

A blue-tinted portrait of Michel Perrin, an older man with glasses, smiling. The portrait is the background for the entire page.

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1250 Eklöf *et al*

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SPECIAL COMMUNICATION

From the American Venous Forum

Revision of the CEAP classification for chronic venous disorders: Consensus statement

Bo Eklöf, MD,^a Robert B. Rutherford, MD,^b John J. Bergan, MD,^c Patrick H. Carpentier, MD,^d Peter Gloviczki, MD,^e Robert L. Kistner, MD,^f Mark H. Meissner, MD,^g Gregory L. Moneta, MD,^h Kenneth Myers, MD,ⁱ Frank T. Padberg, MD,^j Michel Perrin, MD,^k C. Vaughan Ruckley, MD,^l Philip Coleridge Smith, MD,^m and Thomas W. Wakefield, MD,ⁿ for the American Venous Forum International Ad Hoc Committee for Revision of the CEAP Classification, *Helsingborg, Sweden*

The CEAP classification for chronic venous disorders (CVD) was developed in 1994 by an international ad hoc committee of the American Venous Forum, endorsed by the Society for Vascular Surgery, and incorporated into "Reporting Standards in Venous Disease" in 1995. Today most published clinical papers on CVD use all or portions of CEAP.

Rather than have it stand as a static classification system, an ad hoc committee of the American Venous Forum, working with an international liaison committee, has recommended a number of practical changes, detailed in this consensus report. These include refinement of several definitions used in describing CVD; refinement of the C classes of CEAP; addition of the descriptor n (no venous abnormality identified); elaboration of the date of classification and level of investigation; and as a simpler alternative to the full (advanced) CEAP classification, introduction of a basic CEAP version. It is important to stress that CEAP is a descriptive classification, whereas venous severity scoring and quality of life scores are instruments for longitudinal research to assess outcomes. (J Vasc Surg 2004;40:1248-52.)

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The field of chronic venous disorders (CVD) previously suffered from lack of precision in diagnosis. This deficiency led to conflicting reports in studies of management of specific venous problems, at a time when new methods were being offered to improve treatment for both simple and more complicated venous diseases. It was believed that these conflicts could be resolved with precise diagnosis and classification of the underlying venous problem. The CEAP classification¹ (Clinical-Etiology-Anatomy-Pathophysiology) was adopted worldwide to facilitate meaningful communication about CVD and serve as a basis for more scientific analysis of man-

agement alternatives. This classification, based on correct diagnosis, was also expected to serve as a systematic guide in the daily clinical investigation of patients as an orderly documentation system and basis for decisions regarding appropriate treatment.

CREATION OF CEAP CLASSIFICATION

At the Fifth Annual meeting of the American Venous Forum (AVF), in 1993, John Porter suggested using the same approach as the TNM classification (Tumor/Node/Metastasis) for cancer in developing a classification system for venous diseases. After a year of intense discussions a consensus conference was held at the Sixth Annual Meeting of AVF in February 1994, at which an international ad hoc committee, chaired by Andrew Nicolaides and with representatives from Australia, Europe, and the United States, developed the first CEAP consensus document. It contained 2 parts: a classification of CVD and a scoring system of the severity of CVD. The classification was based on clinical manifestations (C), etiologic factors (E), anatomic distribution of disease (A), and underlying pathophysiologic findings (P), or CEAP. The severity scoring system was based on 3 elements: number of anatomic segments affected, grading of symptoms and signs, and disability. The CEAP consensus statement was published in 25 journals and books, in 8 languages (Table I, online only), truly a universal document for CVD. It was endorsed by the joint

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Competition of interest: none.

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Table II. Members of American Venous Forum ad hoc committee on revision of CEAP classification

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Robert Rutherford, MD
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councils of the Society for Vascular Surgery and the North American Chapter of the International Society for Cardiovascular Surgery, and its basic elements were incorporated into venous reporting standards.² Today most published clinical papers on CVD use all or portions of the CEAP classification.

OTHER DEVELOPMENTS RELATED TO CEAP

In 1998, at an international consensus meeting in Paris, Perrin et al³ established a classification for recurrent varicose veins (Recurrent Varices After Surgery [REVAS]), the evaluation of which is ongoing. In 2000 Rutherford et al⁴ and the ad hoc Outcomes committee of AVF published an upgraded version of the original venous severity scoring system. The validity of the new severity score has been evaluated by Meissner et al⁵ and Kakkos et al.⁶ An evaluation of the system by 398 French angiologists was reported by Perrin et al.⁷

Uhl et al⁸ established a European Venous Registry based on CEAP, and reported studies on intraobserver and interobserver variability that showed significant discrepancies in the clinical classification of CEAP, which prompted improved definitions of clinical classes C₀ to C₆.

An international consensus meeting in Rome in 2001 suggested definitions and refinements of the clinical classification, the C in CEAP,⁹ which were published with a commentary by the first author of the current revision of the venous reporting standards.¹⁰ These not only contributed to CEAP, but formed the basis for its ultimate modification, as recommended below.

REVISION OF CEAP

Diagnosis and treatment of CVD is developing rapidly, and the need for an update of the classification logically follows. It is important to stress that CEAP is a descriptive classification. Venous severity scoring⁴ was developed to enable longitudinal outcomes assessment, but it became apparent that CEAP itself required updating and modification. In April 2002 an ad hoc committee on CEAP was appointed by AVF to review the classification and make recommendations for change by 2004, 10 years after its introduction (Table II). An international ad hoc committee was also established to ensure continued universal use (Table III). The 2 committees held 4 joint meetings, with

Table III. International ad hoc committee on revision of CEAP classification

American Venous Forum ad hoc committee*
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Mark Malouf, MD, Australia
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Kenneth Myers, MD, Australia*
Peter Neglén, MD, United States
Andrew Nicolaides, MD, Cyprus
Tomo Ogawa, MD, Japan
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Michel Perrin, MD, France*
Eberhard Rabe, MD, Germany
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Vaughan Ruckley, MD, United Kingdom*
Ulrich Schultz-Ehrenburg, MD, Germany
Jean Francois Uhl, MD, France
Martin Veller, MD, South Africa
Yuqi Wang, MD, China
Zhong Gao Wang, MD, China

*Editorial committee

key members contributing in the interim to the revised document. The following passages summarize the results of these deliberations by describing the new aspects of the revised CEAP.

The recommended changes, detailed below, include additions to or refinements of several definitions used in describing CVD; refinement of the C classification of CEAP; addition of the descriptor n (no venous abnormality identified); incorporation of the date of classification and level of clinical investigation; and the description of "basic CEAP," introduced as a simpler alternative to the full (advanced) CEAP classification.

TERMINOLOGY AND NEW DEFINITIONS

The CEAP classification deals with all forms of CVDs. The term "chronic venous disorder" includes the full spectrum of morphologic and functional abnormalities of the venous system, from telangiectasies to venous ulcers. Some of these, such as telangiectasies, are highly prevalent in the healthy adult population, and in many cases use of the term "disease" is not appropriate. The term "chronic venous insufficiency" implies a functional abnormality of the venous system, and is usually reserved for more advanced disease, including edema (C₃), skin changes (C₄), or venous ulcers (C₅₋₆).

It was agreed to maintain the present overall structure of the CEAP classification, but to add more precise definitions. The following recommended definitions apply to the clinical (C) classes of CEAP:

atrophie blanche (white atrophy) Localized, often circular whitish and atrophic skin areas surrounded by dilated capillaries and sometimes hyperpigmentation. Sign of severe CVD, and not to be confused with healed ulcer scars. Scars of healed ulceration may also exhibit atrophic skin with pigmentary changes, but are distinguishable by history of ulceration and appearance from atrophie blanche, and are excluded from this definition.

corona phlebectatica Fan-shaped pattern of numerous small intradermal veins on medial or lateral aspects of ankle and foot. Commonly thought to be an early sign of advanced venous disease. Synonyms include malleolar flare and ankle flare.

eczema Erythematous dermatitis, which may progress to blistering, weeping, or scaling eruption of skin of leg. Most often located near varicose veins, but may be located anywhere in the leg. Usually seen in uncontrolled CVD, but may reflect sensitization to local therapy.

edema Perceptible increase in volume of fluid in skin and subcutaneous tissue, characteristically indented with pressure. Venous edema usually occurs in ankle region, but may extend to leg and foot.

lipodermatosclerosis (LDS) Localized chronic inflammation and fibrosis of skin and subcutaneous tissues of lower leg, sometimes associated with scarring or contraction of Achilles tendon. LDS is sometimes preceded by diffuse inflammatory edema of the skin, which may be painful and which often is referred to as hypodermatitis. LDS must be differentiated from lymphangitis, erysipelas, or cellulitis by their characteristically different local signs and systemic features. LDS is a sign of severe CVD.

pigmentation Brownish darkening of skin, resulting from extravasated blood. Usually occurs in ankle region, but may extend to leg and foot.

reticular vein Dilated bluish subdermal vein, usually 1 mm to less than 3 mm in diameter. Usually tortuous. Excludes normal visible veins in persons with thin, transparent skin. Synonyms include blue veins, subdermal varices, and venulectasies.

telangiectasia Confluence of dilated intradermal venules less than 1 mm in caliber. Synonyms include spider veins, hyphen webs, and thread veins.

varicose vein Subcutaneous dilated vein 3 mm in diameter or larger, measured in upright position. May involve saphenous veins, saphenous tributaries, or nonsaphenous superficial leg veins. Varicose veins are usually tortuous, but tubular saphenous veins with demonstrated reflux may be classified as varicose veins. Synonyms include varix, varices, and varicosities.

venous ulcer Full-thickness defect of skin, most frequently in ankle region, that fails to heal spontaneously and is sustained by CVD.

REFINEMENT OF C CLASSES IN CEAP

The essential change here is the division of class C₄ into 2 subgroups that reflect severity of disease and carry a different prognosis in terms of risk for ulceration:

C₀ No visible or palpable signs of venous disease.

C₁ Telangiectasies or reticular veins.

C₂ Varicose veins; distinguished from reticular veins by a diameter of 3 mm or more.

C₃ Edema.

C₄ Changes in skin and subcutaneous tissue secondary to CVD, now divided into 2 subclasses to better define the differing severity of venous disease:

C_{4a} Pigmentation or eczema.

C_{4b} Lipodermatosclerosis or atrophie blanche.

C₅ Healed venous ulcer.

C₆ Active venous ulcer.

Each clinical class is further characterized by a subscript for the presence of symptoms (S, symptomatic) or absence of symptoms (A, asymptomatic), for example, C_{2A} or C_{5S}. Symptoms include aching, pain, tightness, skin irritation, heaviness, muscle cramps, and other complaints attributable to venous dysfunction.

REFINEMENT OF E, A, AND P CLASSES IN CEAP

To improve the assignment of designations under E, A, and P a new descriptor, n, is now recommended for use where no venous abnormality is identified. This n could be added to E (E_n, no venous cause identified), A (A_n, no venous location identified), and P (P_n, no venous pathophysiology identified). Observer variability in assigning designations may have been contributed to by lack of a normal option. Further definition of the A and P has also been afforded by the new venous severity scoring system,⁴ which was developed by the ad hoc committee on Outcomes of the AVF to complement CEAP. It includes not only a clinical severity score but a venous segmental score. The venous segmental score is based on imaging studies of the leg veins, such as duplex scans, and the degree of obstruction or reflux (P) in each major segment (A), and forms the basis for the overall score.

This same committee is also pursuing a prospective multicenter investigation of variability in vascular diagnostic laboratory assessment of venous hemodynamics in patients with CVD. The last revision of the venous reporting standards² still cites changes in ambulatory venous pressure or plethysmographically measured venous return time as objective measures of change. The current multicenter study aims to establish the variability of, and thus limits of, "normal" for venous return time and the newer noninvasive venous tests as an objective basis for claiming significant improvement as a result of therapy, and it is hoped will provide improved reporting standards for definitive diagnosis and results of competitive treatments in patients with CVD.

DATE OF CLASSIFICATION

CEAP is not a static classification; disease can be reclassified at any time. Classification starts with the patient's initial visit, but can be better defined after further investigations. A final classification may not be complete until

after surgery and histopathologic assessment. We therefore recommend that any CEAP classification be followed by the date, for example, C_{4bS}, E_pA_{s,p} P_r (2003-08-21).

LEVEL OF INVESTIGATION

A precise diagnosis is the basis for correct classification of a venous problem. The diagnostic evaluation of CVD can be logically organized into 1 or more of 3 levels of testing, depending on the severity of the disease:

Level I: office visit, with history and clinical examination, which may include use of a hand-held Doppler scanner.

Level II: noninvasive vascular laboratory testing, which now routinely includes duplex color scanning, with some plethysmographic method added as desired.

Level III: invasive investigations or more complex imaging studies, including ascending and descending venography, venous pressure measurements, computed tomography (CT), venous helical scanning, or magnetic resonance imaging (MRI).

We recommend that the level of investigation (L) should also be added to the classification, for example, C_{2,4b,S}, E_pA_{s,p} Pr (2003-08-21, L II).

BASIC CEAP

A new basic CEAP is offered here. Use of all components of CEAP is still encouraged. However, many use the C classification only, which is a modest advance beyond the previous classifications based solely on clinical appearance. Venous disease is complex, but can be described with use of well-defined categorical descriptions. For the practicing physician CEAP can be a valuable instrument for correct diagnosis to guide treatment and assess prognosis. In modern phlebologic practice most patients will undergo duplex scanning of the venous system of the leg, which will largely define the E, A, and P categories.

Nevertheless, it is recognized that the merits of using the full (advanced) CEAP classification system hold primarily for the researcher and for standardized reporting in scientific journals. It enables grouping of patients so that those with the same types of disease can be analyzed together, and such subgroup analysis enables their treatments to be more accurately assessed. Furthermore, reports that use CEAP can be compared with each another with much greater certainty. This more complex classification, for example, also allows any of the 18 named venous segments to be identified as the location of venous disease. For example, in a patient with pain, varicose veins, and lipodermatosclerosis in whom duplex scans confirm primary reflux of the greater saphenous vein and incompetent perforators in the calf, the classification would be C_{2,4b,S}, E_pA_{s,p} P_{r2,3,18}.

While the detailed elaboration of venous disease in this form may seem unnecessarily complex, even intimidating, to some clinicians, it provides universally understandable descriptions, which may be essential to investigators in the field. To serve the needs of both, the full CEAP classification, as modified, is retained as "advanced CEAP," and the following simplified form is offered as "basic CEAP."

In essence, basic CEAP applies 2 simplifications. First, in basic CEAP the single highest descriptor can be used for clinical classification. For example, in a patient with varicose veins, swelling, and lipodermatosclerosis the classification would be C_{4b}. The more comprehensive clinical description, in advanced CEAP, would be C_{2,3,4b}. Second, in basic CEAP, when duplex scanning is performed, E, A, and P should also be classified with the multiple descriptors recommended, but the complexity of applying these to the 18 possible anatomic segments is avoided in favor of applying the simple s, p, and d descriptors to denote the superficial, perforator and deep systems. Thus, in basic CEAP the previous example, with painful varicosities, lipodermatosclerosis, and duplex scan-determined reflux involving the superficial and perforator systems would be classified as C_{4b,S}, E_pA_{s,p} P_r, rather than C_{2,4b,S}, E_pA_{s,p} P_{r2,3,18}.

