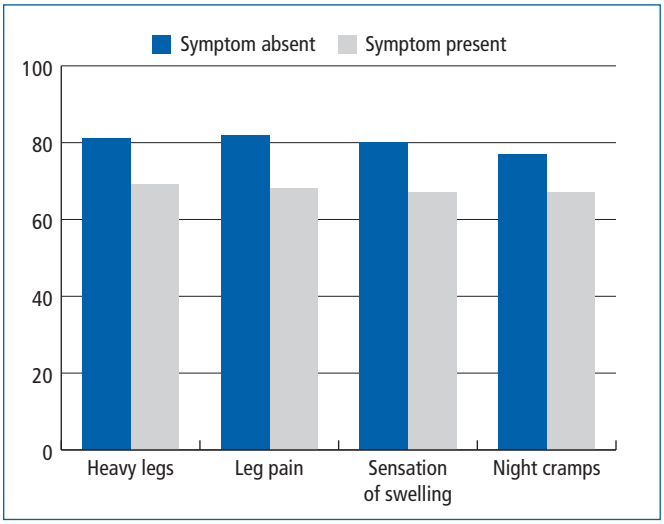


***Figure 2.*** *Quality of life assessment in subjects participating in the Vein Consult Program according to the presence or absence of venous symptoms (C0s to C6 patients; N=35495)*

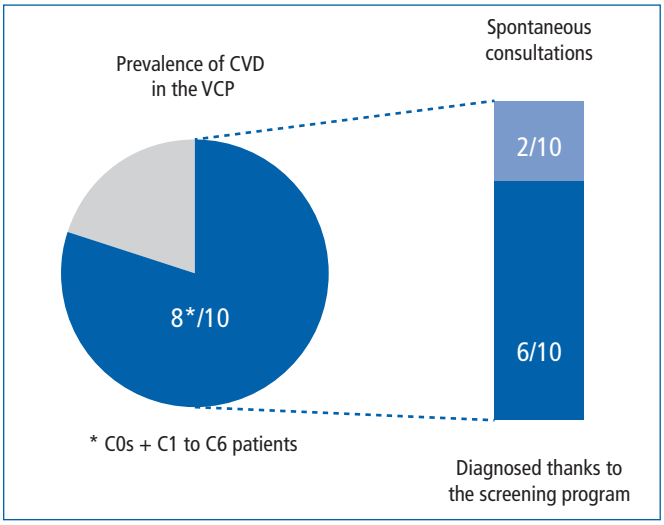


***Figure 3.*** *Prevalence of symptomatic subjects and percentage of subjects consulting spontaneously for leg complaints in the Vein Consult Program*

Globally, 63% of screened subjects in the VCP were considered to have CVD by their GPs.[13] Subjects with symptoms only (C0s class) were less likely to be considered as having CVD and to be liable for treatment than those with signs. The presence of a symptom was not the trigger for starting CVD treatment. While 63% of screened subjects were considered to have CVD by GPs, only 22% (one-third) were referred to venous specialists. Referral to a venous specialist was associated with severity of disease, as this increases with higher clinical CEAP class from 4% in C0s to 60% in C6. It is not until severe stages are present that GPs refer their patients to a venous specialist. Despite this, it appears that a systematic search for venous symptoms, as was performed in the VCP, could help detect CVD in 6 out of 10 subjects (it is of note that 50% of these were C0s or C1s). Only 2 out of 10 subjects spontaneously sought help for their venous problems [13] *(Figure 3)*.

These facts raise the question of why venous symptoms are so often overlooked. The underestimation of venous pain and symptoms may have multiple causes, such as:

- They mostly affect women.
- They are not specific for venous disease.
- They are subjective per se and not systematically related to clinical signs or reflux.
- They are very common whatever the geographical area.
- Improvements are more important for the patient than the physician.

In conclusion, venous pain should be considered a part of CVD as a systematic search for symptoms may help detect the disease, and relief of symptoms leads to improvements in QOL, which is meaningful to patients.

## WHAT IS THE BURDEN OF CHRONIC VENOUS DISEASE FOR SOCIETY?

CVD is a very common disease among adults and is estimated to be the seventh most common reason for physician referral in the US. Approximately 1% of the adult population has an ulcer of venous origin at any one time with 4% at risk. Venous ulcers are often lengthy medical problems and can last for several years and are associated with high recurrence rates.[14]

In the VCP, subjects diagnosed with CVD after GP examination were requested to complete a self-administered questionnaire reporting features about their professional activities and QOL (using CIVIQ-14 and scoring 0 for a poor QOL to 100 for a very good QOL).

A total of 35 495 questionnaires from 17 countries (Armenia, Colombia, France, Georgia, Hungary, Indonesia, Mexico, Romania, Russia, Serbia, Singapore, Slovakia, Slovenia, Thaïland, UAE, Ukraine, Venezuela) were analyzed. Seven percent of patients had been hospitalized and 4% had changed their professional activities because of CVD. Loss of work days was reported in 15% of patients *(Figure 4)*. The number of lost work days did not exceed 1 week for most (40%), while 33% had lost more (21% > 1 week and 12% > 1 month). QOL scores decreased with higher frequency of lost work days (from 68.5 ±19.5 for 1 time to 51.2 ± 22.9 for >3 times) and with duration of absence from work (from 76.0 ±_18.7 for <1 week to 55.3 ± 22.8 for >1 month). This was also true with increasing severity of CVD, ranging from 80.5 ± 16.4 in patients with telangiectasias to 54.8 ± 22.4 in those with an ulcer, and with presence of CVD symptoms: GIS was 84.0 ±16.5 in patients without pain versus 67.8 ± 19.9 in those with pain (unpublished data).

| Events over the last 5 years for venous leg problems | Statistics |
|---|---|
| Surgery or sclerotherapy | 12.1% |
| Changes in professional activities or job | 3.7% |
| Hospitalizations | 6.1% |

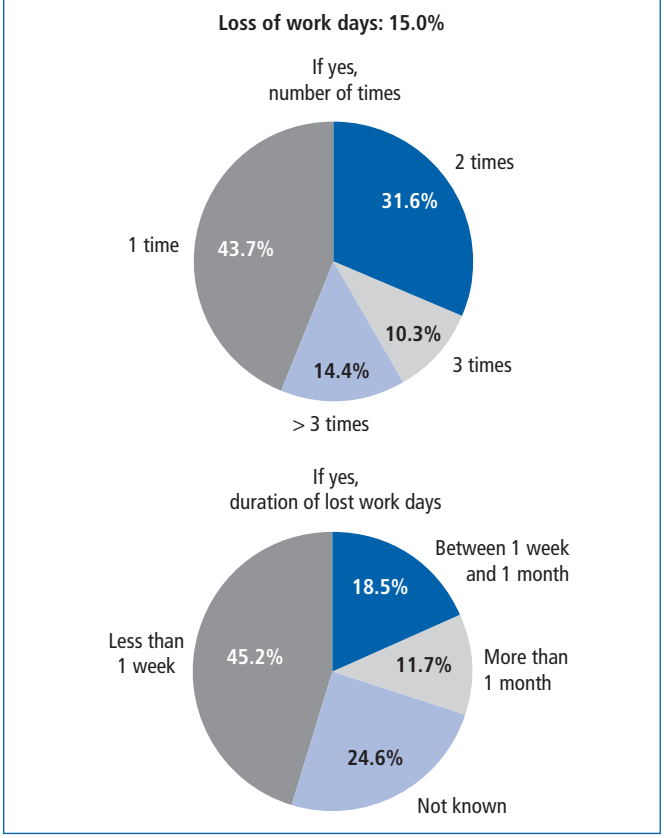


***Figure 4.*** *Appraisal of the costs of chronic venous disorders in the Vein Consult Program*

## SPECIFIC TOOLS FOR ASSESSING QUALITY OF LIFE IN CVD

The use of comprehensive QOL instruments has shown greater consistency of results than those drawn from simple reporting of individual symptoms. A review of the literature shows that CVD is associated with reduced QOL, particularly in relation to pain, physical functioning and mobility, and also with negative emotional reactions and social isolation.[15] Patients with varicose veins have reduced QOL compared with the general population,[16,17] and treatment with surgery[18,19] or sclerotherapy[20] has been shown to improve QOL. However, it is important to distinguish the contribution of the varicose veins themselves from that of other concomitant manifestations of CVD.[17]

A large-scale study in 2404 patients that used the generic SF-36 questionnaire found significant associations between QOL and CVD, which was assessed by visual inspection and by ultrasonography. Worsening of QOL was proportional to disease severity.[21]

A multivariate analysis has shown that QOL (assessed with the disease-specific QOL scale CIVIQ-20) of patients with CVD depends mainly on symptoms, and is less affected by the presence of reflux, the CEAP class to which the patient is assigned, the patient's age, body mass index, or duration of disease. [22]

Early symptomatic treatment, for example with Daflon 500 mg, is aimed at alleviating CVD symptoms, which are now acknowledged to reduce QOL and handicap patients' daily lives.