REVISION OF CEAP AN ONGOING PROCESS

With improvement in diagnostics and treatment there will be continued demand to adapt the CEAP classification to better serve future developments. There is a need to incorporate appropriate new features without too frequent disturbance of the stability of the classification. As one of the committee members (F. Padberg) stated in our deliberations, "It is critically important that recommendations for change in the CEAP standard be supported by solid research. While there is precious little that we are recommending which meets this standard, we can certainly emphasize it for the future. If we are to progress we should focus on levels of evidence for changes rather than levels of investigation. While a substantial portion of our effort will be developed from consensus opinion, we should still strive to achieve an evidence-based format."

REVISION OF CEAP: SUMMARY

Clinical classification

- C₀: no visible or palpable signs of venous disease
- C₁: telangiectasies or reticular veins
- C₂: varicose veins
- C₃: edema
- C_{4a}: pigmentation or eczema
- C_{4b}: lipodermatosclerosis or atrophie blanche
- C₅: healed venous ulcer
- C₆: active venous ulcer
- S: symptomatic, including ache, pain, tightness, skin irritation, heaviness, and muscle cramps, and other complaints attributable to venous dysfunction
- A: asymptomatic

Etiologic classification

- Ec: congenital
- Ep: primary
- Es: secondary (postthrombotic)
- En: no venous cause identified

1252 Eklöf et al

JOURNAL OF VASCULAR SURGERY
December 2004

Anatomic classification

As: superficial veins
Ap: perforator veins
Ad: deep veins
An: no venous location identified

Pathophysiologic classification

Basic CEAP

Pr: reflux
Po: obstruction
Pr,o: reflux and obstruction
Pn: no venous pathophysiology identifiable

Advanced CEAP: Same as basic CEAP, with addition that any of 18 named venous segments can be used as locators for venous pathology

Superficial veins

Telangiectasies or reticular veins
Great saphenous vein above knee
Great saphenous vein below knee
Small saphenous vein
Nonsaphenous veins

Deep veins

Inferior vena cava
Common iliac vein
Internal iliac vein
External iliac vein
Pelvic: gonadal, broad ligament veins, other
Common femoral vein
Deep femoral vein
Femoral vein
Popliteal vein
Cruel: anterior tibial, posterior tibial, peroneal veins (all paired)
Muscular: gastrocnemial, soleal veins, other

Perforating veins:

Thigh
Calf

Example

A patient has painful swelling of the leg, and varicose veins, lipodermatosclerosis, and active ulceration. Duplex

scanning on May 17, 2004, showed axial reflux of the great saphenous vein above and below the knee, incompetent calf perforator veins, and axial reflux in the femoral and popliteal veins. There are no signs of postthrombotic obstruction.

Classification according to basic CEAP: C_{6,S}, E_p, A_{s,p,d}, P_r.
Classification according to advanced CEAP: C_{2,3,4b,6,S}, E_p, A_{s,p,d}, P_{r2,3,18,13,14} (2004-05-17, L II).

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Additional material for this article may be found online at www.mosby.com/jvs.

Table I, online only. Journals and books in which
CEAP classification has been published

Actualités Vasculaires Internationales 1995;31:19-22
Angiologie 1995;47:9-16
Angiology News 1996; 9:4-6
Australia and New Zealand Journal of Surgery 1995;65:769-72
Clinica Terapeutica 1997;148:521-6
Dermatologic Surgery 1995;21:642-6
Elleniki Angiochirurgiki 1996;5:12-9
European Journal of Vascular and Endovascular Surgery 1996;
12:487-91
Forum de Flebologia y Limphologia 1997;2:67-74
Handbook of Venous Disorders 1996;652-60
International Angiology 1995;2:197-201
Japanese Journal of Phlebology 1995;1:103-8
Journal of Cardiovascular Surgery 1997;38:437-41
Journal of Vascular Surgery 1995;21:635-45
Journal des Maladies Vasculaires 1995;20:78-83
Mayo Clinic Proceedings 1996;71:338-45
Minerva Cardioangiologica 1997;45:31-6
Myakkangaku 1995;31:1-6
Phlébologie – Annales Vasculaires 1995;48:275-81
Phlebologie [German version] 1995;24:125-9
Phlebology 1995;10:42-5
Przegląd Flebologiczny 1996;4:63-73
Scope on Phlebology and Lymphology 1996;3:4-7
VASA 1995;24:313-8
Vascular Surgery 1996;30:5-11

JOURNAL OF VASCULAR SURGERY
Volume 43, Number 2

Perrin, Labropoulos, and Leon Jr 329

328 Perrin, Labropoulos, and Leon Jr

JOURNAL OF VASCULAR SURGERY
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From the American Venous Forum

Presentation of the patient with recurrent varices after surgery (REVAS)

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Aim: To identify in patients with recurrent varices after surgery (REVAS) the clinical, etiologic, anatomic, and pathophysiologic patterns according to the CEAP classification, as well as the site, source, causes of recurrence, and contributory factors by using the REVAS classification.

Methods: Centers from eight countries enrolled patients with superficial vein reflux that had had a previous operation. A physical examination and a duplex ultrasound scan were performed at the first visit. This was repeated between 2 to 8 weeks after by the same physician and by another physician within the same time frame. The perforator, deep, and superficial veins systems as well as their accessories and tributaries were examined. A form based on the CEAP and the REVAS classification was used and the data were entered in a customized database.

Results: Fourteen institutions enrolled 170 patients (199 lower limbs) in 1 year. Their mean age was 56 years, and 69% were women. Most of them had undergone one surgical procedure before enrollment (76.6%). Most had varicose veins and swelling (70.9%), and the rest had skin damage (29.1%). More than 90% had primary etiology. The saphenofemoral junction (47.2%) and leg perforators (54.7%) were the areas most often involved by recurrent reflux. Reflux in deep veins was detected in 27.4%. Class 2 (varicose veins) alone was present in 24.6% of limbs, two classes were present in 43%, and three in 24%. Neovascularization was as frequent as technical failure (20% vs 19%); both were seen in 17%. In 35%, the cause was uncertain or unknown. When recurrence occurred at a different site, development of reflux in new sites was found in 32% of limbs. Of the contributing factors, family history and lifestyle had the highest prevalence. Women had significantly more procedures than men, despite a clear trend toward more severe disease in the latter.

Conclusions: Most patients were symptomatic with several clinical forms of presentation. The REVAS classification, together with CEAP, gives significant and more appropriate information for evaluating and following-up patients with chronic venous disease who have had an intervention. (J Vasc Surg 2006;43:327-34.)

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Results: Fourteen institutions enrolled 170 patients (199 lower limbs) in 1 year. Their mean age was 56 years, and 69% were women. Most of them had undergone one surgical procedure before enrollment (76.6%). Most had varicose veins and swelling (70.9%), and the rest had skin damage (29.1%). More than 90% had primary etiology. The saphenofemoral junction (47.2%) and leg perforators (54.7%) were the areas most often involved by recurrent reflux. Reflux in deep veins was detected in 27.4%. Class 2 (varicose veins) alone was present in 24.6% of limbs, two classes were present in 43%, and three in 24%. Neovascularization was as frequent as technical failure (20% vs 19%); both were seen in 17%. In 35%, the cause was uncertain or unknown. When recurrence occurred at a different site, development of reflux in new sites was found in 32% of limbs. Of the contributing factors, family history and lifestyle had the highest prevalence. Women had significantly more procedures than men, despite a clear trend toward more severe disease in the latter.

Conclusions: Most patients were symptomatic with several clinical forms of presentation. The REVAS classification, together with CEAP, gives significant and more appropriate information for evaluating and following-up patients with chronic venous disease who have had an intervention. (J Vasc Surg 2006;43:327-34.)

Residual and recurrent varicose veins are a common problem after interventions to correct reflux in patients with chronic venous disease (CVD).¹ In 1998, an international consensus group met in Paris and developed a classification for patients with recurrent varices after surgery (REVAS)¹ to be used in complement with the CEAP classification.² REVAS is a clinical definition that includes true recurrences, residual refluxing veins, and varicose veins caused by progression of the disease. Until the CEAP and REVAS classifications, it was difficult to report these occurrences. The frequency of REVAS has been reported to be between 20% and 80%, depending on the definition of the condition and the duration of the follow-up.¹ The current data in the literature suffer from the lack of uniformity when defining recurrences, and different lengths of follow-up and methods used for pre- and postoperative assessment make this assessment difficult.

This study was designed to identify in patients with REVAS (1) the clinical, etiologic, anatomic, and pathophysiologic patterns according to the CEAP classification, and (b) the site, source, causes of recurrence, and possible contributory factors according to the REVAS classification.

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PATIENTS AND METHODS

Multiple centers from different countries were selected for the study. These centers were chosen for their long-standing experience in diagnosing and treating patients with CVD. All patients were consecutive and had a previous operation and therefore could be classified according to REVAS. These patients were not asked to come to the vascular clinic, but they presented to the different centers seeking advice for their signs and symptoms of CVD. All patients presented with at least varicose veins.

A form based on the CEAP and the REVAS classification was filled in at the first assessment, which included a physical examination and a duplex investigation. The REVAS form was completed again 2 to 8 weeks after the first examination by the same physician and by another physician within the same time frame.

The CEAP classification can be used in two ways. In the basic CEAP, only the single highest class of the C is used; and only the first descriptor is used for E (etiology), A (anatomy), and P (pathophysiology). In the advanced CEAP, all the signs described in the clinical classes are provided, and for A or P (or both) the 18 named venous segments are used to locate venous pathology.

The duplex investigation was performed at each investigation. Investigations were performed either by technologists (in most cases) or by the investigator. The physicians had a written report and images when they completed the REVAS form. As the patients in this study were evaluated

REVAS Classification sheet

Date of examination
Day Month Year

Patient rename:

First name or given name

Last name or family name

✓ Topographical sites of REVAS

Since more than one territory may be involved, several boxes may be ticked

- Groin ☐
- Thigh ☐
- Popliteal fossa ☐
- Lower leg including ankle and foot ☐
- Other ☐

✓ Source(s) of recurrence

Since more than one source may be involved, several boxes may be ticked

- No source of reflux ☐
- Pelvic or abdominal ☐
- Saphenofemoral junction ☐
- Thigh perforator(s) ☐
- Saphenopopliteal junction ☐
- Popliteal perforator ☐
- Gastrocnemius vein(s) ☐
- Lower-leg perforator(s) ☐

✓ Reflux

Only one box can be ticked

- PROBABLE Clinical significance R+ ☐
- UNLIKELY Clinical significance R- ☐
- UNCERTAIN Clinical significance R? ☐

✓ Nature of sources

Only one box can be ticked

N classifies the source as to whether or not it is the site of previous surgery and describes the cause of recurrence.

• N Ss is for same site

Only one box can be ticked

- Technical failures ☐
- Tactical failures ☐
- Neovascularization ☐
- Uncertain ☐
- Mixed ☐

• N Ds is for different (new) site

Only one box can be ticked

- Persistent ☐
(Known to have been present at the time of previous surgery)
- New ☐
(Known to have been absent at the time of previous surgery)
- Uncertain/not known ☐
(insufficient information at the time of previous surgery)

✓ Contribution from persistent incompetent saphenous trunks

Since more than one territory may be involved, several boxes may be ticked

- AK great saphenous (above knee) ☐
- BK great saphenous (below knee) ☐
- SSV short saphenous ☐
- 0 neither/other ☐

Comment: _____

✓ Possible contributory factors

Several boxes may be ticked

• General factors

- Family history ☐
- Obesity ☐
- Pregnancy* ☐
- Oral contraceptive ☐
- Lifestyle factors** ☐

* Pregnancy since the initial operation

** Prolonged standing, lack of exercise, chair-sitting

• Specific factors

Several boxes may be ticked

- Primary deep vein reflux ☐
- Post-thrombotic syndrome ☐
- Iliac vein compression ☐
- Angiodysplasia ☐
- Lymphatic insufficiency ☐
- Calf pump dysfunction ☐

Table I. Classification of limbs according to basic CEAP

C*	n (%)	E†	n (%)	A	n (%)	P	n (%)
0	0 (0)	E _C	8 (4)	A _S	70 (35.3)	R	190 (95.4)
1	0 (0)	E _P	181 (91)	A _{S+P}	74 (37.3)	O	0 (0)
2	99 (49.8)	E _S	10 (5)	A _P	0 (0)	R+O	9 (4.6)
3	42 (21.1)	E _{P+S}	0 (0)	A _{S+D}	20 (10)		
4	39 (19.5)			A _D	0 (0)		
5	15 (7.6)			A _{S+P+D}	35 (17.4)		
6	4 (2)						

Total limbs: 199

C, Clinical classification; E, etiologic classification (E_C, congenital; E_P, primary; E_S, secondary); A, anatomic classification (A_S, superficial; A_P, perforator; A_D, deep); P, pathophysiologic classification (R, reflux; O, obstruction); n, number of patients.

*Symptoms were present in 76.8%.

†E_P was found in 125 women and 45 men ($P < .001$), E_S in 5 women and 4 men, and E_C in 1 woman and 7 men ($P < .001$ when E_S and E_C are combined).

twice (duplex scan and clinical exam), information concerning the reproducibility of the data collected was assessed. These data have been currently submitted to the *European Journal of Vascular and Endovascular Surgery*.

Most of the patients consulting for REVAS in this study had previous operations in other centers. Often it was impossible to know precisely the type of the procedure performed because the time elapsed between the last operation and the inclusion in the survey varied from 1.8 to 692 months (average, 136 months). Consequently, any type of surgical procedure was included such as ligation, stripping, and phlebectomy. Endovenous laser and radiofrequency ablation were not included.

The clinical significance of reflux was determined in a subjective manner by the physician as it was described in original publication of REVAS.¹ Clearly, it is not easy to quantify the degree of reflux from various sites. The significance of reflux was based on the estimate from the duplex scanning (DS) information and the physicians' evaluations of how the degree of reflux related to the overall clinical situation. R+ was used for clinical significance probable, R- for clinical significance unlikely, and R? for clinical significance uncertain. For example, a patient who had varicosities but only knee pain was classified as R-, whereas a patients with calf varicosities and swelling and pain around the involved area was classified as R+.

Technical failure was defined as an incorrect procedure, mostly nonflush ligation of the saphenofemoral or saphenopopliteal junctions (SFJ, SPJ) that could be identified easily by DS investigation. The presence of a stump at the previous SFJ or SPJ with refluxing tributaries connecting to these junctions was classified as a technical failure.

Neovascularization was identified on DS as the presence of reflux in thin, serpentine veins in previously ligated SFJ or SPJ. No quantitative criteria (size of the vessels) were used.

Imaging was performed in the different centers by using linear array transducers. The method of evaluating reflux in the superficial,³ tributary,⁴ perforator,⁵ and deep⁶ veins has been previously described. Briefly, the femoropopliteal, deep calf veins, the great (GSV) and small saphenous (SSV) and nonsaphenous veins, as well as their acces-

sories and tributaries, were examined with the patient in the standing position. Veins that were not a part of the GSV or SSV were termed nonsaphenous.⁷ Reflux in the recurrent or residual varicose veins was defined as a retrograde flow >0.5 seconds.⁸ Patients often had to rotate to trace these veins circumferentially and encompass all their trajectories. The distribution and extent of reflux in these veins and their tributaries, as well as their connections with perforating and deep veins, were recorded in detail.

The REVAS form (Fig) includes six items: *T* is for *topographic* sites of REVAS; *S* is for *sources* of reflux; *R* is for *degree of reflux*; *N* is for *nature* of sources (*Ns* for same site of previous surgery and *Nds* for different sites); *P* is for *contribution* from a *persistent* incompetent saphenous trunk; and *F* is for possible contributory *factors* *Eg* for general and *Fs* for specific factors).¹

All the recorded information was sent to the core center in Clinique du Grand Large, Decines, France. All data were entered in a customized database designed for the study.

Statistical analysis. Analysis of the patients' characteristics was performed by descriptive statistics. Differences in proportions were analyzed with the χ^2 test, the likelihood ratio, and trend analysis. Fisher's exact test was used when the expected value in any cell was <5. The difference in age was compared with unpaired *t* test. The statistical significance was set at $P = .05$.

RESULTS

Fourteen institutions from eight countries enrolled 170 patients (199 lower limbs) in 1 year. Their mean age was 55.6 ± 12 years (SD) (range, 27 to 82 years) and 69% were women. Most of these patients had undergone one surgical procedure before enrollment (76.6%), 21.9% had two procedures, and 1.5% had three. High ligation, stripping, and phlebectomies were the main interventions performed. The mean time between the last surgical intervention and office consultation was 136 months (range, 1.8 to 692 months).

The clinical, etiologic, anatomic, and pathophysiologic characteristics of this cohort are summarized in Table I. Most patients had varicose veins and swelling (70.9%), and the rest had skin damage (29.1%). More than 90% had

Table II. Clinical classification using advanced CEAP

<i>Clinical class</i>	<i>Number of limbs</i>	<i>Percentage</i>
C2	49	24.62
C2,C6	2	1.01
C2,C5	5	2.51
C2,C4	11	5.53
C2,C3	18	9.15
C2,C3,C6	1	0.50
C2,C3,C5	1	0.50
C2,C3,C4	8	4.02
C1,C2	50	25.13
C1,C2,C5	3	1.51
C1,C2,C4	10	5.03
C1,C2,C3	24	12.16
C1,C2,C3,C6	1	0.50
C1,C2,C3,C5	6	3.02
C1,C2,C3,C4	10	5.03
Total	199	100

Table III. Association between symptomatology and CEAP class C

	<i>Asymptomatic</i>	<i>Symptomatic</i>	<i>Total</i>
C2	30 (15.6)	62 (32.3)	92 (47.9)
C3-6	10 (5.2)	90 (46.9)	100 (52.1)
Total	40 (20.8)	152 (79.2)	192 (100.0)

C2 vs C3-C6 for the presence of symptoms $P = .0001$.

The numbers in parenthesis are percentages of the total number at the last column.

primary etiology. By definition from the study design, all patients had superficial vein involvement, and their pathophysiology was reflux. Reflux in perforator veins was detected in 54.7% and in the deep veins in 27.4%. With the advanced CEAP classification, more information can be given in the clinical class as presented in Table II. Only one quarter presented with class 2 alone, and two clinical classes were present in 43%, three in 24%, and four classes in 9% of limbs. Symptoms were more likely to be present in classes 3 to 6 compared with class 2 (Table III).

Reflux was identified at the groin region in 37% of cases, at the thigh in 68%, at the popliteal fossa in 23%, at the lower leg in 85%, and in other areas in 11%. The different sources of reflux are summarized in Table IV. The SFJ and leg perforators were the areas most frequently involved by recurrent reflux. This reflux was found to be of probable clinical significance in 164 limbs (82%), unlikely to be significant in 20 (10%), and its clinical importance was uncertain in 15 (8%). One or two sources of reflux were identified in 68% of patients and more than two in 22%.

When the recurrence occurred on the same site of a previous operation, the cause was ticked uncertain in 20%, mixed in 17%, and unknown in 14%. The numbers for technical failure, tactical failure, and neovascularization were, respectively, 19%, 10%, and 20%. When the varices were present on the site not previously operated on (different site), the answers were persistent (known to have been

Table IV. Sources of reflux

	<i>Number of limbs</i>	<i>Percentages</i>
Source of reflux		
No source	19	9.55
Pelvic or abdominal	33	16.58
Saphenofemoral junction	94	47.24
Thigh perforators	60	30.15
Saphenopopliteal junction	49	24.62
Popliteal perforators	9	4.52
Gastrocnemial veins	17	8.54
Lower leg perforators	85	42.71
Sources of reflux-number		
Unknown	19	9.55
1	73	36.68
2	63	31.66
3	29	14.57
4	14	7.04
5	1	0.5
Total	199	100

Table V. Nature of sources

<i>Site</i>	<i>Nature</i>	<i>Number of limbs</i>	<i>Percentages</i>
Same	Technical failure	38	19.1
	Tactical failure	19	9.6
	Neovascularization	40	20.1
	Uncertain	39	19.6
	Mixed	33	16.6
Different	Unknown	30	15.1
	Persistent	23	11.6
	New	63	31.7
	Uncertain/unknown	42	21.1
	Info not given	71	35.7

present at the time of previous surgery) in 12%, new (known to have been absent at the time of previous surgery) in 32%, uncertain/unknown in 21%, and information was not given in 35%.

Ultrasound assessment of the sources of reflux and their nature was performed (Table V). Technical or tactical failure accounted for 29% of all recurrences at the same site, and neovascularization was found to be responsible for 20%. When a different site of reflux was diagnosed, newly incompetent segments were found in 32% of cases.

Persistent reflux in the above-knee GSV was found in 78 limbs (39.2%), in the below-knee segment in 60 (30.2%), in the SSV in 48 (24.1%), and in nonsaphenous trunks in 73 (36.7%). The below-knee saphenous trunks had a higher prevalence than did the above-knee ($P < .01$).

Of the possible contributing factors (Table VI), family history and lifestyle had the highest prevalence. Multiple factors were present in many patients, however. One factor was present in 99 limbs (49.25%), and the rest had multiple factors.

Gender had a significant influence on the number of procedures performed. Women had a significantly higher number of procedures than men, despite a clear trend toward more severe disease in male patients (Table VII).

Table VI. Possible contributory factors

Factor type	Factor	Number of limbs	Percentages
General	None	31	15.4
	Family history	135	67.8
	Lifestyle factors	85	42.7
	Obesity	47	23.6
	Pregnancy	21	10.6
	Contraceptives	11	5.5
Specific	Primary deep reflux	24	12.1
	Calf muscle pump dysfunction	20	10.1
	Post-thrombotic syndrome	10	5.0
	Angiodysplasia	5	2.5
	Lymphatic insufficiency	1	0.5

Table VII. Gender, number of procedures, and disease severity

	Males (%)	Females (%)	Total (%)
Number of procedures			
1	49 (84.5)	95 (72.5)	144
2	7 (12.1)	36 (27.5)	43
3	2 (3.5)	0 (0)	2
Total	58	131	189
$P = .006$			
Disease severity			
C2	25 (13.4)	72 (38.5)	97 (51.9)
C3	9 (4.8)	31 (16.6)	40 (21.4)
C4	14 (7.5)	21 (11.2)	35 (18.7)
C5	7 (3.7)	4 (2.1)	11 (5.9)
C6	1 (0.5)	3 (1.6)	4 (2.1)
Total	56 (29.9)	131 (70.1)	187 (100.0)

 χ^2 for trend, $P = .049$; likelihood ratio, $P = .064$.

Perforator vein and SSV trunk incompetence were associated with a greater number of procedures; conversely, the presence of symptoms and deep vein abnormality were not (Table VIII).

DISCUSSION

Recurrence is common after varicose vein surgery. Van Rij et al⁹ prospectively studied 92 consecutive patients with symptomatic varicose veins that required superficial vein surgery. Recurrence was seen in 14% of limbs at 3 months, 32% at 1 year, and 52% after 3 years. A uniform identification of the causes and patterns of recurrence has not been reported, however. Disparate results have often been found, mainly because of the lack of consistency in defining recurrence, initial therapy, and the method and duration of follow-up.

This prompted a consensus meeting led by one of the authors (M. P.) in 1998 that proposed guidelines for REVAS. Only one report so far has been published using these guidelines. Kostas et al¹⁰ studied 113 operated legs and found a 25% recurrence rate in a 5-year follow-up. Because of the small sample size with recurrences ($n = 28$), only a descriptive analysis was performed.

Table VIII. Number of procedures, presence of symptoms and perforator, small saphenous vein trunk incompetence, and deep vein involvement

	1 (%)	2 (%)	3 (%)	Total
Perforator vein				
No	79 (88.8)	10 (11.2)	0 (0)	89
Yes	73 (66.4)	34 (30.9)	3 (2.7)	110
Total	152	44	3	199
$P = .0008$				
SSV				
Yes	29 (60.4)	18 (37.5)	1 (2.1)	48
No	123 (81.5)	26 (17.2)	2 (1.3)	151
Total	152	44	3	199
$P = .011$				
Symptoms				
Asymptomatic	115 (75.7)	34 (22.4)	3 (2.0)	152
Symptomatic	31 (77.5)	9 (22.5)	0 (0)	40
Total	146	43	3	192
$P = .669$				
Deep vein				
Yes	41 (74.6)	14 (25.5)	0 (0)	55
No	111 (77.1)	30 (20.8)	3 (2.1)	144
Total	152	44	3	199
$P = .458$				

SSV, Small saphenous vein.

The mean age (55 years) of patients in our study was higher than that in previous reports. Labropoulos et al¹¹ found among 90 patients before surgical intervention a mean age of 49, and Kostas et al¹⁰ found a mean age of 48 years. This is not surprising, because patients who seek treatment after their first intervention are likely to be older as a significant time elapses for the recurrence of the disease.

Clinical grade based on CEAP system was higher in men, but women underwent significantly more interventions. Those differences may be explained by the fact that women care more about the appearance of their legs than men and seek medical advice at an earlier stage. Women also had a higher primary and lower congenital etiology compared with men as seen in Table I. A possible explanation for the higher congenital etiology is the male preponderance in cases of Klippel-Trenaunay syndrome.^{12,13}

The use of the advanced CEAP is more appropriate for REVAS patients as it allows a more defined description and better comparison among different patient groups. This is evident from Tables I and II, where in the latter the whole clinical spectrum of the disease is given for each limb. For example, the advanced CEAP system offers the ability to identify patients with varicose veins only, which in our patients was 25%. Likewise, edema was present in 35% of REVAS limbs, whereas when the basic system was used, many cases of limb edema were missed (21% only). The basic CEAP provides limited and inaccurate information.

Most of the REVAS patients were symptomatic (77%). Labropoulos et al¹¹ reported a 85% prevalence of symptomatic nonoperated limbs. Kostas et al¹⁰ reported a 72% prevalence of symptomatic operated limbs. Although early after intervention the prevalence of symptoms should be lower, in our study it was high owing to the long follow-up

period. The presence of symptoms was not related to a higher number of interventions.

The number of REVAS patients consulting for skin changes was higher than that of patients screened for epidemiologic studies who had varices and had not been operated on. Carpentier et al¹⁴ found a 2.8% occurrence of skin changes in women and 5.4% in men in a random sample of 835 subjects in the general population in France. Kaplan et al¹⁵ reported a 6.3% prevalence among 2404 patients screened in the San Diego study who had a similar mean age with our cohort. However, patients who are referred to clinics seeking treatment may have a similar prevalence of skin damage compared with the REVAS patients. Labropoulos et al¹¹ found a prevalence of 25% (29/116), which was comparable to the 29% (58/159) in the current study ($P = .5$). The preponderance of skin changes in the REVAS patients may be due to their older age (49 vs 55.6 years, $P < .01$).

Pelvic or abdominal reflux was detected in 17%. The prevalence of this reflux is not known. Its frequency may be higher in this study than is usually seen because one of the centers has many referrals. Nonsaphenous vein reflux is found in about 10% of people presenting with CVD.⁸ Often, tributaries of such veins in the leg are thought to be part of the saphenous system, and technical and tactical failure can occur. In REVAS patients, the higher occurrence was expected given that 70% of our patients were women, who have significantly higher prevalence of nonsaphenous veins than men.⁸

Reflux was present in the SFJ in 47% of cases. Up to 60% of limbs of patients surviving >30 years after ligation and stripping demonstrate incompetence at or near the SFJ.¹⁶ This has been attributed to neovascularization, to failure in ligating the SFJ, or to overlooked junctional tributaries. In our study, neovascularization occurred as often as incorrect ligation (20% and 19% respectively).

Perforator incompetence was identified in 55% of REVAS limbs. Reflux in these veins is very common and has been described in many studies. Labropoulos et al¹⁷ showed that 57% had incompetent perforator veins among 134 REVAS limbs. In a prospective study of patients operated on for varicose veins, van Rij et al¹⁹ found that reflux in perforator veins increased progressively. The same group¹³ studied 822 incompetent perforators after intervention. At a 3-year follow-up, 397 incompetent perforators were noted, with the main cause for recurrence being changes in pre-existing perforators in other locations, followed by neovascularization at sites of ligation and a very small number of missed vessels. Furthermore, the number of incompetent perforators correlated significantly with the clinical severity of the disease.

The exact cause of reflux has been subject of intense debate. Poor surgical technique¹⁸ and neovascularization were the most common reasons accounting for most cases of REVAS.¹⁹ Neovascularization accounted for 20% of REVAS cases in our series when reflux was identified in the same site and technical or tactical failure for 29%.

The item concerning the nature of sources was difficult to complete, as the investigators did not always have information on the previous interventions. Consequently, the answers *uncertain*, *unknown*, or *information not given* were frequently notched. Only a prospective study using the REVAS classification can provide accurate information.

The below-knee saphenous trunks had a higher prevalence of reflux compared with the above knee. This is because the GSV is most often stripped to the knee level, and the SSV is often ligated without stripping. High prevalence of recurrent GSV varicosities in the thigh can be attributed to ligation of the SFJ without stripping. It has been shown that GSV stripping correlates with less recurrence in long-term follow-up.¹⁷

Reflux recurrence in the popliteal region has been attributed to insufficient excision of an incompetent SSV. Among REVAS patients, SSV reflux was responsible for 29% of cases.¹⁷ An analysis of 125 popliteal interventions for REVAS after excision of an incompetent SSV identified 14% of patients with an intact SSV.²⁰ A retrospective study²¹ of 59 patients after saphenopopliteal junction (SPJ) disconnection revealed that 47% had reflux after the operation because of tactical or technical failure at the SPJ and persisting superficial vein incompetence. The survey by the Vascular Surgical Society of Great Britain and Ireland showed a wide variation in the management of SSV owing to the lack of proper clinical trials in this area.²²

Gastrocnemial vein incompetence has a prevalence of up to 30% among patients with varicose veins.²³ Most practitioners do not treat this vein. Also, incompetent perforators through this vein at the posteromedial calf may be overlooked or missed.

Calf muscle dysfunction may cause recurrence or persistence of ulcerations.^{24,25} Rhodes et al²⁶ demonstrated significantly lower hemodynamic improvement in calf muscle pump function with perforator interruption alone than when performed with concomitant saphenous ablation. However, no specific test was used for identifying calf pump failure in our study other than known joint and muscle problems and, therefore, some cases may have been missed.