## IS PAIN REDUCTION A MEANINGFUL TREATMENT OUTCOME?

According to Peter Neglen (Cyprus) and colleagues, the importance of targeting pain in the treatment of chronic venous disorders is emphasized by the fact that the CEAP classification, the Venous Clinical Severity Score (VCSS) and hemodynamic parameters are not sufficient assessment methods to judge the success of a treatment.[4] Yet these methods are often the only ones used by Insurance Companies to reimburse venous treatments in certain countries.[4]

Patient-reported symptoms, in particular pain, and their assessment with QOL scales such as CIVIQ might be

| Symptom | Expectation of significant improvement | Expectation of moderate (but not significant) improvement | Legs [n=365] or patients [n=281] where expectations were not met |
|---|---|---|---|
| **Pain** | 37% | 63% | 20% |
| **Itch** | 32% | 68% | 21% |
| **Tingling** | 24% | 76% | 18% |
| **Cramps** | 30% | 70% | 23% |
| **Restless legs** | 29% | 71% | 22% |
| **Swelling** | 37% | 63% | 27% |
| **Heaviness** | 37% | 63% | 18% |
| **Aspect of lifestyle** | | | |
| **Appearance of the legs** | 60% | 30% | 12% |
| **Choice of clothes that can be worn** | 30% | 40% | 25% |
| **Performance at work** | 27% | 40% | 25% |
| **Enjoyment of leisure activities** | 27% | 40% | 14% |
| **Relationships** | 10% | 15% | 30% |

***Table IV.*** *Percentage of legs [n=373] or patients [n=281] associated with pre-operatively expectations of significant or moderate improvement in symptoms and lifestyle respectively, and where expectations were not met 6 months post-operatively.* [24]

the best way to consider the value and the benefit of a treatment.

This consideration is reinforced by patient expectations from treatment. For patients affected by CVD, treatment must be highly effective in terms of improving and even eradicating symptoms.[23-25]

According to previous studies, 75% to 100% of patients expect improvements in symptoms and lifestyle, and only 20% of patients in one study did not have their high expectations met.[24] *(Table IV)*

Expectations for improvements in lifestyle are also high, with around 70% expecting improvements in the choice of clothes, enjoyment of leisure activities and performance at work, and 25% expecting an improvement in relationships.[25] Patients also associated CVD with a high risk of morbidity. DVT and ulceration were deemed probable events by patients, and some patients also believed gangrene was a very high risk.[25]

All these CVD-related expectations and fears need to be addressed by providing clear information and by choosing adequate treatment. This is in line with the recommendations drawn from the VCP. Venoactive drugs have a place in the treatment strategy for CVD.

## THE PLACE OF DAFLON 500 MG IN THE TREATMENT STRATEGY TO REDUCE SYMPTOMS IN CVD

Daflon 500 mg has a number of vein-specific anti-inflammatory effects that relieve symptoms at all stages of CVD. In several placebo-controlled trials, micronized purified flavonoid fraction (MPFF; Daflon 500 mg) was associated with a significantly greater improvement in many of the symptoms of CVD after 2 months compared with placebo ($P<0.001$ MPFF vs placebo) or nonmicronized diosmin ($P<0.05$ MPFF vs simple diosmin). Importantly, symptom relief with MPFF was achieved rapidly and maintained in the long term.[26]

In a meta-analysis of 459 patients, MPFF significantly reduced the symptoms associated with venous ulcers after 4 and 6 months of treatment.[27] MPFF is also beneficial for post-surgery pain,[28,29] and pain associated with pelvic congestion syndrome.[20] Patients receiving MPFF 2 weeks before and continuing for 14 days after varicose vein surgery required significantly less

| Indication | Venoactive drug | Recommendation | Quality of evidence | Grade |
|---|---|---|---|---|
| Relief of venous symptoms (C0s to C6s) and edema (C3) | **MPFF** | **Strong** | **Moderate** | **1B** |
| | Simple diosmins | Weak | Poor | 2C |
| | Rutosides (O-betahydroxyethyl) | Weak | Moderate | 2B |
| | Calcium dobesilate | Weak | Moderate | 2B |
| | HCSE | Weak | Moderate | 2B |
| | Ruscus extracts | Weak | Moderate | 2B |
| | Gingko biloba | Weak | Poor | 2C |
| | Other VADs | Weak | Poor | 2C |
| Adjunctive treatment of primary venous ulcer (C6) | **MPFF** | **Strong** | **Moderate** | **1B** |

***Table V.*** *Recommendations for venoactive drugs from the international consensus meeting in Cyprus, November 2012.*

analgesic use than a control group.[28,29] In a cross-over study, women were randomized to receive either MPFF or placebo. After 6 months, mean pain scores were significantly lower in the MPFF group compared with placebo ($P<0.05$).[30]

## PLACE OF DAFLON 500 MG IN RECENT INTERNATIONAL GUIDELINES

In recent guidelines for the management of CVD, Daflon 500 mg has been assigned a high level of recommendation as a first-line treatment for venous symptoms at any stage of CVD.[14] Recommendations for the use of venoactive drugs in the guidelines are based on the 'Grading of Recommendations Assessment, Development and Evaluation' (GRADE) system.[31,32] The GRADE system differs from other schemes described in the guidelines in that separate levels are assigned for the recommendation for treatment and for the quality of evidence on which the recommendation is based. Recommendations are classified as either strong (grade 1) or weak (grade 2), and quality of evidence as high (grade A), moderate (grade B) or low (grade C). Importantly, the GRADE system recognizes that large observational studies may provide evidence of moderate or even high quality, particularly if the estimate of the magnitude of the treatment effect is very large.

Recommendations are summarized in *Table V*. It should be noted that the recommendation for Daflon 500 mg is strong, based on benefits that clearly outweigh the risks and evidence of moderate quality (grade 1B) for the indication of relief of venous symptoms in C0s to $C6_s$ patients, including those with CVD-related edema. Daflon 500 mg retains its strong recommendation for use as adjunctive therapy in treating venous ulcers. [14]

Venoactive drugs may be the only alternative available when patients cannot comply with compression therapy. In patients with CVD complications, venoactive drugs–and in particular Daflon 500 mg–may be used in conjunction with sclerotherapy, surgery and/or compression therapy, and be considered as adjunctive therapy in patients with active venous ulcers, especially in those with large ulcers of long standing. [14]

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# Pelvic congestion syndrome: an update

Javier LEAL MONEDERO[1]
Santiago ZUBICOA EZPELETA[1]
Michel PERRIN[2]

*1. Hospital Ruber Internacional, Madrid, Spain*
*2. Clinique du Grand Large, Chassieu, Lyon, France*

## ABSTRACT

Pelvic congestion syndrome is a common cause of chronic pelvic pain in women caused by abnormal ovarian and pelvic varices. The diagnosis is established using Duplex ultrasonography followed by selective venography according to an investigation algorithm, in order to obtain anatomic and hemodynamic information. This allows the precise detection of any anomaly present and whether it is responsible for the symptoms of pelvic congestion syndrome. If treatment is indicated, a number of options are available, but endovenous procedures are usually the first-line treatment as they provide clear benefits over conventional surgery. Further prospective randomized studies are needed to optimally refine this technique and assess long-term patient outcomes.

## BACKGROUND

In the mid-19th century, the association between chronic pelvic pain and the presence of varicose veins in the utero-ovarian plexus was noted by Richet who also described the presence of pelvic varices.