Multiple factors contribute in the development of recurrent disease. The weight of each factor has not been determined, as there are no prospective studies with adequate sample size. Family history of venous disease had by far the highest prevalence (68%), however. This is not surprising, as a prominent role of heredity in the development of venous disease has been shown.²⁷

A higher number of procedures were performed in our patients with perforator vein and SSV incompetence. These findings may be explained by the fact that perforator veins can be easily missed on preoperative assessment. Glociczki et al²⁸ found a 30% rate of persistent or new incompetent perforator veins in 30 patients at a mean time of 16 months after surgery (1 to 50 months). Neovascularization and the development of new veins from dilatation of those missed at surgery have been proposed as the most likely mechanisms.^{13,29,30} Van Rij and Hill,¹³ in a 3-year follow-up, identified 397 recurrent incompetent veins that were most

often in the medial paratibial compartment. Changes in pre-existing perforator veins at other sites were responsible for 61% of cases, followed by neovascularization in 35%, and inadequate surgery accounted for only 0.4%.

Small saphenous vein reflux has been recognized as an important cause of CVD.³¹ Iafrati et al³² recognized that a more conservative attitude to treat SSV reflux was a contributor for CVD recurrence after surgical intervention. Inaccurate preoperative duplex examination and surgeons' bias towards certain types of surgical interventions might have a role in our recurrence rates.

Deep vein involvement was not associated with a higher number of procedures. The importance of deep venous reflux in CVD has been better identified only recently, and the benefit of deep reconstructive surgery remains controversial.³³ This type of surgery is only performed by very few selected centers worldwide; therefore, patients with deep vein reflux may have not been adequately treated in most centers in our study.

CONCLUSION

Most patients were symptomatic with various clinical patterns of presentation. There was female preponderance for primary CVD and number of interventions. The use of the advanced CEAP is more appropriate for the REVAS patient. The sources of reflux feeding the recurrence were of multiple origins, and present at the SFJ in almost half of the patients. Ten percent had no apparent source of reflux; in 17%, it was of pelvic or abdominal origin. About 75% of limbs have incompetent perforator veins. Neovascularization was as frequent as technical failure (20% vs 19%), and a combined presentation was found in 17%. In 35% of cases, the cause was uncertain or unknown. When recurrence occurred at a different site, development of reflux in new sites was found in 32% of limbs. The use of the REVAS classification together with CEAP gives significant information for evaluating and following-up patients with CVD who underwent an intervention.

REVAS group

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Writing the article: N.L., L.R.L.
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334 Eklöf

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February 2006

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INVITED COMMENTARY

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The credo of the American Venous Forum (AVF) is that the cornerstone for management of chronic venous disorders (CVD) is an accurate diagnosis and classification of the underlying venous problem, which creates the base for correctly directed treatment. The AVF, together with international experts, created the CEAP classification at a 1994 meeting in Hawaii. In 2004, 10 years after its introduction, a revision of CEAP was established by an AVF international ad hoc committee and published in the *Journal of Vascular Surgery*¹—we have got an internationally accepted classification of CVD, “we can speak the same language.”

Recurrent varices after surgery (REVAS) is a common, complex, and costly problem, and the data in the literature suffer from a lack of uniformity. I had the privilege to participate in the consensus meeting organized by Michel Perrin, the first author of the present report, and his French colleagues in Paris in July 1998, at the same time as the French team won the World Cup in soccer a few blocks away from the meeting. The goal was to create a classification for REVAS to be used as a complement to CEAP, which was expanded to define the sites, nature, and sources of recurrence, as well as the magnitude of the reflux and possible contributory factors. Factors responsible for recurrence and recommendations for primary prevention were debated.

The need for well-planned prospective studies was obvious. Several future studies were recommended, and this report is one such outcome. It is a multicenter, prospective, observational study

of 170 patients with recurrent varicose veins after previous surgery from 14 institutions in 8 countries. The aim of the study was to classify the patients according to the CEAP and REVAS classifications by using physical examinations and duplex scanning. The REVAS form was filled in again 2 to 8 weeks after the first examination by the same physician and by another physician. The data on reproducibility of the REVAS information has been submitted for publication to the *European Journal of Vascular and Endovascular Surgery*. In this study, 70.9% had varicose veins and swelling (C2, 3) and the rest (29.1%) had skin damage (C4, 5, 6). More than 90% had primary etiology. The saphenofemoral junction and leg perforators were the areas most often involved by recurrent reflux. Neovascularization was as frequent as technical failure (20% vs 19%).

This is an interesting report confirming that the use of proper classification will lead to better understanding of the underlying venous problem and, hopefully, improved initial treatment of patients with CVD.

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590 Gillet, Perrin, and Allaert

JOURNAL OF VASCULAR SURGERY
September 2006

From the American Venous Forum

Clinical presentation and venous severity scoring of patients with extended deep axial venous reflux

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Background: The objective of this study was to evaluate the prevalence and profile of patients presenting with chronic venous insufficiency (class C3-C6) and cascading deep venous reflux involving femoral, popliteal, and crural veins to the ankle.

Methods: From September 2001 to April 2004, 2894 patients were referred to our center for possible venous disorders. The superficial, deep, and perforator veins of both legs were investigated with color duplex scanning. The criterion for inclusion in this study was the existence of cascading deep venous reflux involving the femoral, popliteal, and crural veins to the ankle whose duration had to be longer than 1 second for the femoropopliteal vein and longer than 0.5 seconds for the crural vein. The advanced CEAP classification, the Venous Clinical Severity Score (VCSS), the Venous Segmental Disease Score (reflux; VSDS), and the Venous Disability Score (VDS) were used.

Results: Seventy-one limbs in 60 patients were identified. Eleven limbs (15.5%) were classified as C3, 36 (50.7%) as C4, 21 (29.6%) as C5, and 3 (4.2%) as C6. A primary etiology was identified in 11 (15.5%) limbs, and a postthrombotic etiology was identified in 60 limbs (84.5%). In the latter group, all but four patients were aware that they had had a previous deep venous thrombosis. In addition to femoropopliteal and calf veins, reflux was present in the common femoral vein in 60 (84.5%), the deep femoral vein in 27 (38%), and the muscular calf veins in 62 (87.3%). Incompetent perforator veins were identified in 53 (74.6%) limbs. Fifty-one (71.8%) limbs had a combination of superficial venous insufficiency (AS₂, AS_{2,3}, AS₄, or their combination) previously treated or present. Of these, 11 had primary etiology alone, and 40 had a secondary etiology with or without primary disease. Means and 95% confidence intervals of the VCSS, VSDS, and VDS were 9.72 (8.91-10.53), 7.2 (6.97-7.42), and 1.08 (0.83-1.32), respectively. A significant increase in the VCSS and in the VSDS ($P < .0001$) paralleled the CEAP clinical class. The VDS was higher in the C3 and C6 classes but did not reach significance. There was a significant link between the pain magnitude in the VCSS and the VDS ($P < .0001$). Severity of pain and high VDS did not depend on the wearing of elastic compression stockings. VCSS increased significantly according to the presence of an incompetent perforator vein ($P < .05$) and/or reflux in the deep femoral vein ($P < .05$).

Conclusions: This study confirmed the value of the Venous Severity Score as an instrument for evaluation of chronic venous insufficiency. A significant increase in the VCSS and VSDS paralleled CEAP clinical class; VDS was higher in classes C3 and C6 without reaching significance, probably because of the small size of the samples. Some clinical and anatomic features need to be clarified to facilitate scoring. (J Vasc Surg 2006;44:588-94.)

From the American Venous Forum

Clinical presentation and venous severity scoring of patients with extended deep axial venous reflux

Jean Luc Gillet, MD,^a Michel R. Perrin, MD,^b and François André Allaert, MD, PhD,^c *Bourgoin-Jallieu, Chassieu, and Dijon, France*

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The CEAP classification was conceived and created at the sixth annual meeting of the American Venous Forum in Maui, Hawaii, in 1994 by an international ad hoc committee.¹ It is an internationally recognized classification. It has been published in 25 medical journals or books, has been translated into 8 languages, and was recently revised.² This classification is only descriptive in scope and cannot quantify the severity of chronic venous disorders (CVD). The Venous Severity Score (VSS) has supplemented the original classification³ and was updated in 2000 (the VSS is also available online at <http://www.jvascsurg.org>; click on the Special Collection section and then the Reporting Stan-

dards section).⁴ With the CEAP classification and the VSS, we now have an instrument that is descriptive and can quantify CVD. However, although the CEAP has been widely circulated among physicians specializing in venous disease and is used in scientific research, an analysis of the literature shows that use of the VSS continues to be limited.

The objective of this study was to evaluate the prevalence of and profile of patients presenting with chronic venous insufficiency (CVI) and cascading deep postthrombotic or primary venous reflux involving the femoral, popliteal, and crural veins to the ankle⁵ (C3-C6; primary etiology, s; Ad, s, p).

METHODS

From September 2001 to April 2004 (32 months), 2894 patients were referred to our center for possible venous disorders (C0s-C6). The superficial, deep, and perforator veins of both legs in all patients were investigated with color duplex scanning (DS). The criteria for inclusion in this study were the presence of CVI (C3-C6 according to the updated CEAP²) and cascading deep venous reflux involving in all cases the femoral, popliteal, and crural veins

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to the ankle, whose duration had to be longer than 1 second for the femoropopliteal vein and longer than 0.5 seconds for the crural vein.^{6,7} We used DS with the Vivid 3 scanner from General Electric Healthcare Technologies (Vingmed) (Waukesha, Wis) and a linear probe (frequency, 7.5 MHz; range, 5-10 MHz) to investigate the lower limbs and a phased array probe (frequency, 2.5 MHz; range, 2.25-5 MHz) to investigate the abdomen and pelvis.

In all patients, three protocols were successively used to assess deep vein reflux. The first consisted of performing a Valsalva maneuver with the patient in a supine position. We considered a reflux significant if its duration was greater than or equal to 1 second in the common femoral vein and was greater than or equal to 0.5 seconds in the deep femoral vein (DFV),^{6,7} measured 2 or 3 cm from its termination into the common femoral vein. In a second phase, with the patient standing with his or her back to the examiner and holding onto a frame, with the knee flexed slightly and the calf muscle relaxed, we looked for the existence of a reflux in the femoral vein, the popliteal vein, and the gastrocnemial and soleal veins by exerting manual compression on the calf with sudden release. In a third phase, the patient was installed seated at the edge of the examining table with his or her legs hanging, resting on a stool. By exerting compression at the base of the calf muscle and the plantar sole of the foot, we looked for a reflux in the peroneal and posterior tibial veins in the lower third of the leg, as well as in the gastrocnemial veins and the soleal veins.

The gastrocnemial veins were evaluated at their termination and along their intramuscular course. A reflux whose duration was greater than or equal to 1 second in the femoral vein at mid thigh and in the popliteal vein and of at least 0.5 seconds in the axial and muscular calf veins was considered significant.^{6,7}

A reflux in the thigh and/or calf perforator veins was sought by means of manual compression of the lower third of the thigh and/or the calf followed by sudden release, with the patient in the standing position and then in the sitting position as previously described. An outward flow whose duration was greater than 0.5 seconds⁸ was considered significant.

The following patients were excluded from the study:

1. Patients presenting with a concomitant obstructive postthrombotic syndrome (PTS)⁹ so that the hemodynamic disorder induced by the obstructive syndrome did not interfere with that of the reflux. The criterion used for qualifying obstruction was the one described by Rutherford et al⁴: total vein occlusion at some point in the segment or more than 50% narrowing of at least half of the segment.
2. Patients with PTS secondary to a deep vein thrombosis (DVT) that occurred less than 1 year previously.
3. Bedridden patients or subjects with only very limited mobility and those who presented with an altered mental condition that made it impossible to interview them.

PTS was differentiated from primary deep venous insufficiency by the demonstration of morphologic abnor-

malities in deep vein trunks by venous DS investigation that showed evidence of postthrombotic valvular or transmural vein wall abnormalities. In some patients, venography or DS previously performed at the time of an acute episode provided evidence of an initial DVT. The advanced CEAP classification, the Venous Clinical Severity Score (VCSS), the Venous Segmental Disease Score (reflux; VSIDS), and the Venous Disability Score (VDS) Française were used in all patients.

Quantitative data are reported as means \pm SD, and qualitative data are reported as percentages and sample sizes. The between-group comparisons were performed by one-way χ^2 tests and Kruskal-Wallis tests. The statistical computer software SAS version 8.2 (SAS Institute, Cary, NC) was used for analysis. Values of $P < .05$ were considered to be significant.

RESULTS

Seventy-one lower limbs in 60 patients were identified, yielding a prevalence of 2% in patients referred to our institution for possible CVD. Forty-two left lower limbs and 29 right lower limbs were involved. There were 11 cases of bilateral involvement (reflux). Thirty-four women and 26 men were enrolled in the study (age [mean \pm SD], 65 ± 14 years; range, 29-85 years; median, 69 years; interquartile range, 59-75 years).

CEAP classification

Clinical classification. Each patient was described by his or her highest clinical class. Eleven limbs (15.5%) were classified as C3, 36 (50.7%) as C4, 21 (29.6%) as C5, and 3 (4.2%) as C6. According to the criteria at inclusion, no patient was identified C0 to C2. Sixty-one (85.9%) patients were symptomatic.

Etiologic classification. A primary etiology was identified in 11 (15.5%) and a postthrombotic etiology in 60 (84.5%) limbs. In the latter group, all but four patients were aware that they had had a previous DVT. The initial DVT occurred on average 25.5 years previously (SD, 15.6 years; range, 2-58 years; median, 25.0 years; 95% confidence interval [CI], 21.3-29.7 years). Thirty-nine patients reported that they had had only 1 episode of lower limb DVT, whereas 21 patients may have presented with several episodes of DVT in the lower limb.

Anatomic classification

Superficial (As). Fifty-one limbs (71.8%) had a combination of superficial venous insufficiency As2, As2, 3, As4, or their combination as defined in the CEAP classification,¹ previously treated or present. Of these, 11 had a primary etiology alone, and 40 had secondary etiology with or without primary disease. Superficial venous insufficiency was significantly ($P < .05$) more frequent in patients with primary etiology (11/11; 100%) than in those with postthrombotic etiology (40/60; 66.6%).

Deep (Ad). All of the patients had grade 4 deep axial venous reflux (inclusion criterion), whose segmental description is listed in Table I. Two patients presented with an

Table I. Deep venous reflux segmental description

Segmental localization (Ad classification)	n (%)
CFV (Ad 11)	60 (84.5)
DFV (Ad 12)	27 (38)
FV (Ad 13)	71 (100)
PV (Ad 14)	71 (100)
Calf vein(s) (Ad 15)	71 (100)
Muscular vein(s) (Ad 16)	62 (87.3)

CFV, Common femoral vein; DFV, deep femoral vein; FV, femoral vein; PV, popliteal vein.

The number after Ad is the number used in the anatomic description of the CEAP classification.

abnormal external iliac vein (Ad 9) without an obstruction pattern.

Perforator veins (Ap). The existence of at least 1 incompetent perforator vein in the calf (Ap 18) was observed in 53 limbs (53/71; 74.64%). An incompetent perforator vein in the thigh was also present concomitantly in six limbs (Ap 17-18). We did not observe the isolated existence of an incompetent perforator vein in the thigh. In limbs classified as C3, an incompetent perforator vein was identified in 6 (54.5%) of 11. In limbs classified C4, an incompetent perforator vein was recognized in 27 (75%) of 36. In limbs classified C5, an incompetent perforator vein was recognized in 17 (80.9%) of 21. At least one incompetent perforator vein was identified in each of three limbs (100%) classified as C6. An increased incidence of incompetent perforator veins according to clinical class was observed but did not reach statistical significance.

Severity scores

Means, ranges, and 95% CIs of the VCSS, VSDS, and VDS were 9.72, 4.00 to 23.00, and 8.91 to 10.53; 7.20, 5.00 to 9.50, and 6.97 to 7.42; and 1.08, 0.00 to 3.00, and 0.83 to 1.32, respectively. The VDS could not be determined in five patients who were unable to carry out usual activities but were not wearing compression stockings and did not submit to limb elevation. This group is unlisted in the VDS scoring. Table II lists the values of each score according to the clinical class. A significant increase in the VCSS (Kruskal-Wallis, 23.22; $P < .0001$) and in the VSDS (Kruskal-Wallis, 23.22; $P < .05$) paralleled the CEAP clinical class.

The VDS was higher in the C3 and C6 classes but did not reach significance. Table III shows the distribution by number and percentage of VDS scores according to the CEAP clinical class.

We analyzed the pain item in the VCSS in all lower limbs and according to clinical class. Then we classified the patients into two groups: pain absent or mild (scoring 0 or 1) in 84.5% ($n = 60$) and moderate or severe (scoring 2 or 3) in 15.5% ($n = 11$). Pain rated 2 or 3 was statistically more frequent (Fisher test; $P < .01$) in classes C3 and C6 than in classes C4 and C5.

We also analyzed activity according to clinical class; 62 (87.3%) limbs allowed normal activity (VDS 0, 1, or 2), and

9 (12.7%) did not (VDS 3; unlisted). Activity was more adversely affected (Fisher test; $P < .01$) in classes C3 and C6 than in classes C4 and C5. However, these results should be interpreted cautiously because of the small sample size studied.

Table IV shows that there was a significant link between pain magnitude and the VDS (Fisher test; $P < .0001$). In other words, when the pain was absent or mild, the patient was disabled in 95% of cases; conversely, patients with moderate or severe pain were either handicapped or not (54.5% vs 45.5%).

We analyzed pain severity and VDS in patients who were wearing elastic compression stockings or not, knowing that only stockings exerting 15 mm Hg of pressure at the ankle were taken into account. No significant difference was found between groups.

We sought to determine whether pain severity, the existence of at least one incompetent perforator vein (Ap 17 or 18), an incompetent saphenous vein (As 2, 3, or 4), or a reflux in the DFV (Ad 12) resulted in an increase in VCSS. VCSS increased, but not significantly (Kruskal-Wallis, 5.72; not significant), according to pain scoring.

The existence of an incompetent perforator vein produced a significant increase in the VCSS (Kruskal-Wallis, 5.89; $P < .05$). In the group of patients ($n = 53$) who presented with at least one incompetent perforator vein, the mean \pm SD of VCSS was 10.25 ± 3.59 (range, 5-23; median, 10; 95% CI, 9.25-11.24). It was 8.17 ± 2.33 (range, 4-14; median, 8; 95% CI, 7.01-9.33) in the group of patients ($n = 18$) without an incompetent perforator vein.

The existence of reflux in the DFV also produced a significant increase in the VCSS (Kruskal-Wallis, 2.20; $P < .05$). In the group of patients ($n = 27$) who had a reflux in the DFV, the mean \pm SD VCSS was 11.07 ± 4.23 (range, 6-23; median, 10; 95% CI, 9.40-12.75). It was 8.89 ± 2.54 (range, 4-16; median, 9; 95% CI, 8.12-9.66) in the group of patients ($n = 44$) without reflux in the DFV.

The existence of an incompetent saphenous vein produced an increase in the VCSS, but this did not reach significance (Kruskal-Wallis, 1.29). In the group of patients with an incompetent saphenous vein ($n = 41$), the mean \pm SD VCSS was 10.00 ± 3.57 (range, 4-23; median, 9; 95% CI, 8.87-11.13). In the group of patients who did not have an incompetent saphenous vein ($n = 30$), this mean was 9.33 ± 3.24 (range, 5-21; median, 9; 95% CI, 8.12-10.54).

DISCUSSION

In agreement with most authors, we considered the duration of reflux as the selective or more reliable parameter. Our cutoff values were those chosen by most authors.^{6,7,10} In perforating veins, the cutoff value used in most studies is 0.5 seconds; however, a recent study suggests that it could be decreased to 0.35 seconds.⁷

Study protocols differ with different teams of investigators. The patient can be assessed in the supine position, standing position, or sitting position. Pneumatic cuff com-

Table II. Mean \pm SD, median, range, and 95% CI of the VSS according to clinical class

Variable	C class				Kruskal-Wallis
	C3	C4	C5	C6	
VCSS					
Mean \pm SD	6.73 \pm 1.85	9.33 \pm 2.37	10.48 \pm 2.58	20.00 \pm 3.61	
Median (range)	6 (4-10)	9 (6-17)	10 (5-16)	21 (16-23)	23.22
95% CI	5.49-7.97	8.53-10.13	9.30-11.65	11.04-28.96	$P < .0001$
VSDS					
Mean \pm SD	6.77 \pm 0.93	7.03 \pm 0.93	7.62 \pm 0.89	7.83 \pm 0.76	
Median (range)	6.5 (5-9)	7 (5-9.5)	7.5 (6-9.5)	8 (7-8.5)	10.52
95% CI	6.15-7.40	6.71-7.34	7.21-8.03	5.94-9.73	$P < .05$
VDS					
Mean \pm SD	1.60 \pm 0.97	0.91 \pm 0.98	0.95 \pm 0.97	2.50 \pm 0.71	
Median (range)	1.5 (0-3)	1 (0-3)	1 (0-2)	2.5 (2-3)	7.29
95% CI	0.91-2.29	0.56-1.26	0.51-1.40	-3.85-8.85	NS

CI, Confidence interval; VSS, Venous Severity Score; VCSS, Venous Clinical Severity Score; VSDS, Venous Segmental Disease Score; VDS, Venous Disability Score; NS, not significant.

Table III. Distribution of the Venous Disability Score (VDS) according to clinical class and total number

VDS	C3	C4	C5	C6	Total
0	1 (9.1)	16 (44.4)	10 (47.6)	0 (0)	27 (38.0)
1	4 (36.4)	5 (13.9)	2 (9.5)	0 (0)	11 (15.5)
2	3 (27.3)	11 (30.6)	9 (42.9)	1 (33.3)	24 (33.8)
3	2 (18.2)	1 (2.8%)	0 (0)	1 (33.3)	4 (5.6)
U	1 (9.1)	3 (8.3)	0 (0)	1 (33.3)	5 (7)

Data are n (%).

U, Patient unable to carry out usual activities but not wearing compression stockings and not submitting to limb elevation.

Table IV. Activity according to pain magnitude

Pain scoring	VDS 0-2	VDS 3, U	P value (Fisher test)
0-1	95% (57/60)	5% (3/60)	<.0001
2-3	45.5% (5/11)	54.5% (6/11)	

VDS, Venous Disability Score; U, patient unable to carry out usual activities but not wearing compression stockings and not submitting to limb elevation.

pression provides reproducible results for the measurement of reflux.⁷ We chose to perform distal manual compression with sudden release, which is easier to perform in daily practice insofar as this method accurately induces a reflux compared with pneumatic compression.^{6,11} Apart from the femoral junction, which we believe can be investigated more readily with the patient in the supine position by means of a Valsalva maneuver,⁶ we investigated patients in both the standing and sitting positions.

The rate of secondary etiology was very high (85%). This rate might be related to the fact that patients were investigated only by DS without complementary venography.

We identified 27 cases (27/71; 38%) of reflux in the DFV. According to Labropoulos et al,⁷ this vein is rarely the site of reflux. It is possible that the incidence of reflux in the DFV may be higher if such a reflux is sought by compressing the termination of the femoral vein.

The criteria necessary to estimate the obstructive component of PTS vary in the literature. Haenen et al⁶ considered that a vein is noncompressible when it is not totally compressed under gentle pressure of the duplex probe. Insofar as we used the Rutherford venous severity scoring,⁴ we used the criteria defining obstruction as proposed in the same article. Certainly, endoluminal ultrasonography¹² would make it possible to better assess the obstructive component of a PTS, but it is an invasive method used mainly to assess the iliac veins.

We included in this study three lower limbs with an obstructive component (femoral or popliteal) that did not meet the above-mentioned criteria. It is worth noting that during the same period, we identified 14 lower limbs in patients presenting with a significant obstructive venous syndrome.

All patients with a primary etiology had a combination of superficial venous insufficiency previously treated or present (AS₂, AS_{2,3}, AS₄, or their combination). This concept is in agreement with published data.¹³ Superficial venous insufficiency was less frequently observed in patients with PTS ($P < .05$).

We observed an increase in the incidence of incompetent perforator veins based on clinical class, but this did not reach significance, probably as the result of inadequate statistical power. This increased incidence is in agreement with published data.¹⁴⁻¹⁸

The CEAP classification is widely used internationally by venous disease specialists. It provides a precise description of patients presenting with CVD, but it does not quantify the severity of this disorder. Various rating scales to quantify it have been developed, but none of them has truly been validated in daily phlebologic practice. We will mention the scale used by Prandoni et al,¹⁹ in which five symptoms (heaviness, pain, cramps, pruritus, and paresthesia) and six signs (edema, induration, hyperpigmentation, new venous ectasia, redness, and pain during calf compression) are scored from 0 to 3.

The VSS,⁴ by differentiating the clinical features, the anatomical and pathophysiologic components, and the effect of CVD on the patient's activity, opens up new perspectives. However, these tools are little used in everyday clinical practice, and only the VCSS has been validated.²⁰ Originally designed to evaluate the efficacy of treatments of CVD, they have been used to determine the severity of CVD or to determine the presence of the disease.²¹ In this study, we simultaneously evaluated the three scores. In our opinion, they represent a true advance in the evaluation of a group of patients with CVI, but some points need to be clarified so that they can be fully usable in daily phlebologic practice.

In VCSS, isolated insufficiency of the small saphenous vein has not been identified as a separate entity. We gave a score of 2 to this case. In the same way, we scored edema that develops in the afternoon and remains limited to the ankle as 2 points and edema that exists from the morning as 3 points, even if it does not require a change in the patient's usual activity or elevation of the affected limb. Widespread pigmentation above the lower third of the leg and of long duration was scored 3.

Compression therapy requires a few comments. A patient can wear elastic compression stockings daily but may not elevate his or her legs (we scored this situation as 3). No mention was made of the force of compression. When a patient wears compression stockings that are not suited to his or her clinical condition, scoring is difficult.

For VSDS (reflux), the number of incompetent perforator veins was not differentiated (one or more). We assigned a score of 0.5 points and 1 point to the existence of one or more incompetent perforator veins in the thigh and the leg, respectively.

In the calf, the VSDS attributes two points when multiple veins are incompetent and one point when only the posterior tibial veins are incompetent. When only the fibular veins are incompetent, scoring is difficult. We assigned two points to this situation. We also noted that isolated incompetence of leg muscular calf veins was not taken in account.

Scoring of incompetence of the great saphenous vein can give rise to debate. To assign a full score, all valves in the segment have to be incompetent. It is worth noting that this situation is not the most frequent one.^{22,23}

Calculation of the VDS also calls for several comments. Usual activities, defined as patients' activities before the onset of disability from venous disease, are sometimes

difficult to assess in patients in whom venous disease has been present for a long duration. Bilateral involvement (16.4% of patients in our series) logically interferes with this score. We suggest that the VDS score for each patient should be based on the worst limb in forthcoming studies. For limb elevation, practice and compliance are difficult to estimate. A patient may not be able to carry out usual activities but may not wear compression stockings (or may use an unsuitable type of compression) or elevate his or her lower limbs. No score then can be assigned.

In our series, all of the patients evaluated presented with CVI. A significant increase in the VCSS paralleled the CEAP clinical class. This notion has been highlighted in studies by Meissner et al²⁰ and Ricci et al²¹ in less selective groups of patients. We have confirmed this in a series of patients with a CVI and with grade 4 deep vein reflux. Besides, we found a significant increase in the VSDS that paralleled the clinical class.

Pain scoring was more severe in the C3 and C6 classes compared with C4 and C5; VDS was also more severe, although not significantly, in the C3 and C6 classes compared with C4 and C5: this demonstrates that the C class is not a good tool to measure the severity of disease and disability. VSS seems more suitable for this purpose.

Patients with edema had more limitation of activities and a higher pain score than patients classified as C4 and C5. Because patients were enrolled before 2004, the updated C4 group² was not used. The C4 updated group, subdivided into C4a and b, might have shown a significant difference between these two subgroups. Healed ulcer (C5) was not responsible for major pain and activity reduction. All of the patients in this group had normal activity without ($n = 12$) or with ($n = 9$) elastic compression. Although the sample size of the C6 group was small, all of the patients in this group presented with pain and major impairment in their activity.

It is difficult to assess the effect of wearing elastic compression stockings on pain severity and VDS. Nevertheless, among the 62 patients with normal activity (VDS 0-2), two thirds (42/62; 67.7%) wore elastic compression stockings. Pain was absent or occasional in 61 (85.9%) of 71, and 46 of 71 wore elastic compression stockings. Compression did not influence pain severity and VDS; this is not in disagreement, because patients with severe pain and VDS were in most cases compliant with compression since the onset of signs of CVI. Only three patients (4.2%) presenting with severe pain did not wear elastic compression stockings.

The part played by incompetent perforator veins in the pathophysiology of CVI remains controversial. In our studied population, we observed that the existence of at least one incompetent perforator vein resulted in a significant increase in VCSS.

In the North American Subfascial Endoscopic Perforator Surgery (NASEPS),²⁴ the patient's clinical condition was improved after ligation of the perforator veins, but this condition was not assessed by VSS. If the criterion evalu-

ated was recurrence of venous ulcer, then the recurrence rate was much higher when PTS had been identified.

The existence of an incompetent saphenous vein resulted only in nonsignificant elevation of the VCSS. The existence of reflux in the DFV produced a significant increase in the VCSS. This confirmed the dominance of deep venous reflux over superficial venous reflux in the pathophysiology of clinical disorders observed in patients presenting concomitantly with extended deep axial and superficial venous reflux.^{25,26}

Some studies have evaluated VSS in daily phlebologic practice. Meissner et al²⁰ evaluated the validity and reliability of the VCSS. This score was measured in 64 patients (128 lower limbs) consulting for CVD; 47.2% (60/128) were CVI patients. The mean score was highly correlated with CEAP clinical class. Scores in 68 limbs evaluated twice by the same observer differed by a mean of only 0.8 ($P = .15$), with a reliability coefficient of 0.6. Three observers (a vascular nurse and two vascular surgeons) scored the patients the same day in the assessment of intraobserver variability. Mean scores of 8.0 ± 5.1 , 7.2 ± 5.1 , and 8.0 ± 5.4 were obtained in 63 limbs evaluated by all 3 investigators ($P = .02$). Only the component scores for pain, inflammation, and pigmentation showed significant ($P < .05$) variability. In agreement with Meissner et al, we suggest that the VCSS could benefit from minor clarifications.