## EPIDEMIOLOGY

Pelvic congestion syndrome (PCS) is a common condition and reports indicate that more than one-third of women will experience pain in the lower abdomen at some point during their life.[1]

## ETIOLOGY, PATHOLOGY, AND PHYSIOPATHOLOGY

Two venous systems are known to be involved in PCS: the ovarian and internal iliac veins. Incompetence in these veins is responsible for reflux and varices in various internal iliac vein tributaries or in the lower extremities. Ovarian vein and internal vein tributary incompetence may have several different etiologies. Congenital incompetence is caused by the absence of valves. The main cause of secondary incompetence is multiparity, but ovarian dilatation and reflux may also be due to compression as a result of abdominal or retroperitoneal tumors (benign or malign), nutcracker syndrome (left ovarian vein), or iliac vein compression. The most frequent type of compression is compression of the left common iliac vein, also known as May-Thurner syndrome.

**Keywords:**
compression; iliac vein; investigation; May-Thurner syndrome; nutcracker syndrome; pelvic congestion syndrome; pelvic pain; ovarian vein

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## CLINICAL PRESENTATION

Pain may or may not be associated with other symptoms such as pelvic heaviness, dyspareunia, dysmenorrhea, lumbar pain, urinary frequency, signs of vulvar and lower limb varices, and hemorrhoids. It is accepted that these symptoms must be present for at least 6 months before a diagnosis of PCS can be considered.

## PELVIC CONGESTION SYNDROME INVESTIGATION

Many protocols can be used to identify the presence of PCS and no comparative trials have been carried out so far. Nevertheless, there is a general consensus that selective venography is the best procedure to identify the anatomical and pathophysiological anomalies of PCS. However, as selective venography is an invasive procedure, investigations should begin with a noninvasive duplex scan, which may give clues indicative of PCS. In our practice, we use an investigation algorithm when female patients consult with the signs and symptoms mentioned above (*Figure 1*).[2]

The first step is to rule out any gynecological disease or pudendal nerve compression, which is less common. Once these conditions have been excluded, transvaginal echo Doppler (TED) ultrasonography should be performed. This investigation provides both anatomical and hemodynamic information. If pelvic varices with substitute continuous flow that cannot be modified by the Valsalva maneuver are identified, the next step is to perform abdominal transparietal echo Doppler (ATED) ultrasonography to determine if there is vein compression. ATED can identify either left renal vein compression or, more frequently, iliac vein compression. When compression is identified by ATED, complementary venography is undertaken to distinguish between left renal vein compression with ovarian reflux (*Figure 2*) and iliac vein compression with reflux in the internal iliac vein tributaries (*Figure 3*).

Conversely, for pelvic varices without continuous flow but displaying flow augmentation and dilatation induced by the Valsalva maneuver during TED, selective venography is the recommended next step, as compression is highly unlikely. Brachial access is best for this procedure and will confirm the absence of compression in the left renal vein and iliac vein. The presence of reflux is investigated by selective venography in the gonadal veins (*Figure 4*) or iliac vein tributaries (*Figure 5*).

In summary, this investigation algorithm allows a step-by-step and precise determination of the type of anomaly present and whether it is responsible for PCS.

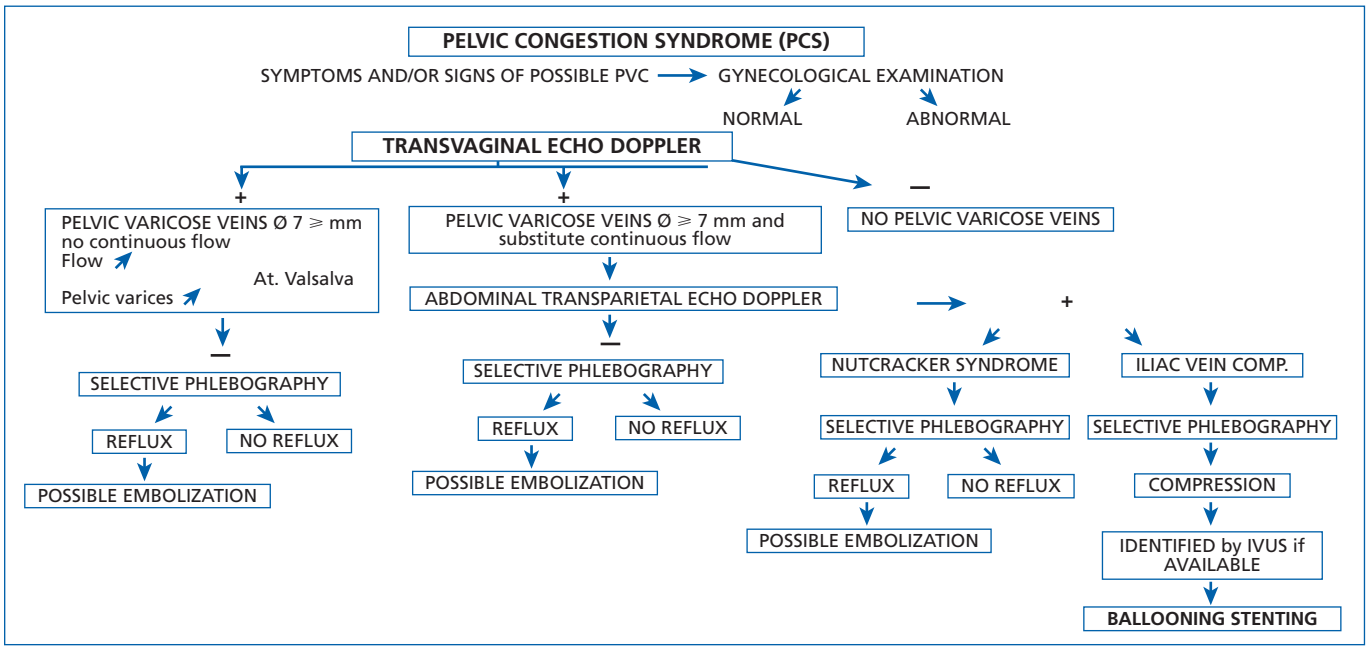


***Figure 1.*** *Investigation algorithm for pelvic congestion syndrome.*
*Abbreviations: Ø, diameter; PVC, pelvic venous congestion ; IVUS, intravascular ultrasound.*

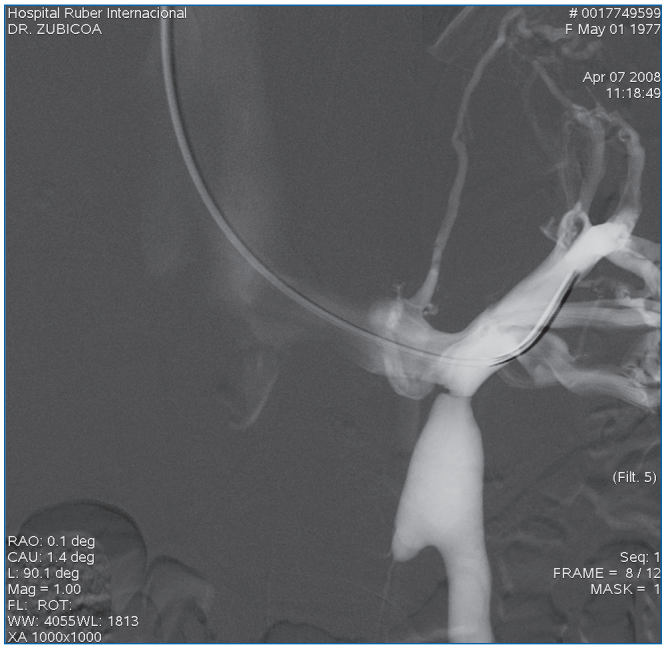


***Figure 2.*** *Venography using brachial access. Left renal vein compression is associated with left ovarian vein reflux.*