Ricci et al²¹ evaluated the relationship between venous ultrasound scan and VCSS. VCSS was measured in 210 patients (420 lower limbs) in a kindred population with protein C deficiency. Few lower limbs were affected by CVI, because VCSS was 0 in 283 limbs and the highest total score in any limb was 8. A good correlation was seen with the VCSS and venous ultrasound scan abnormalities. In this study, the VCSS was not used to quantify the severity of the CVD. This study found that it was a useful screening tool to separate patients with and without CVD. Kakkos et al²⁷ conducted an observational study to validate the VCSS, VSDS, and VDS and to evaluate the VCSS, VDS, and CEAP clinical class and score in quantifying the outcome of varicose vein surgery. Forty-five patients who underwent superficial venous surgery for primary etiology were prospectively included. CEAP clinical score, VCSS, and VDS demonstrated a linear association with CEAP clinical class ($P < .001$, $P = .001$, and $P = .002$, respectively). VSDS demonstrated a weak correlation with VCSS ($R = 0.29$; $P = .048$) and VDS ($R = 0.31$; $P = .03$).

An observational survey²⁸ was conducted on a representative sample of French angiologists. The objective was to test and evaluate the interest in and usefulness of the daily practice of VCSS, VSDS, and VDS for CVD. The scores were tested on 1900 patients by 398 angiologists, who completed an opinion questionnaire. Because they were assessed as relevant by most, their use in daily practice for C4, C5, and C6 patients was considered by a minority of the angiologists: 42.0% for the VCSS, 32.9% for the VSDS, and 38.7% for the VDS. These percentages were lower for C1, C2, and C3 patients. Their opinion was that these scores seem difficult to use in daily practice, and in partic-

ular they seem applicable to evaluate therapeutic efficacy in CVD.

In conclusion, the CEAP classification, internationally recognized and widely used, accurately describes patients who present with CVD. Its aim is not to quantify the latter, even though the CEAP clinical class has sometimes been used for this purpose. This function applies to the VSS. In a group of patients with CVI and cascading deep venous reflux involving the femoral, popliteal, and crural veins to the ankle, ie, the most severe anatomic/hemodynamic form of deep vein reflux,^{25,26} we demonstrated that a significant increase in the VCSS and in the VSDS paralleled the CEAP clinical class but that VDS was higher in classes C3 and C6, without reaching significance, probably because of the small size of the samples. Determination of VSS proved easy in the studied population provided that a precise venous DS protocol for examination was followed and that a few clarifications were made. In the future, this should result in a much wider use of VSS with the aim of evaluating the efficacy of treatments of CVD and also determining the severity of the disease, at least in the most serious forms, ie, CVI.

AUTHOR CONTRIBUTIONS

Conception and design: JLG, MRP

Analysis and interpretation: JLG, MRP, FAA

Data collection: JLG

Writing the article: JLG, MRP

Critical revision of the article: JLG, MRP, FAA

Final approval of the article: JLG, MRP, FAA

Statistical analysis: FAA

Overall responsibility: JLG, MRP

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Short-term and mid-term outcome of isolated symptomatic muscular calf vein thrombosis

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Background: Although muscular calf vein thrombosis (MCVT) is commonly seen in everyday practice, no treatment guidelines are available. This study evaluated short-term and mid-term outcome of isolated symptomatic MCVT.

Method: We included prospectively and consecutively all patients referred to an outpatient clinic with isolated MCVT. Clinical signs were pain or edema, or both, of the calf. Diagnosis was established with duplex ultrasound (DUS) examination. Not completely occlusive and asymptomatic MCVTs were excluded. Patients were followed up clinically and with DUS at 1, 3, and 9 months, and up to 36 months. Anticoagulant therapy at curative dosage associated with compression was prescribed for 1 month and was extended for 2 additional months in case of incomplete recanalization at 1 month or if risk factors for venous thromboembolism (VTE) were present.

Results: Included were 128 patients (78 women, 50 men) presenting with 131 MCVTs. Their mean age was 57.02 ± 15.36 years (range, 20 to 87 years). Thrombus was present in the soleal veins (SoV) in 73 patients (55.7%) and in the medial gastrocnemius veins (MGV) in 58 (44.3%). Initial symptoms were isolated pain in the calf in 90 patients, isolated edema of the calf in six, and pain plus edema in 32. Anticoagulant therapy was prescribed in 53 patients (41.4%) for 1 month, in 59 (46.1%) for 3 months, and in 13 (10.2%) for ≥ 6 months. At baseline, nine pulmonary embolisms (7%), complicated with MCVT, were observed in six MGV patients (10.3%) and three SoV patients (4.1%; $P = .18$). Two nonfatal hemorrhagic events occurred. Three patients died during the follow-up after anticoagulant therapy had been discontinued. Recanalization of MCVT was considered complete at 1, 3, and 9 months in 54.8%, 84.7%, and 96% of cases, respectively, with no significant difference between the MGV and the SoV groups. Twenty-nine VTE symptomatic recurrences (PE, $n = 6$; DVT including MCVT, $n = 23$) were observed in 24 patients (18.8%), with similar figures in both thrombosis groups: none at 3 months, 11 between 3 and 9 months and 18 between 9 and 36 months. No extension of the MCVT or a recurrence of VTE was observed in patients treated with anticoagulant therapy. Twelve cases of superficial thrombophlebitis occurred during the follow-up period.

Conclusion: This study confirms the place of MCVT in VTE disorders. Pulmonary embolism at the MCVT initial diagnosis was not rare, and mid-term follow-up (mean, 26.7 months) revealed that 18.8% of patients had at least one VTE recurrence. The treatment of acute MCVT needs to be standardized because no guidelines currently exist. (*J Vasc Surg* 2007;46:513-9.)

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Duplex ultrasound (DUS) examination has evolved to become the imaging method of choice for investigating calf vein thrombosis. Most vascular laboratories in France routinely assess the calf deep veins in patients suspected of having an acute deep vein thrombosis (DVT) of the lower limbs. Complications, including propagation of thrombus to proximal veins, pulmonary embolism (PE), and post-thrombotic abnormalities have been reported, albeit sometimes with conflicting data, and the precise prevalence of these complications remains unclear.¹⁻¹²

In the calf, we distinguished^{13,14} the crural veins, including the posterior tibial veins, the anterior tibial veins, the peroneal veins, all paired, from the muscular or sural

veins, including the soleal veins (SoV), the medial gastrocnemius veins (MGV) and the lateral gastrocnemius veins (LGV). Although muscular calf vein thrombosis (MCVT) has long been recognized¹⁵⁻¹⁸ and several publications^{5,9,10,17,19-21} have underlined its frequency, few studies have been published on this topic and no treatment guidelines are available. Management of this disease remains controversial, although MCVT is commonly seen in everyday practice. The objective of this study was to evaluate the short-term and mid-term outcome of isolated symptomatic acute MCVT. The crural veins were not a part of the study.

METHODS

This study was conducted between July 1997 and June 2004. Patients were referred from local general practitioners to our outpatient Vascular Medicine Clinic for suspicion of DVT in the lower limbs. We included prospectively and consecutively all patients presenting with isolated MCVT. Clinical signs were pain or edema, or both, of the calf.

Patients with nonmuscular DVT associated with MCVT were not included. We excluded patients with not completely occlusive and asymptomatic MCVT to be sure

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to include only patients with acute vein thrombosis, patients with a contraindication to anticoagulant therapy, and patients who could not be followed up to 9 months.

Diagnosis was established by DUS imaging. We used the Vivid 3 scanner (Vingmed; GE Healthcare Technologies Waukesha, Wis) and a linear probe (frequency, 7.5 MHz; range, 5 to 10 MHz) to investigate the lower limbs and a phased array probe (frequency, 2.5 MHz; range, 2.25 to 5 MHz) to investigate the abdomen and pelvis. All the deep veins in both lower extremities, including the calf muscular veins, were examined from the vena cava to the calf veins.

The following protocol was used to assess calf vein thrombosis. The patient was seated at the edge of the examining table with his or her legs hanging, resting on a stool. The calf veins were imaged individually in both longitudinal and transverse planes from the ankle to the knee. The gastrocnemius veins were first identified near their confluence with the popliteal vein and were followed within the muscle belly down into the calf. MGVT and LGVT were both assessed. The SoV were found first just below the sural triangle and were followed in both directions.¹⁰

The criteria used to confirm the diagnosis of MCVT was incompressibility of the vein with probe pressure that induced pain combined with the absence of venous flow, spontaneous or with distal compression. Most often, an intraluminal thrombus was visualized.

The clinical examination and the history identified clinical signs and symptoms suggestive of DVT, the existence of a triggering factor (surgery, trauma, lengthy air or car travel), a symptom suggestive of PE, and also the patient's personal and family history of previous venous thromboembolism (VTE). In case of a symptom of PE, a ventilation-perfusion lung scan or a helical computed tomography scan was performed.

Screening for risk factors in patients with MCVT involved the routine investigations used in our Vascular Medicine Clinic in patients presenting with any type of DVT. The risk factors assessed included neoplasm, thrombophilia, iliac, femoral, or popliteal deep venous abnormality, hormone replacement therapy, and obesity.

Ultrasound imaging of the abdomen and pelvis, a chest radiograph, and investigation of the prostate to detect a possible neoplasm were performed in men aged >50 years old, with more specific investigations depending on clinical findings to guide the choice of tests.

Screening for thrombophilia was performed in subjects aged <40 years old or in patients with a history of DVT. It included measurement of protein C, protein S, antithrombin, antiphospholipid (APL) antibodies, and screening for a mutation in coagulation factor V (presence of factor V Leiden) and factor II G20210A.

Abnormalities in the iliac, femoral, and popliteal veins indicative of post-thrombotic syndrome (PTS) or primary deep vein insufficiency (PDVI) were sought and identified with DUS.²² PTS was differentiated from PDVI by the demonstration of morphologic abnormalities in deep vein trunks by venous DUS investigation, that showed evidence

of post-thrombotic venous wall or valvular thickening. The criterion used for qualifying obstruction was the one described by Rutherford et al²³: total vein occlusion at some point in the segment or >50% narrowing of at least half of the segment. The criterion for reflux was the identification of a deep venous reflux involving the popliteal vein of >1 second.^{22,24,25} In some patients, venography or DUS previously performed at the time of an acute episode provided evidence of an initial DVT.

Women were asked about contraceptive method or hormone replacement therapy of menopause, and body mass index ($\text{BMI} \geq 28 \text{ kg/m}^2$) was used to assess obesity.

Anticoagulant therapy at curative dosage and elastic compression stockings exerting at least 15 mm Hg ankle pressure were prescribed to all patients for 1 month. We used fluindione to obtain an international normalized ratio (INR) of between 2 and 3. Walking was advised. Anticoagulant therapy was extended 2 additional months when DUS at 1 month showed incomplete recanalization of the MCVT or if risk factors for VTE were present, including a history of recurrent venous thrombosis, PTS, thrombophilia, and malignancy.

Patients were followed up both clinically and with DUS at 1, 3, and 9 months. The objectives of these examinations were:

1. to identify possible complications of anticoagulant therapy;
2. to seek clinical signs or symptoms, or both, of extension of the initial thrombosis or a recurrence of VTE defined as any new symptomatic event of PE, DVT, or MCVT involving the vein initially thrombosed after its recanalization or involving another muscular calf vein, and confirmed by DUS or radiography; and
3. to assess recanalization of the MCVT.

Recanalization was considered complete when no abnormality other than venous wall or valvular thickening was observed in the DUS examination. In other cases, it was recorded as incomplete. The risk factors for VTE were collected and analyzed. After month 9, patients were followed up clinically and with DUS up to month 36 to detect a recurrence of VTE.

Statistics analysis. Data analysis was performed using the SAS 8.2 software (SAS Institute, Cary, NC). Quantitative variables were expressed as means \pm standard deviation and were compared with the Student *t* test or a nonparametric test such as the Mann-Whitney Wilcoxon test. The proportions of qualitative variables were tested with nonparametric tests (Fisher exact test), and $P < .05$ was considered significant.

RESULTS

During the study period, 131 isolated MCVTs were identified in 128 symptomatic patients, consisting of 78 women (60.9%) and 50 men (39.1%). The average age was 57.02 ± 15.36 years (median, 57; range, 20 to 87 years). Seventy-three thromboses (55.7%) involved the SoV, and 58 (44.3%) involved the MGVT. Three patients presented with both SoV and MGVT thrombosis. We did not observe

Table I. Distribution of patients according to the number of thrombotic veins*

Veins (n)	Patients, n (%)	
	MGVT	SVT
1	10 (17.24)	41 (56.16)
2	25 (43.1)	23 (31.51)
3	7 (12.07)	7 (9.59)
4	15 (25.86)	2 (2.74)
5	0	0
6	1 (1.72)	0
Total	58 (100)	73 (100.00)

MGVT, Medial gastrocnemius vein thrombosis; SoVT, soleal vein thrombosis.

*Every gastrocnemius or soleal vein identified individually by duplex ultrasound imaging was counted separately.

any isolated LGV thrombosis. Thrombosis was located in the right calf in 69 patients (53.9%) and in the left calf in 59 (P = .47). In 30 (23.4%) of 128 patients, the MCVT was combined with superficial thrombophlebitis (ST) in the calf. Initial symptoms were isolated pain in the calf in 90 patients, isolated edema of the calf only in six patients, and pain combined with edema in 32 patients. Sixty patients (46.9%) reported that they had had a previous DVT, confirmed or not.

A triggering factor was identified in 85 patients (66.4%). The most common factors were previous surgery in 23, trauma in 16, and a long car trip in 7 or lengthy air travel in 6.

The risk factors for VTE were cancer in 7 patients (5.5%), in all cases known at the time of the MCVT diagnosis; thrombophilia in 19 (14.8%), including heterozygous factor V Leiden in 16, protein S deficiencies in 2, protein C deficiency in 1, and APL antibodies in 1; both heterozygous factor V Leiden and protein S deficiency in 1; obesity in 29 (22.7%); and 20 (25.6%) women were receiving hormone replacement therapy (contraceptive in 13; hormonal therapy of menopause in 7). No additional cases of cancer were discovered during the follow-up. An abnormality of the deep venous system (iliac, femoral, or popliteal vein) was identified in 12 patients (9.4%): 10 with PTS, including reflux in 7, obstruction in 2, and reflux and obstruction in 1; and 2 with PDVI.

The distribution of patients according to number of thrombotic veins is listed in Table I, and the distribution of patients according to the diameter of the venous lumen filled by the clot is summarized in Table II.

In the MGVT group, the thrombosis involved one to six veins, but 82.8% of patients presented several veins involved by the thrombosis. The diameter of the thrombosis measured in the transverse plane with DUS varied from 5 to 17 mm, and 58.6% presented a thrombosis in which the diameter measured ≥ 8 mm. The thrombosis was confined to the intramuscular segment of the vein in 35 patients (60.3%), an extension into the extramuscular gastrocnemius vein was observed in 23 (39.7%), and extension of from 1 to 3 cm into the popliteal vein but without

Table II. Distribution of patients according to the diameter of the vein lumen filled by the clot

Diameter (mm)	Patients, n (%)	
	MGVT	SVT
5	4 (6.90)	3 (4.11)
6	8 (13.79)	19 (26.03)
7	12 (20.69)	13 (17.81)
8	12 (20.69)	13 (17.81)
9	7 (12.07)	12 (16.44)
10	6 (10.34)	5 (6.85)
11	6 (10.34)	2 (2.74)
12	1 (1.72)	3 (4.11)
13	0	3 (4.11)
14	0	3 (4.11)
15	1 (1.72)	0
17	1 (1.72)	0
Total	58 (100)	73 (100)

MGVT, Medial gastrocnemius vein thrombosis; SoVT, soleal vein thrombosis.

complete occlusion of this vein was observed in nine (15.5%).