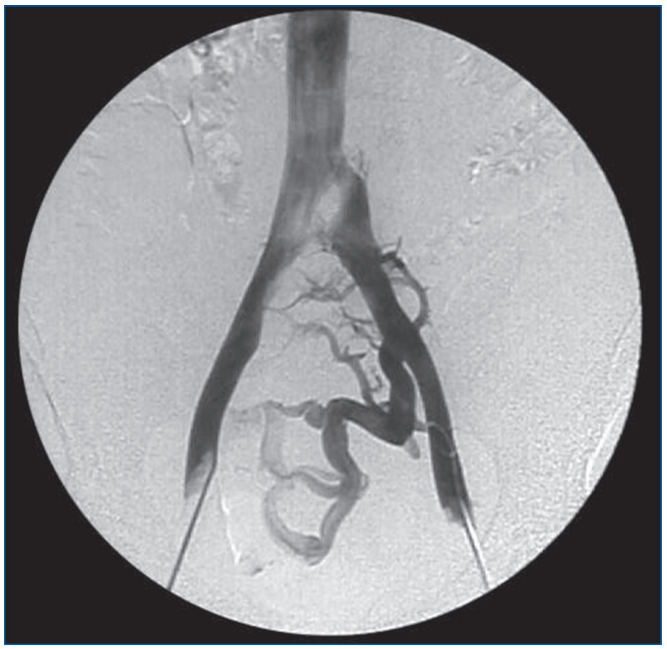

***Figure 3.*** *Venography using femoral access showing left common iliac vein compression and reflux in the left internal iliac vein tributary.*

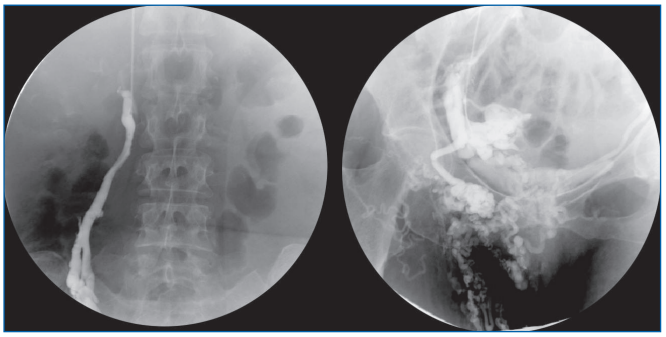

***Figure 4.*** *Venography using brachial access and selective ovarian vein catheterization. Valsalva maneuver: unilateral ovarian vein reflux filling pelvic varices through a round ligament vein as well as lower-limb varicose veins.*

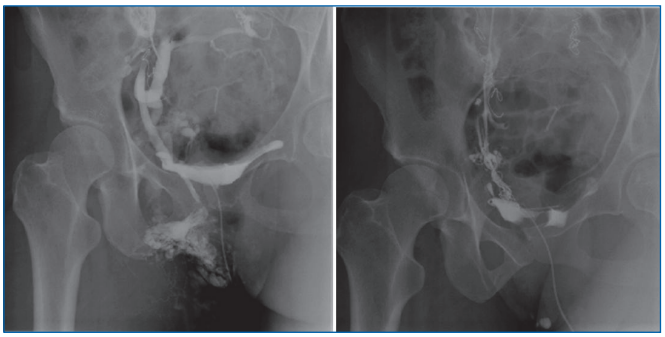

***Figure 5.*** *Venography using brachial access and internal iliac vein tributary vein catheterization.*
*A. Reflux filling both pelvic varices and lower-limb varicose veins is identified after injection into the internal pudendal vein and Valsalva maneuver.*
*B. The same patient, after embolization. There is no longer any reflux into the internal iliac vein tributary.*

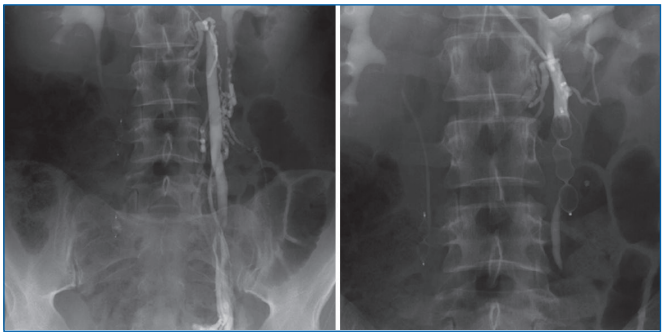

***Figure 6.*** *Venography using brachial access. Incompetent left ovarian vein before and after embolization (Amplatzer).*

## TREATMENT OF PELVIC CONGESTION SYNDROME

### Medical treatment

Drugs such as medroxyprogesterone and micronized purified flavonoid fraction have been used to provide short-term improvement, but there are no data on long-term efficacy.

### Sclerotherapy

Sclerotherapy has been associated with poorly documented and inconclusive results. Various open and

laparoscopic surgery techniques have been reported including ovarian or iliac vein ligation or resection. Poor-to-good outcomes in small series have been reported and were published, for the most part, over 10 years ago.

Endovenous treatment with distal embolization of the refluxed veins by a coil and/or foam sclerosing agent (*Figure 6*), and/or by ballooning and stenting iliac vein compression (*Figure 7*) has progressively replaced surgery (*Table I*).[3-12]

## TREATMENT INDICATIONS

The decision to treat PCS is based on the severity of the symptoms as well as the presence of vulvar and lower limb varices. When operative treatment is considered, endovenous procedures are the first-line treatment with

| Reference | Number of patients | Embolization | Material | Follow-up in months (range) | Clinical outcome |
|---|---|---|---|---|---|
| **Capasso et al,** *Cardiovasc Intervent Radiol. 1997.*[3] | 19 | Ovarian embolization: 13 unilateral<br>6 bilateral | Coil and/or sclerosing agent | 15.4 | Total relief: 58.5% |
| **Maleux et al.** *J Vasc Interven Radiol. 2000.*[4] | 41 | Ovarian embolization: 32 unilateral<br>9 bilateral | Gel foam +/-sclerosing agent | 19.9 (1-61) | Total relief: 58.5%<br>Partial relief: 9.7%<br>No relief: 31.8% |
| **Venbrux et al.** *J Vasc Interv Radiol. 2002.*[5] | 56 | 56 bilateral ovarian<br>43 bilateral internal iliac | Coils | 22.1 (6-38) | Significant/partial relief: 96%; no change: 4% |
| **Pieri et al.** *Radiol Med (Torino). 2003.*[6] | 33 | 1 right ovarian<br>11 left ovarian<br>21 bilateral ovarian | Sclerosing agent | 6-12 | Significant pain relief: 100% |
| **Chung et al.** *Tohoku. 2003.*[7] | 52 | Gonadal vein | Coil | 6-12 | Total evaluation<br>Significant pain relief |
| **Kim et al.** *J Vasc Interv Radiol. 2006.*[8] | 127 | 106 bilateral ovarian vein + 95 internal iliac vein<br>20 unilateral ovarian vein + 13 internal iliac vein | Sclerosing agent and coil | 45 (mean) in 97 patients | Overall evaluation<br>Improved: 83%<br>Unchanged: 13%<br>Worsened: 4% |
| **Creton et al.** *Eur J Vasc Endovasc Surg. 2007.*[9] | 24 | 11 left ovarian + 7 ovarian and internal iliac + 5 unilateral internal iliac + 1 bilateral internal iliac | Coil | 36 | Overall evaluation<br>Improved: 76% |
| **Kwon et al.** *Cardiovasc Interv Radiol. 2007.*[10] | 67 | 64 left ovarian, 1 right ovarian, 2 bilateral | Coil | 44.8 | Significant relief: 82%<br>No relief:15%<br>Worsened: 3% |
| **Gandini et al.** *Cardiovasc Interv Radiol. 2008.*[11] | 38 | Bilateral ovarian | Sclerosing agent | 12 | Significant relief: 100% |
| **Asciutto et al.** *Eur J Vasc Endovasc Surg. 2009.*[12] | 35 | 28 left ovarian + 5 iliac vein + 2 ovarian and iliac vein | Coil | 45 (mean) | Overall evaluation<br>Improved: 47%<br>Unchanged: 36%<br>Worsened: 17% |

***Table I.*** *Outcome of endovenous treatments.*

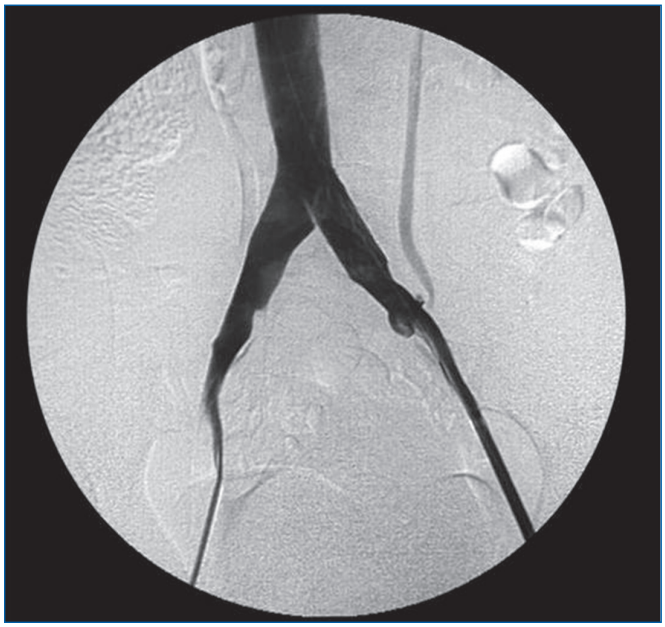

***Figure 7.*** *Venography using femoral access. This is the same patient as in Figure 3, after stenting. Reflux is no longer observed.*

clear benefits over conventional surgery as they are less invasive and associated with very few complications and low morbidity.