In the SoV thrombosis group, the thrombosis involved one to four veins, but 56% presented with a thrombosis limited to a single vein. The diameter varied from 5 to 14 mm, and 56.2% of patients presented with a thrombosis with a diameter of ≥ 8 mm.

Anticoagulation therapy at a curative dosage was prescribed for 1 month in 53 patients (41.4%), for 3 months in 59 (46.1%), and for ≥ 6 months in 13 (10.2%) because they presented with a PE or major risk factors for VTE. In three patients, the duration of AT was not known.

Nine PEs (7%), clinically suspected and confirmed with radiographs, which were complicated with MCVT, were observed in the baseline examination: six (10.3%) of 58 in the MGVT group and three (4.1%) of 73 in the SoVT group. The difference was not significant (P = .18). No patients with PE had PTS or PDVI. We did not observe a PE in the three patients presenting with both SoV and MGVT thrombosis. None of those patients died or presented severe clinical signs or major abnormalities evidenced by laboratory methods.

PE was diagnosed with ventilation-perfusion lung scan in eight patients and with helical computed tomography imaging in one. The symptoms suggestive of PE were chest pain in five patients and dyspnea in four. In addition, one patient presented with hemoptysis. Regarding the features of the MCVTs, eight of nine patients presented with two to four veins involved by the thrombosis. In all patients, the diameter of the venous thrombosis was > 8 mm. In the subgroup of the six patients with MGVT thrombosis and PE, the thrombus was confined to the intramuscular segment of the vein in two patients, extended into the extramuscular gastrocnemius vein in two, and into the popliteal vein in two.

Follow-up of at least 1 month was achieved in 125 (97.7%) patients (127 MCVTs), at least 3 months in 120

Table III. Recanalization rate

Time period	MGVT, % (n)	SVT, % (n)	P*
1 month			0.62
0	52.1 (25)	56.7 (38)	
1	47.9 (23)	43.3 (29)	
3 months			0.97
0	84.9 (45)	84.6 (55)	
1	15.1 (8)	15.4 (10)	
9 months			1.00
0	95.8 (46)	96.1 (49)	
1	4.2 (2)	3.9 (2)	

MGVT, Medial gastrocnemius vein thrombosis; SoVT, soleal vein thrombosis; 0, complete recanalization (ie, no postthrombotic anatomic abnormality except for venous wall or valvular thickening); 1, incomplete recanalization. *Fisher exact test.

(93.8%) patients (122 MCVTs), and at least 9 months in 110 (85.9%) patients (111 MCVTs). Beyond 9 months, 94 patients (73.4%) were followed up with a mean of 26.7 months. There was no difference in the distribution of the followed up patients in the SoV thrombosis and MGVT thrombosis groups at the different times (P was .12, .66, .20 and .35 at 1, 3, 9, and beyond 9 months, respectively).

Three patients with SoV thrombosis died, but at the time of death, anticoagulation therapy had been discontinued. The cause of death was myocardial infarction in one patient, aortic aneurysm rupture in another, and cachexia in a patient with metastatic disease.

Two (1.56%) of 128 patients presented with a serious but nonfatal hemorrhagic event: a patient with gastric cancer required a blood transfusion for digestive bleeding, and a hematoma in the upper limb occurred after venipuncture in a patient whose INR was 4.8 (the fluindione dosage was reduced and the hematoma did not require any specific treatment).

Recanalization (Table III) was complete at 1, 3, and 9 months in 54.8%, 84.7%, and 96%, respectively, in all MCVTs, without a significant difference between the SoV thrombosis and MGVT thrombosis groups at the different times of follow-up. Table III shows that the numbers of DUS performed at the three follow-up visits were lower than the numbers of followed up patients because some patients in whom prolonged anticoagulation therapy had been prescribed were not assessed by DUS at every visit.

Twenty-nine symptomatic VTE recurrent events (Table IV) occurred in 24 patients (18.8%): none at 3 months, 11 between 3 and 9 months, and 18 between 9 and 36 months. One patient presented with three VTE recurrent events, and three patients with two events. There was no significant difference in the SoV thrombosis and MGVT thrombosis groups comparing the numbers of patients with VTE recurrences or the numbers of VTE events. Two (8.3%) of 24 patients had PTS with reflux. We did not observe extension of the MCVT or VTE recurrence in patients treated with anticoagulant therapy. Six nonfatal PEs were observed, four (6.9%) of 58 in the

Table IV. Venous thromboembolism recurrence events*

Initial Thrombosis	9 months	9-36 months	No. total (%)
MGVT	MCVT (n = 2) Crural (n = 1) PE (n = 1)	MCVT (n = 5) Crural (n = 1) Proximal (n = 1) PE (n = 3)	14/58 (24.1%)
SoVT	MCVT (n = 5) Crural (n = 1) PE (n = 1)	MCVT (n = 7) PE (n = 1)	15/73 (20.5%)

MGVT, Medial gastrocnemius vein thrombosis; SoVT, soleal vein thrombosis; MCVT, muscular calf vein thrombosis; PE, pulmonary embolism.

*No thrombosis occurred at 1 or 3 months.

MGV thrombosis group and two (2.7%) of 73 in the SoV thrombosis group ($P = .40$); as were 23 DVTs, including 19 MCVTs. Ten MCVTs (MGV, 5; SoV, 5) were observed in the muscle in which the initial MCVT occurred after its recanalization. In addition, 12 STs were identified during the follow-up.

DISCUSSION

DUS is the imaging method of choice for the diagnosis of DVT in symptomatic patients, including calf vein thrombosis. DUS has been reported to have a diagnostic sensitivity of 94% to 100%, a specificity of 91% to 100%, a positive-predictive value of 80%, and a negative-predictive value of 94% for detection of crural vein thrombosis.^{4,9,12,26,27}

Compared with contrast venography, DUS has an overall sensitivity, specificity, and accuracy of >87% for MCVT diagnosis.^{10,12} Although MCVT is commonly seen in everyday practice, few publications address this subject and no treatment guidelines are available. We were not able to determine the precise prevalence of isolated MCVT diagnosed in our Vascular Medicine Clinic during the study period because the overall number of DVTs was not determined during the MCVT inclusion period. This prevalence of all lower limb DVTs varies in publications^{10,19-21,28} between 12.5% and 25%. Labropoulos et al¹⁰ detected 742 DVTs (14%) in 5250 patients referred to the vascular laboratory for clinical suspicion of DVT. An isolated calf DVT was detected in 282 limbs (33.8%) in 251. An isolated MCVT was found in 113 limbs (SoV, n = 57; MGVT, n = 48; SoV plus VGM, n = 8), yielding a prevalence of 15% of all DVTs.

We observed a similar distribution between MGVT and SoV thrombosis in agreement with some publications.^{10,20} In other series,^{12,29} SoV thrombosis was more common. In our series we observed that in 30 patients (23.4%), MCVT was combined with a ST. This association is not surprising: in a previous article³⁰ we had identified that ST was frequently combined with DVT and particularly with MCVT.

In our series, pain was the most common symptom suggesting DVT in patients presenting with MCVT. Pain was often severe and disabling especially with MGVT thrombosis. Isolated edema was rare, observed in 4.7% (6/128).

The natural history of MCVT is poorly known. MacDonald et al¹² included 219 isolated MCVTs in 185

patients (SoV, 170; MGv, 42; SoV plus MGv, 7). Their aim was to establish the incidence of propagation of untreated isolated MCVT into the deep veins of the calf and thigh. Each patient was evaluated by DUS on the first day of presentation, with a repeat examination of the involved leg 5, 9, 14, 30, and 90 days later. At 3 months, 84 (38.4%) of 219 thromboses were excluded because the patients were lost to follow-up or for various other reasons (some of them had had been treated with anticoagulant therapy). During their study, 22 patients died, although none of these deaths seemed related to thromboembolic events. Postmortem examinations were not done, so the authors reported that death from thromboembolism could not definitively be ruled out. Within their 3-month follow-up, 22 (16.3%) of the 135 limbs with isolated MCVT had thrombus extension to the level of adjacent tibial or peroneal veins or higher, 20 (91%) of 22 of which occurred within 2 weeks of the initial DUS. Four (3%) of 135 extensions to the popliteal vein were identified.

In this series, recanalization of the MCVT seemed to be less satisfactory than in our series. Indeed the MacDonald et al study¹² reported a complete recanalization at 1 and 3 months in 20.7% and 44.6% of MCVT, respectively, vs 54.8% and 84.7% in our series. One hypothesis to explain this difference is that the patients in our series were treated with anticoagulant therapy. However, we cannot exclude that the assessment criteria were different in the two studies given that we considered veins with simple wall thickening as completely recanalized. We did not assess the presence or absence of post-thrombotic reflux because patients with a history of DVT were not excluded.

No treatment guidelines currently exist. Schwarz et al³¹ conducted a prospective, nonrandomized study including 84 MCVTs. He investigated the outcome in two cohorts of consecutive patients. The first received compression therapy and heparin for 10 days at therapeutic doses, and the second received compression therapy alone. In the 52 patients who received heparin at therapeutic dosage, no progression to DVT occurred. A statistically significant higher rate of progression into the deep calf veins (25%) was shown in the 32 patients without anticoagulant therapy. The studies by MacDonald et al¹² and Schwarz et al³¹ showed that the rate of extension of the thrombosis was high in patients not treated with anticoagulant therapy, and suggested that in most of the patients, the extension occurred early after the diagnosis.

The Seventh American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy³² recommended that, "patients with acute DVT require long-term anticoagulant treatment (...). This observation applies to patients with proximal vein thrombosis and also to patients with thrombosis confined to the deep veins of the calf." However MCVT was not specifically referenced in this recommendation.

In our series, we did not observe extension or VTE recurrence during the anticoagulant therapy period.

Even though the clinical significance of extension of the thrombus into the deep veins is not clearly established, our

results, reinforced by the results of MacDonald¹² and Schwarz et al,³¹ indicate that MCVT should be treated with anticoagulant therapy. The issue is to determine the minimum duration of anticoagulant therapy to prevent the extension of the venous thrombosis with no major risk of bleeding. This risk depends on the duration of anticoagulant therapy. With an INR target range of between 2 and 3, the yearly risk of major bleeding is estimated at 3%.³³ For this reason, in our opinion, long-term anticoagulant therapy as recommended in Chest³² seems excessive. In our series we observed only two nonfatal bleeding events; both occurred in frail patients: one had metastatic disease and the other was 79 years old. We suggest that anticoagulant therapy at a curative dosage, associated with compression therapy and walking, is necessary to prevent an extension of the thrombus into the deep veins, for at least 15 to 30 days and probably longer when a risk factor for VTE is present. Management without anticoagulant therapy could be used in patients with a major risk for bleeding, but this would require monitoring with repeated DUS examinations.

The association between MCVT and PE is controversial. Three publications have reported PE in patients with isolated MCVT with a prevalence of 15%, 37.5%, and 50% respectively.^{20,21,29}

- Guias et al²⁰ conducted a retrospective study on 848 symptomatic DVTs of the lower limbs; 106 patients (12.5%) presented with isolated MCVT (MGV, 48; SoV, 50; MGV plus SoV, 8). In 106 patients with symptoms suggestive of PE, 16 (15%) were diagnosed with PE with radiographs. Although it was retrospective, this study confirmed the high prevalence of isolated MCVT in patients with calf vein thrombosis and showed a high rate of PE associated with isolated MCVT.
- Ohgi et al²⁹ analyzed a series of 33 distal DVTs in 28 patients. Fourteen patients presented with isolated SoV thrombosis and two with isolated MGv thrombosis. Six (37.5%) of 16 symptomatic PEs (in all isolated MCVTs) were diagnosed by lung perfusion scanning or pulmonary angiography. All six patients had isolated SoV thrombosis.
- Hollerweger et al²¹ identified 45 patients presenting with isolated MCVT in a series of 179 DVTs of the lower limbs. PE was diagnosed in 50% of the MCVT patients, but the inclusion criteria used for investigating PEs were not clearly defined. A limitation of these two studies is the small number of patients with MCVT.

In our prospective series we have identified 7% of PEs, all of which were nonfatal and with no clinical or hemodynamic signs of seriousness. In designing this study we discussed whether to include patients with MCVT complicated by symptomatic PE at the initial examination. It is indeed impossible to identify the precise location of the venous thrombosis source of the PE. At the time of clot migration, was the venous thrombosis confined to a muscular vein, or was extension of the venous thrombosis into

the deep venous system present? Probably both are possible; the migration of a thrombus from the muscle can cause a distal subsegmental PE. We decided to include patients with PE in our study insofar as the inclusion criterion was the identification of an isolated MCVT by DUS in suspected patients for DVT of the lower limbs.

In our series, all patients with PE, except one, presented with extended MCVTs (several veins involved by the thrombosis), and all had a large venous thrombosis (diameter >8 mm). These data confirm the result of Ohgi et al²⁹ results, because in that series, all patients with PE presented a large SoV thrombosis measuring >7 mm.

It is difficult to estimate whether PE is more frequently associated with MGVT thrombosis or with SoV thrombosis. In our series, the prevalence of PE seemed higher in patients with MGVT thrombosis than in patients presenting SoV thrombosis, but the difference was not significant. Ohgi et al²⁹ identified PE only in patients with SoV thrombosis. The distribution of PEs was similar in the two groups of MCVT in Guis et al²⁰ publication.

As we have previously discussed, it is impossible to identify the precise origin of the PE. Are we entitled to speak of embolic risk of isolated MCVT? We can only note that in published reports, MCVT is associated with PE with a prevalence of 7% to 50%.

The patient profile with MCVT does not appear to be very different from the patient profile with any other DVT location. A triggering factor was identified in 66.8% of patients, the most frequent being surgery. The risk factors for VTE identified in our series were similar to those reported in other DVT publications. MCVT does not always appear as an isolated VTE event in the patient's life: 47% of patients reported that they had had a previous DVT (confirmed or not), and post-thrombotic anomalies (iliac, femoral, or popliteal vein) were identified in 8% of patients at the initial DUS examination. Furthermore, we observed a high rate of VTE recurrence (18.8%, with 6 PEs) with a mean follow-up of 26.7 months, and we cannot exclude that the real incidence of VTE recurrence was higher, because 27% of patients (34/128) were not followed up beyond 9 months. Consequently, and regarding the PE risk as well, MCVT should not be considered a minor venous thrombosis.

Schwarz et al³⁴ reported one case of recurrent MCVT due to a venous aneurysm of the SoV. We also observed a feature of aneurysm of the MGVT in two patients who presented a recurrent MGVT thrombosis. The 12 STs observed during the follow-up were not taken into account as a VTE recurrence but suggest that some additional patients had a thrombotic profile. We did not assess the risk factors for VTE recurrence because we did not perform systematic screening at the initial examination.