## CONCLUSION

Pelvic congestion syndrome is underestimated and its diagnosis relies on precise investigation techniques. Endovenous treatment is the recommended operative technique to treat this condition.

**Corresponding author**
Javier LEAL MONEDERO
Angiology and Vascular Surgery Unit
Hospital Ruber Internacional
C/La Masó 38 - Mirasierra
28034 Madrid - Spain

E-mail:
angiovascularlyz@ruberinternacional.es

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# A retrospective study of 100 patients with varicose veins treated with radiofrequency ablation and stripping

Andrian O. TONEV,
Stoyan G. GENADIEV,
Svetoslav G. DIMITROV,
Todor T. ZAHARIEV,
Gencho K. NACHEV

*Clinic of Vascular Surgery and Angiology*
*"St. Ekaterina" University Hospital*
*Sofia, Bulgaria*

## ABSTRACT

The management of varicose veins has changed rapidly in recent years. Saphenofemoral ligation and stripping of the great saphenous vein (GSV), which once used to be the standard treatment for GSV reflux, has been challenged–and in some areas replaced–by endovenous therapies. We retrospectively analyzed the records of 100 consecutive patients with chronic saphenofemoral insufficiency. Between 2009 and 2011, 50 patients underwent endovenous ablation using radiofrequency with ClosureFAST™ catheter (Group 1) and 50 underwent classic stripping of the GSV (Group 2). In both groups, phlebectomies with microincisions of varicose veins below the knee were performed simultaneously with the selected procedure. The present study shows improved results using the new ClosureFAST™ technique leading to good venous closure with minimal complications and with improved patient comfort. The outcomes with radiofrequency obliteration of saphenous vein reflux were comparable to those of traditional stripping and ligation at 1-year follow up. Radiofrequency ablation is associated with fewer complications and when they do occur they are time-limited and usually of minor consequence.

## INTRODUCTION

Chronic venous insufficiency of the lower limbs is a common condition afflicting 25% of women and 15% of men, with venous reflux at the saphenofemoral junction (SFJ) being the most common cause leading to varicose veins.[1] The management of varicose veins has changed rapidly in recent years. Saphenofemoral ligation and stripping of the great saphenous vein (GSV) was once the standard treatment for GSV reflux, but more recently it has been challenged–and in some areas replaced–by endovenous therapies (EVT).[2-5] Over the last decade, technological progress has enabled the development and application of new minimally invasive therapies such as VNUS Closure endovenous radiofrequency ablation (RFA) and endolaser.[5-7] In the last 2 years, developments in the technology related to the use of RFA catheters have led to the introduction of the ClosureFAST™

**Keywords:**
ablation, radiofrequency, stripping, varicose vein

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catheter. Evidence supports the use of endovenous modalities in terms of reduced postoperative hospital stay, early return to work, and low complication rates.[8]

## PATIENTS AND METHODS

We retrospectively analyzed the records of 100 consecutive patients with chronic saphenofemoral insufficiency. Between 2009 and 2011, a total of 50 patients underwent endovenous ablation using RFA with the ClosureFAST™ catheter (Group 1) and 50 underwent classic stripping of the GSV (Group 2). In both groups, phlebectomies with microincisions of varicose veins below the knee were performed simultaneously with the selected procedure (*Figure 1*). Follow-up visits performed at 2 weeks, 3 months, and 1 year were also analyzed. All patients had symptomatic varicose veins and the inclusion criteria for the study were based on the clinical, etiological, anatomical, pathophysiological (CEAP) classification. All patients with C1-C5 disease (C1: spider veins, C2: varicose veins, C3: ankle edema, C4: lipodermatosclerosis, and C5: healed ulcer) were included in the study. Patients in C6 stage with active ulcers and those with postthrombotic etiology were excluded. The diagnosis was based on both clinical and color Doppler examination. Patients who demonstrated venous reflux in the long saphenous vein with a duration equal to or more than 0.5 seconds were included in the study. Exclusion criterium for RFA was a GSV diameter of more than 16 mm.

Venous Clinical Severity Score (VCSS) was calculated for each patient. The VCSS scores characteristic features of venous disease on a severity scale from 1 to 3 (mild, moderate, and severe) and the scores are then added to score a maximum of 30.[9] The disease characteristics are: pain, varicose veins, venous edema, pigmentation, inflammation, induration, fatigue, cramps, compression use, and overall response. We also looked for and recorded the following complications: hyperpigmentation, thrombophlebitis, saphenous paresthesias, ecchymosis, hematoma, infection, and thermal injury.

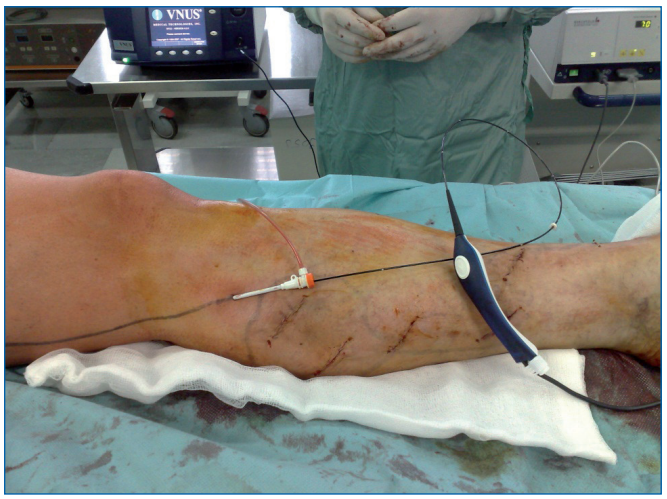



***Figure 1.*** *Final stage of radiofrequency ablation.*

Follow-up clinical and Doppler examinations were performed at 2 weeks, 3 months and 12 months to determine both short- and long-term outcomes, and the final VCSS was determined at 1 year. Any patient with recanalization of a closed vein, recurrent reflux or neovascularization was noted. All patients were advised to take a venoactive drug (micronized purified flavonoid fraction, MPFF*) twice daily for 3 months and to use compression stockings for at least 1 month.

**Registered as: Daflon® 500 mg, Alvenor®, Ardium®, Arvenum® 500, Capiven®, Detralex®, Elatec®, Flebotropin®, Variton®, Venitol®.*

## RESULTS

We conducted a retrospective analysis of data from 100 consecutive patients with saphenofemoral junction incompetence who underwent RFA and stripping. Of these patients, 64 (64%) were female and 36 were male (36%) with a mean age of 36.4 ± 9 and 48.3 ± 12 years, respectively. The mean length of the RFA-treated GSV segment was 35 cm (range, 20 to 60 cm).

All patients were symptomatic for their venous problems, with or without skin changes. The majority were in the C2 group of the CEAP classification (26 patients in Group 1 and 22 in Group 2), followed by C3 (20 patients in Group 1 and 18 in Group 2), and C4-C5 (4 patients in Group 1 and 10 in Group 2) (*Figure 2*). *Figure 2* also illustrates the distribution of patients at 1-year follow-up: C0-C1 (42 patients in Group 1 and 41 in Group 2), C2 (5 patients in both Groups), C3 (2 patients in both Groups), and C4-C5 (1 patient in Group 1 and 2 patients in Group 2).

VCSS scores are displayed in *Figure 3*. The largest number of patients was seen in the moderate group (10-20) with 36 patients from Group 1 and 30 patients from Group 2, followed by the severe group (20-30) with 8 patients from Group 1 and 16 from Group 2, and

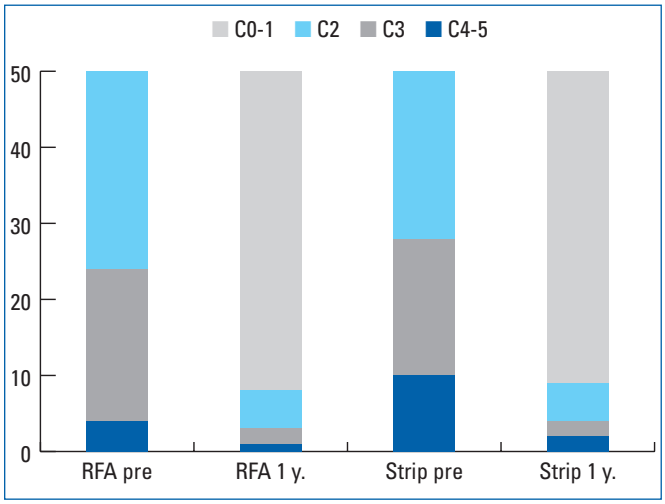



***Figure 2.*** *Comparison of clinical CEAP classes distribution in patients who underwent either radiofrequency (RFA) or stripping (Strip), before and 1 year after the procedure.*

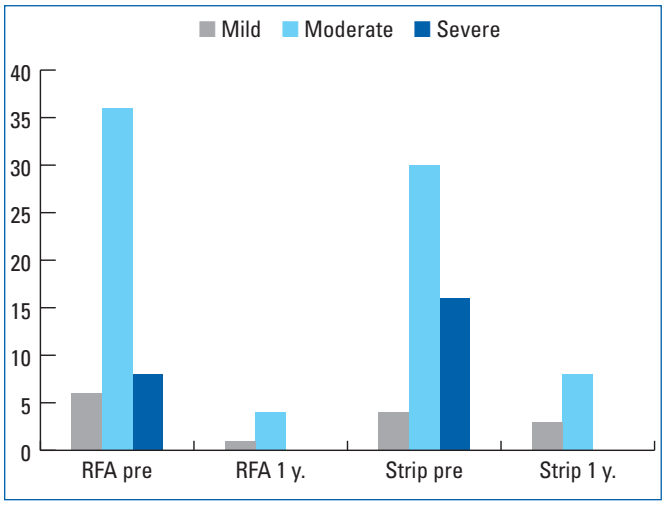



***Figure 3.*** *Comparison of VCSS scores in patients who underwent either radiofrequency (RFA) or stripping (Strip), before and 1 year after the procedure.*

then the mild group (0-10) with 6 patients from Group 1 and 4 from Group 2. Posttreatment VCSS assessment was performed at 12 months and showed significantly reduced scores: only 4 patients from Group 1 and 8 from Group 2 were in the moderate group, followed by 1 patient from Group 1 and 3 patients from Group 2 in the mild group (*Figure 3*).

The complications observed at 2 weeks of follow-up are shown in *Table I*. The most common complications were saphenous paresthesias (1 patient from Group 1 and 5 patients from Group 2), followed by ecchymosis (1 patient from Group 1 and 5 patients from Group 2), hyperpigmentation (2 patients from both Groups), thrombophlebitis in distal varicosities (2 patients from Group 1), hematoma (1 patient from Group 2), and infection of the inguinal-femoral area (1 patient from Group 2). Postprocedural Doppler examinations showed complete vein closure in 100% of patients from Group 1. Reflux-free and vein occlusion rates at 1 year were 100% in Group 1. One patient from Group 2 showed neovascularization and in another patient a de novo reflux was observed in the anterolateral vein, which opened separately into the common femoral vein.

| RFA | Complication | Stripping |
|---|---|---|
| 2 | Hyperpigmentation | 2 |
| 2 | Thrombophlebitis | 0 |
| 1 | Saphenous paresthesia | 5 |
| 1 | Ecchymosis | 5 |
| 0 | Hematoma | 1 |
| 0 | Infection | 1 |
| 1 | Thermal injury | 0 |
| 7 | | 14 |

***Table I.*** *Distribution of complications in both radiofrequency ablation (RFA) and stripping groups.*

The cumulative rate of recurrence of varicose veins at 1 year was 2% (1 patient) in Group 1 and 4% (2 patients) in Group 2.

## DISCUSSION

RFA of the GSV is an alternative treatment option to venous stripping, which can lead to a painful and prolonged postoperative recovery with a high incidence of hematoma formation, nerve injury, and infection.[10-12] Early RFA studies used a slow, incremental, catheter pullback technique, which was associated with a higher incidence of clot formation, early vessel recanalization, and thermal injury. The overall reported success in these studies was 83%-100%.[13,14] The present analysis reports improved results with good venous closure and minimal complications using the new ClosureFAST™ technique, which has overcome the limitations of previous RFA techniques as well as improving patient comfort. The present technique did not require the use of any postprocedure analgesics with the patient being ambulatory the same day, which is a great advantage for early patient recovery. VCSS results at 2 weeks,

3 months and 1 year also showed a significant reduction in scores thus showing an excellent symptomatic recovery with better results in Group 1.

Nerve damage is one of the most common causes of litigation after varicose vein surgery.[15] Paresthesia or numbness may arise following RFA and stripping, but in most cases improves over the course of a few weeks.[16] RFA has been shown to cause less pain and bruising than surgery as well as taking less time.[17] Our study showed a 2% neovascularization rate in Group 2 and no recanalization in Group 1 at 1-year follow-up. The open surgery technique was associated with a recurrence rate of 4% compared with 2% in Group 1. In comparison, the EVOLVeS trial reported a neovascularization rate of 3% with a conventional closure technique and 17% with stripping.[18]

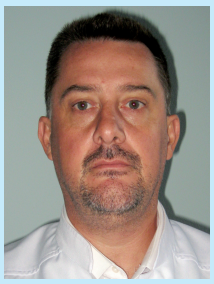
Recanalization of a vein may be due to either reflux from a tributary or an incompetent perforator. Similarly, if the main lumen is patent, reflux from the groin due to an accessory vein can also lead to failure and recurrence.[19] Technical problems such as difficult access, problems in advancing the catheter, or a tortuous GSV can also all play a role in failure of the procedure or incomplete occlusion of the vein and ultimately result in recurrence.[19]

Deep vein thrombosis can develop in the deep veins of the calf, or a thrombus can circulate from the treated superficial veins following RFA and stripping. In our study we observed no thrombus formation in the deep venous system. Deep vein thrombosis after endovenous ablation is extremely rare and most case series and trials show no evidence of it.[2,20]

All patients in Group 1 and 56% of patients in Group 2 returned to normal activities within 1 day of the procedure. This outcome is even better than that observed in the EVOLVeS trial,[18] which used the conventional closure technique and where 80% of patients resumed their normal activities 24 hours after the procedure, compared with only 47% after stripping.

## CONCLUSION

The results from our series of patients suggest that RFA with the ClosureFAST™ technique is a safe and promising tool for the treatment of saphenofemoral junction insufficiency. Outcomes 1-year after RFA obliteration of saphenous vein reflux were comparable to those of traditional stripping and ligation. When complications did occur they were time limited and usually of minor consequence. The significant advantages of RFA over stripping in this series of patients were less pain, early return to normal activities, fewer days off work, and better cosmetic results and quality-of-life scores. Confirmation of whether RFA deserves to be the treatment of choice should be studied in further randomized trials.



**Corresponding author**
Andrian O. TONEV, MD, PhD
"St. Ekaterina" University Hospital
52A Pencho Slaveykov Blvd.
Sofia, 1431
Bulgaria

E-mail: andi.tonev@abv.bg

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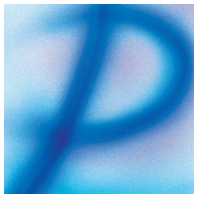

# Differential diagnosis of chronic leg ulcers

Sandra MARINOVIĆ KULIŠIĆ,
Jasna LIPOZENČIĆ

*University Department of Dermatology and Venereology, University Hospital Center Zagreb and School of Medicine, Zagreb, Croatia*

## ABSTRACT

**Background:** Chronic leg ulcers are nonhealing wounds on the distal aspects of the leg. Chronic venous insufficiency occurs when the venous system of the legs becomes inefficient and is a price we pay for our upright posture. The majority of chronic leg ulcers are caused by venous disease, but occasionally ulcers are associated with arterial problems or vessel inflammation (vasculitis).

**Objective:** To describe the varying dermatoses found in patients with chronic leg ulcers.

**Study design:** Literature search and personal experience of differential diagnoses associated with chronic leg ulcers.

**Setting**: Patients with chronic leg ulcers attending the Phlebology Clinic of the University Dermatology Department in Zagreb.

**Methods:** Determination of causes of leg ulcers through medical history, physical examination and laboratory investigations.

**Results:** Authors' recommendations for a general approach to the differential diagnosis of chronic leg ulcers.

**Conclusion:** Leg ulcers associated with chronic venous insufficiency occur in 1% of the population in developed countries and are found in 5% of those aged 80 years or more. The correct diagnosis of the cause of leg ulceration is important as up to 20% are not of venous origin.

Establishing the etiology of a leg ulcer is important as various treatment modalities are available, but the specific treatment will be dependent on the underlying ulcer cause. Most wounds, of whatever etiology, heal without difficulty. Some wounds are subject to factors that impede healing, although healing is not prevented if the wounds are managed appropriately.[1-2]

This short overview on the differential diagnosis of leg ulcers considers chronic leg ulcers, ie, those present for more than 6 weeks, a condition suffered by approximately 0.2%-2% of the European population. At least half of these ulcers have an underlying venous pathology, but the figure can be as high as 80%-90%, especially when ulcers localized to the foot are excluded. The

**Keywords:**
CEAP classification, chronic leg ulcer, chronic venous insufficiency, differential diagnosis

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prevalence of leg ulcers increases proportionately as the population ages.[1-4]

Chronic venous insufficiency (CVI) of the lower extremities is a common medical problem. Sustained venous hypertension produces a cascade of pathologic events clinically graded by clinical manifestations (C), etiologic factors (E), anatomic distribution (A), and underlying pathophysiologic findings (P) – the CEAP classification of chronic venous disease. Approximately 50% of venous ulcers are a consequence of CVI of the superficial venous system (intrafascial superficial veins with or without perforator insufficiency). After venous ulcers, other common chronic leg ulcers include arterial ulcers (5%-10%) (*Figures 1, 2*), neuropathic ulcers caused by a combination of factors (*Figures 3 a-d*), and ulcers associated with skin cancers (*Figure 4*). Lately, an increase in the prevalence of arterial (12%) and mixed (arteriovenous) ulcers (22%) has been observed, probably reflecting aging of the population.[3, 4]

The most difficult diagnostic and therapeutic problems are encountered in patients with leg ulcers in whom the major cause of the ulcer cannot be found, though a certain degree of venous insufficiency exists. In a smaller but significant number of patients, chronic leg ulcer may be a manifestation of a variety of dermatologic, systemic

***Figure 1.*** *Venous ulcer*

- *Localization – low (distal) third of the tibia, perimalleolar*
- *Pain – moderate, it weakens with lying and rest*
- *Debridement – causes venous hemorrhage*
- *Bottom – abundant granulations, humid*
- *Edges – erythematous, inflamed, elevated, and hard*


***Figure 2.*** *Arterial ulcer*

- *Localisation – ulcer is most frequently found in areas of bone strain – acral parts (thumb, ankle)*
- *Round, with sharp edges*
- *Bottom of the ulcer is dry, with little or no granulations, with present necrosis*
- *Deep with affected deeper structures - until tendons*
- *Surrounding skin is dry, cold, pale, shiny and hairless, muscle weakening and atrophy of tibia and foot skin*


***Figure 3a.*** *Vasculitis leukocytoclastica*

- *Vasculitis is an inflammation of the blood vessel wall and affects a variety of organs, including the skin*
- *Immune complex deposition between endothelium and basal capillary membranes and venules*
- *Leading to chronic inflammation and ultimately to cell death, tissue necrosis and ulceration*
- *Symmetrical*

*Figure 3b. Polyarteritis nodosa*

- *Multisystemic necrotic vasculitis*
- *Present with general symptoms*
- *Affects kidneys and peripheral and central nervous systems*
- *Most frequent occurrence bilateral pretibia*
- *Most frequent skin changes are similar to "livedo racemosa" with painful nodules, ulcerations and purpura*

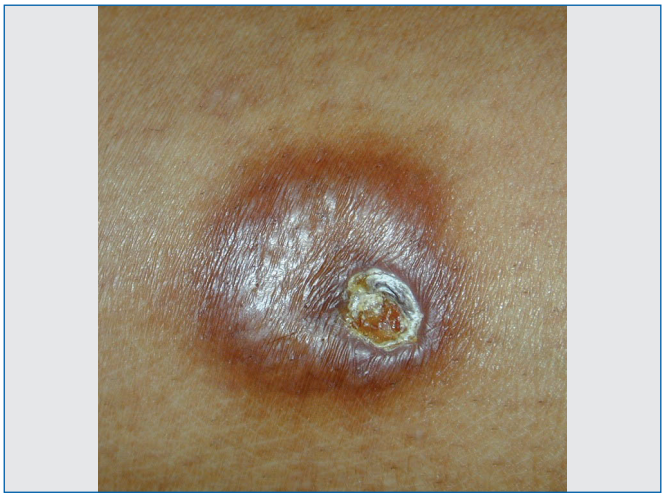

*Figure 3d. Necrobiosis lipoidica diabeticorum*

- *Present in about 60% of diabetes patients*
- *Causative connection between necrobiosis lipoidica and diabetic microangiopathy*
- *Observed as ischemic ulceration*
- *Symmetrical on extensor sides of tibia*
- *In one-third of patients ulceration occurs*
- *It can ulcerate after a trauma*
- *Yellowish ulceration, fat ulcer bases*
- *Heals with difficulty*

*Figure 3c. Pyoderma gangrenosum*

- *Chronic ulcer – gangrenous skin affection of unknown etiology*
- *Starts with occurrence of pustula*
- *Deep necrotic ulcer, with elevated and undetermined livid edge*
- *Rapid peripheral expansion and bizarre shape*
- *If not treated in time it can affect deeper structures including bone*
- *Mostly localised on lower limbs*
- *Painful*

*Figure 4. Basocellular carcinoma*

- *In most cases (sometimes as fibrosaracoma) it occurs in chronic ulcers, especially on lower limbs*
- *Most probably occurs because of increased number of cell divisions on the bottom and the surrounding area of an ulcer*
- *Hypertrophic granulations, indurations and hemorrhage*
- *On area of perforation an ulcer grows, often kidney shaped, with sharp edges*

and infectious diseases. The most important differential diagnoses are those defined by Lautenschlager[2] with our additional modifications (*Table I*).

- Vascular (venous, arterial, lymphatic, vasculitis)
- Metabolic (diabetes, gout)
- Connective tissue disease (inflammatory bowel disease-pyoderma gangrenosum , rheumatoid arthritis, scleroderma, systemic lupus erythematous, bullous pemphigoid, dermatomyositis, polyarteritis nodosa, leukocytoclastic vasculitis)
- Cutaneous microthrombotic ulcers (cryofibrinogenemia, antiphospholipid syndrome, coagulopathies)
- Hematological disease (red blood cell disorders, sickle cell disease; white blood cell disorders, leukaemia; platelet disorders, trombocytosis, thalassemia)
- Neoplastic (basal cell carcinoma, squamous cell carcinoma, malignant melanoma, primary cutaneous B cell lymphoma, Marjolin's ulcer, Kaposi's sarcoma, Bowen's disease – intraepidermal carcinoma)
- Panniculitis (necrobiosis lipoidica)
- Traumatic (pressure ulcer, radiation damage)
- Iatrogenic (drugs)

***Table I.*** *Differential diagnosis of chronic leg ulcers (from Lautenschlager and Eichmann[2] with authors modifications).*

The differential diagnosis of chronic leg ulcers may be straightforward, but at times will require time, effort, and patience by both physician and patient. The search for the cause of a leg ulcer should include a detailed medical history, physical examination, evaluation of arterial and venous blood flow, and suitable laboratory tests (*Table II*).[3,5,6]

Medical history and findings from the physical examination dictate the selection of additional investigations. Due to the many possible causes of leg ulcers, the number of potentially useful diagnostic tests is also large. Depending on the situation, microbiological tests, skin biopsy, radiologic imaging, and epicutaneous patch tests may be indicated.[6] Of all the tests, biopsy is indispensable for the confirmation of vasculitides, tumors, granulomatous inflammation, and many skin infections, especially micobacterial and fungal infections. A correct sample must incorporate both the margin and base of the ulcer.[6-12] If there is uncertaintly about the best place to biopsy, multiple punch biopsies can be taken from different parts of the ulcer. The decision on when to take a leg ulcer biopsy is dependent on a number of criteria, but should be

| Investigation | Rationale |
|---|---|
| Hemoglobin | Anemia may delay healing |
| White cell count | Infection |
| Platelet count | Thrombocytopenia |
| Erythrocyte sedimentation rate;<br>C-reactive protein | Non-specific markers of infection and inflammation; useful in diagnosis and monitoring treatment of infectious or inflammatory ulceration |
| Urea and creatinine, epidermal growth factor receptor (EGFR) | High urea impairs wound healing<br>Renal function important when using antibiotics |
| Albumin | Protein loss delays healing |
| Glucose, hemoglobin $A_{1C}$ | Diabetes mellitus |
| Markers of autoimmune disease<br>(such as rheumatoid factor, antinuclear antibodies, anticardiolipin antibodies, lupus anticoagulant) | Indicative of rheumatoid disease, systemic lupus erythematosus, and other connective tissue disorders |
| Cryoglobulins, cryofibrinogens, prothrombin time, partial thromboplastin time | Hematological disease |
| Deficiency or defect of antithrombin III, protein C, protein S, factor V, XII Leiden, heparin cofactor 2 | Vascular thrombosis |
| Hemoglobinopathy screen | Sickle cell anemia, thalassemia |
| Urine analysis | Useful in connective tissue disease |

***Table II.*** *Laboratory investigations required before treating a wound*[3]

considered with: typical ulcers that do not respond to standard treatment or even worsen with treatment, atypical ulcers where the cause is not venous, arterial or neuropathic ulcers (vasculitis, systemic and other dermatologic diseases), ulcers highly suspicious for malignancy (unusual localization, nodular changes, rolled borders, multiple coalescing ulcers, presence of regional lymphadenopathy), or recent travel to tropical countries.[2,6]

| |
|---|
| **History** |
| Personal medical history (deep venous thrombosis, diabetes, occlusive arterial disease) |
| Family history (diabetes, hypercholesterolemia) |
| Drugs |
| Risk factors (hypertension, homocystinemia, smoking, trauma, hyperlipidemia) |
| When did the ulcer break, did it ever heal, etc. |
| Factors that worsen and alleviate symptoms |
| **Complete physical examination, which should include:** |
| Neurological tests |
| Deep tendon reflexes |
| Light touch, prick sensation, deep sensation, etc |
| Peripheral pulses |
| Ulcer (site, morphology) |
| Surrounding skin (color, sclerosis, purpura, dermatitis, pigmentation…) |
| Clinical tests (capillary refilling time, ABI) |
| **Laboratory investigations** |
| **Microbiological analysis** (semiquantitative and quantitative analysis) |
| **Skin biopsy** |
| **Radiological imaging** (ankle brachial pressure index, duplex ultrasound, arteriography) |

***Table III.*** *General approach to differential diagnosis of chronic leg ulcer (authors' recommendations).*

The most useful approach to diagnose CVI is with Doppler and duplex sonography. Other procedures such as light reflection rheography (LRR), digital photoplethysmography (DPPG), and venous plethysmography (resting and dynamic) can be used as indicated. When deciding on the possibility of surgery for postthrombotic syndrome with secondary varicosities, invasive phlebodynametry (measurement of venous pressure with intravascular needle) is often required. Measurement of the ankle-brachial index (ABI) is a simple and reliable test for the assessment of arterial blood flow in the leg.[6-9] Phlebography is usually not necessary when the above approaches are employed (*Table III*).

**Corresponding author**
Sandra MARINOVIĆ KULIŠIĆ, MD, PhD
University Hospital Centre Zagreb
Department of Dermatology and Venereology
School of Medicine University of Zagreb
Salata 4, 10000 Zagreb, Croatia

E-mail: sandra.marinovic@zg.htnet.hr

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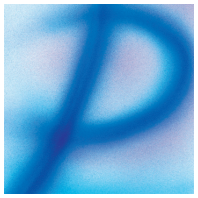

# Congress and conference calendar

| DATES | CONGRESS | COUNTRY | CITY |
|---|---|---|---|
| September 2013 | CHINA VASCULAR SURGREY 12TH | China | TBD |
| September 2013 | CONGRESS OF ROMANIAN NATIONAL SOCIETY OF CARDIOVASCULAR SURGERY | Romania | Brasov |
| 12-14 September 2013 | ASIAN CHAPTER INTERNATIONAL UNION OF ANGIOLOGY - 6TH NATIONAL SYMPOSIUM ON VASCULAR SURGERY | Indonesia | Jakarta |
| 18-20 September 2013 | THE EUROPEAN SOCIETY FOR VASCULAR SURGERY XXVII ANNUAL MEETING | Hungary | Budapest |
| 25th - 28th September 2013 | ANNUAL CONFERENCE OF VASCULAR SOCIETY OF INDIA | India | Kodaikanal |
| 28 September-1 October 2013 | 21ST EUROCHAP - EUROPEAN CONGRESS OF THE INTERNATIONAL UNION OF ANGIOLOGY | Italy | Rome |
| 28 September-1 October 2013 | NATIONAL CONGRESS OF ITALIAN SOCIETY FOR VASCULAR INVESTIGATION - SIDV | Italy | Rome |
| 30 September - 4 October 2013 | BRAZILIAN ANGIOLOGY CONGRESS | Brazil | Florianópolis |
| October 2013 | XIV INTERNATIONAL SYMPOSIUM OF ANGIOLOGY AND VASCULAR SURGERY | Portugal | Oporto |
| October 1, 2013 | CONGRES OF ROMANIAN NATIONAL SOCIETY OF DERMATOLOGY | Romania | Targu Mures |
| 2-5 October 2013 | CONGRESS OF THE EUROPEAN FEDERATION OF INTERNAL MEDICINE (EFIM) | Czech Republic | Prague |
| 3-5 October 2013 | XXIII MLAVS 2013, MEDITERRANEAN CONGRESS OF ANGIOLOGY AND VASCULAR SURGERY, 4TH EDUCATIONAL COURSE ON THROMBOSIS AND ANTITHOMBATIC TREATMENT | Greece | Larissa |
| 30 October - 1 November 2013 | 14È CONGRÈS DE L'UNION DES SOCIÉTÉS SUISSES DES MALADIES VASCULAIRES | Switzerland | Montreux |

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| 20-23 November 2013 | XXXV NATIONAL CONGRESS OF ITALIAN SOCIETY FOR ANGIOLOGY AND VASCULAR MEDICINE - SIAPAV | Italy | Milan |
| 29-30 November 2013 | CHALLENGES & INNOVATIONS VASCULAIRES | France | Paris |
| December 2013 | 4TH LISBON INTERNACIONAL FORUM ON VASCULAR DISEASES | Portugal | Lisbon |
| December 2013 | ANNUAL MEETING OF THE AUSTRIAN SOCITETY OF PHLEBOLOGY | Austria | Vienna |
| 5-6 December 2013 | 6TH SAINT-PETERSBURG VENOUS FORUM (CRISTMAS MEETING) | Russia | Saint-Petersburg |
| Mid March 2014 | XXXIV VENOUS MEETING OF PORTUGUESE SURGICAL SOCIETY | Portugal | Lisbon |
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