CONCLUSION

This study confirms that symptomatic PE is not rare (7%) at the initial diagnosis of isolated MCVT, as shown in previous publications. We did not observe any deaths related to venous thrombosis or anticoagulant therapy; a low

rate (1.5%) of nonfatal bleeding, and no extension of the venous thrombosis or VTE recurrence at 3 months but a high 18.8% rate of VTE recurrence after 3 months during the follow-up period (mean, 26.7 months). These results underline the need for clarifying the treatment of symptomatic MCVT.

We suggest that, apart from patients who present with a major risk of bleeding, symptomatic MCVT requires anticoagulant therapy at curative dosage at least for a short duration of 15 to 30 days, and probably longer when a risk factor for VTE is present, to prevent extension of the thrombus into the deep veins. Only additional prospective and randomized studies with large sample sizes can provide high-grade recommendations. In addition, the high incidence of VTE recurrence underlines the need to follow such patients as well as all patients with any type of DVT and to prescribe the usual preventive measures.

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AUTHOR CONTRIBUTIONS

Conception and design: JG
Analysis and interpretation: JG, MP
Data collection: JG
Writing the article: JG, MP
Critical revision of the article: JG, MP
Final approval of the article: JG, MP, FA
Statistical analysis: FA
Overall responsibility: JG

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INVITED COMMENTARY

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Muscular calf vein thrombosis (MCVT) is commonly seen in everyday practice, and as foam sclerotherapy gains dominance in treatment of venous disorders, this condition will become more prevalent. No treatment guidelines are available, so this study is important.

One hundred twenty-eight patients with 131 MCVTs were included in this study. Seventy-three (55.7%) had thrombosis of soleal veins, and 58 (44.3%) had thrombosis of the medial gastrocnemius veins. In our experience with foam sclerotherapy, the reverse incidence was seen.

Anticoagulation was prescribed (41.4%) for 1 month, 59 (46.1%) for 3 months, and 13 (10.2%) for 6 months or more. Nine patients (7%) had pulmonary emboli confirmed. We have had no suspected pulmonary emboli, but the incidence of MCTV in our

foam sclerotherapy experience is only 0.003%. Six (10.3%) of the patients with thrombi were in the medial gastrocnemius vein group, and three (4.1%) were in the soleal vein group.

Recanalization of MCVT was complete at 1, 3, and 9 months in 54.8%, 84.7%, and 96% of cases, respectively. Our experience is similar except that venous reopening occurred much earlier. Perhaps this was because we administered low-molecular-weight heparin immediately when the diagnosis of MCTV was made.

This study confirms the importance of MCVT in venous thromboembolic disorders, but because this is an initial large report on this condition, the results should be confirmed by additional studies. There is a definite need to standardize the treatment of acute MCVT because no guidelines exist at this time.

JOURNAL OF VASCULAR SURGERY
Volume 49, Number 2

Eklof *et al* 499

500 Eklof *et al*

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SPECIAL COMMUNICATION

From the American Venous Forum

Updated terminology of chronic venous disorders: The VEIN-TERM transatlantic interdisciplinary consensus document

Bo Eklof, MD, PhD,^a Michel Perrin, MD,^b Konstantinos T. Delis, MD, MS, PhD,^c
Robert B. Rutherford, MD,^d and Peter Gloviczki, MD,^e *Helsingborg, Sweden; Lyon, France; Marousi and
Larissa, Greece; Denver, Colo; and Rochester, Minn*

Non-uniform terminology in the world's venous literature has continued to pose a significant hindrance to the dissemination of knowledge regarding the management of chronic venous disorders. This VEIN-TERM consensus document was developed by a transatlantic interdisciplinary faculty of experts under the auspices of the American Venous Forum (AVF), the European Venous Forum (EVF), the International Union of Phlebology (IUP), the American College of Phlebology (ACP), and the International Union of Angiology (IUA). It provides recommendations for fundamental venous terminology, focusing on terms that were identified as creating interpretive problems, with the intent of promoting the use of a common scientific language in the investigation and management of chronic venous disorders. The VEIN-TERM consensus document is intended to augment previous transatlantic/international interdisciplinary efforts in standardizing venous nomenclature which are referenced in this article. (J Vasc Surg 2009;49:498-501.)

SPECIAL COMMUNICATION

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The VEIN-TERM transatlantic interdisciplinary
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Chronic venous disorders (CVD) have a documented socioeconomic impact, involving 50-85% of the western populations, and consuming 2-3% or more of community health budgets. For publications dealing with the management of CVD to have more universal value, standardized reporting practices with uniform terminology are needed.^{1,2} The CEAP classification (1995, 2004),³⁻⁵ the venous severity scoring (2000)⁶ and the nomenclature extensions and refinements of the veins of the lower limbs (2002, 2005)^{7,8} have generated a momentum in the quest for promoting consistency in medical venous reporting. Nevertheless, the increasing universal interest in the proper

management of chronic venous disorders has exposed problems caused by non-uniform use or misuse of a number of venous terms. The lack of universal agreement on the definition of many widely used clinical venous terms has perpetuated their liberal interpretation, and hindered the effective exchange of medical information and the comparison of clinical outcomes.

OBJECTIVE

To report recommendations of uniform usage of venous terms reached by consensus by a transatlantic interdisciplinary faculty of experts (Table) under the auspices of the American Venous Forum (AVF), the European Venous Forum (EVF), the International Union of Phlebology (IUP), the American College of Phlebology (ACP), and the International Union of Angiology (IUA), the goal being a common scientific language for reports on the management of CVD.

METHODS

The aims of this consensus process, along with a working protocol and an organizational framework, were first developed in Feb 2007 as part of plans for an "Arctic Fjords Conference and Workshops on CVD" to be held aboard MS Trollfjord (Oct 2-6, 2007), Hurtigruten, Norway, under the auspices of the European Venous Forum (EVF), the Societas Phlebologica Scandinavica (SPS), and the University of Tromsø, Norway. On October 5, 2007, a group composed of invited faculty attending this workshop held

From the University of Lund,^a Vascular Department, Lyon Hospital,^b Athens Medical Center, Marousi and University of Larissa,^c University of Colorado School of Medicine,^d Mayo Clinic, Rochester.^e

Competition of interest: none.

Presented at the American Venous Forum Twentieth Annual Meeting, Charleston, SC, Feb 20-23, 2008.

The following societies were a part of the terminology guideline consensus:

- The American College of Phlebology
- The American Venous Forum
- The European Venous Forum
- The International Union of Phlebology

The following societies endorsed the terminology guidelines:

- The International Union of Angiology
- The Society for Vascular Surgery

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Table. Faculty

1st VENTERM Meeting

Arctic Fjords Conference and Workshops on Chronic Venous Disorders, October 5, 2007, Hurlgruten, Norway

- | | |
|----------------------------------|--------------------------------|
| 1. Michel Perrin, MD | Vascular Surgery, France |
| 2. Bo Eklöf, MD | Vascular Surgery, Sweden |
| 3. Robert L. Kistner, MD | Vascular Surgery, USA |
| 4. Robert B. Rutherford, MD | Vascular Surgery, USA |
| 5. Hugo Partschi, MD | Dermatology/Angiology, Austria |
| 6. John T. Hobbs, MD | Phlebology, UK |
| 7. Andrew N. Nicolaides, MD | Vascular Surgery, Cyprus |
| 8. Peter Neglen, MD | Vascular Surgery, USA |
| 9. Olle Nelzén, MD | Vascular Surgery, Sweden |
| 10. Marianne Vandendriessche, MD | Phlebology, Belgium |
| 11. Jean Jerome Guex, MD | Angiology, France |
| 12. Konstantinos T. Delis, MD | Vascular Surgery, Greece |

2nd VENTERM Meeting

Twentieth Annual Meeting of the American Venous Forum, February 20-23, 2008, Charleston, SC, USA

Participants of the first meeting (except RBR, MV, JTH) in addition to:

- | | |
|---------------------------|---|
| 1. John J. Bergan, MD | Vascular Surgery, USA |
| 2. Peter Gloviczki, MD | Vascular Surgery, USA |
| 3. Nicos Labropoulos, PhD | Vascular Physiology/
Ultrasound, USA |
| 4. Mark H. Meissner, MD | Vascular Surgery, USA |
| 5. Eberhard Rabe, MD | Dermatology, Germany |
| 6. Claudio Allegra, MD | Angiology, Italy |
| 7. Steven Zimmer, MD | Phlebology/Dermatology, USA |
| 8. Joann M. Lohr, MD | Vascular Surgery, USA |
| 9. Thomas Proebstle, MD | Dermatology, Germany |

the first VEIN-TERM meeting, co-chaired by M. Perrin (M.P.) and B. Eklöf (B.E.) with K.T. Delis as secretary. A second consensus meeting, also chaired by B.E. and M.P., was held at the time of the Twentieth Annual Meeting of the American Venous Forum (AVF), February 20-23, 2008, Charleston, SC, USA, under the auspices of the AVF. Between these meetings, a consensus draft was circulated and refined. At the first meeting, a list of problematic CVD terms was identified and provisional definitions were set forth. Between meetings, a draft of these was circulated by open e-mail communications to the entire faculty for further refining comments, which were provisionally incorporated into the main draft. This process was repeated, with additional input from those invited to attend the second meeting, and three additional drafts were circulated in this manner prior to the second meeting at the AVF in Feb 2008 where the original faculty was enlarged to include those not present at the first meeting but contributing to the draft refinements. This second face-to-face meeting at the AVF on Feb 16, 2008, produced further refinements in wording and document organization. These were incorporated into a final draft reflecting the consensus of the assembled faculty. This article, then, represents the final consensus agreement on venous terminology reached at the second VEIN-TERM meeting at the Twentieth Annual Meeting of the AVF, Charleston, SC, USA. Its make-up includes broadly used venous terms

related to the management of CVD of the lower extremities, which were agreed to have variable applicability and interpretation in reports in the venous literature. Excluded were terms previously defined in the CEAP documents³⁻⁵ and prior venous nomenclature refinements,^{7,8} and those pertaining to a congenital etiology. In the section below, the venous terms selected for inclusion in the VEIN-TERM consensus are stratified into three different groups: Clinical, Physiological, and Descriptive, although some degree of overlap was unavoidable.

THE VEIN-TERM UPDATE ON TERMINOLOGY OF CHRONIC VENOUS DISORDERS

Clinical venous terms.

- Chronic venous disorder:** This term includes the full spectrum of morphological and functional abnormalities of the venous system.
- Chronic venous disease:** (Any) morphological and functional abnormalities of the venous system of long duration manifested either by symptoms and/or signs indicating the need for investigation and/or care.
- Chronic venous insufficiency (C3*-C6):** A term reserved for advanced CVD, which is applied to functional abnormalities of the venous system producing edema,* skin changes, or venous ulcers. (C3*: moderate or severe edema as stratified by Rutherford et al.⁶) (Explanation: It was unanimously accepted that the term "chronic venous disorder" would encompass the full spectrum of venous abnormalities, and after much deliberation, it was further agreed that "chronic venous disease" would represent that major subset of individuals with venous complaints and/or manifestations requiring investigation and/or care. The term "chronic venous insufficiency" was then reserved for those with advanced signs and/or symptoms).^{1,2,9-11}
- Venous symptoms:** Complaints related to venous disease, which may include tingling, aching, burning, pain, muscle cramps, swelling, sensations of throbbing or heaviness, itching skin, restless legs, leg-tiredness and/or fatigue. Although not pathognomonic, these may be suggestive of chronic venous disease, particularly if they are exacerbated by heat or dependency in the day's course, and relieved with leg rest and/or elevation. Existing venous signs and/or (non invasive) laboratory evidence are crucial in associating these symptoms with CVD.
- Venous signs:** Visible manifestations of venous disorders, which include dilated veins (telangiectasia, reticular veins, varicose veins), leg edema, skin changes, ulcers, as included in the CEAP classification.⁵
- Recurrent varices:** Reappearance of varicose veins in an area previously treated successfully.
- Residual varices:** Varicose veins remaining after treatment.
- PREVAIT:** This acronym means PREsence of Varices (residual or recurrent) After InTervention.

(Explanation: Although recurrent varices, taken as those reappearing in an area previously treated successfully, and residual varices, taken as those remaining after treatment, were both felt to be clearly defined, the difficulty in correctly classifying the results of initial procedures done by others prompted the need for an all-inclusive term for varices presenting for treatment after prior intervention. The acronym PREVAIT, which was introduced to facilitate reporting in clinical scenarios where varices could not be definitely classified as recurrent or residual, was therefore accepted.)

9. **Post-thrombotic syndrome:** Chronic venous symptoms and/or signs secondary to deep vein thrombosis and its sequelae.
10. **Pelvic congestion syndrome:** Chronic symptoms, which may include pelvic pain, perineal heaviness, urgency of micturition, and post-coital pain, caused by ovarian and/or pelvic vein reflux and/or obstruction, and which may be associated with vulvar, perineal, and/or lower extremity varices.
11. **Varicocele:** Presence of scrotal varicose veins.
12. **Venous aneurysm:** Localized saccular or fusiform dilatation of a venous segment with a caliber at least 50% greater than the normal trunk.

Physiological venous terms.

1. **Venous valvular incompetence:** Venous valve dysfunction resulting in retrograde venous flow of abnormal duration.
2. **Venous reflux:** Retrograde venous flow of abnormal duration in any venous segment.
Primary: Caused by idiopathic venous valve dysfunction.
Secondary: Caused by thrombosis, trauma, or mechanical, thermal, or chemical etiologies.
Congenital: Caused by the absence or abnormal development of venous valves.
3. **Axial reflux:** Uninterrupted retrograde venous flow from the groin to the calf.
Superficial: Confined to the superficial venous system.
Deep: Confined to the deep venous system.
Combined: Involving any combination of the three venous systems (superficial, deep, perforating).
4. **Segmental reflux:** Localized retrograde flow in venous segments of any of the three venous systems (superficial, deep, perforating) in any combination in the thigh and/or the calf, but **NOT** in continuity from the groin to calf.

(Explanation: The now recognized significance of axial reflux in the pathophysiology of venous leg ulcers¹² justified distinctions made to clarify the definitions of different types of lower extremity venous reflux with axial reflux defined as uninterrupted retrograde venous flow from the groin to the calf in continuity. It was accepted that axial reflux might be confined to the superficial or the deep systems, but could also involve

any combination of the superficial, deep, and the perforator systems. This is in contradistinction to “segmental reflux”, defined as localized retrograde flow in any of the three venous systems, **but without continuity** from the groin to the calf.)

5. **Perforator incompetence:** Perforating veins with outward flow of abnormal duration.
6. **Neovascularization:** Presence of multiple new small tortuous veins in anatomic proximity to a previous venous intervention.
7. **Venous occlusion:** Total obliteration of the venous lumen.
8. **Venous obstruction:** Partial or total blockage to venous flow.
9. **Venous compression:** Narrowing or occlusion of the venous lumen as a result of extra-luminal pressure.
10. **Recanalization:** Development of a new lumen in a previously obstructed vein.
11. **Iliac vein obstruction syndrome:** Venous symptoms and signs caused by narrowing or occlusion of the common or external iliac vein.
12. **May-Thurner syndrome:** Venous symptoms and signs caused by obstruction of the left common iliac vein due to external compression at its crossing posterior to the right common iliac artery.

(Explanation: Venous symptoms and signs may be caused by narrowing or occlusion of the common or external iliac vein, yet not be due to the May-Thurner syndrome, as described. The term Iliac Vein Obstruction syndrome is, thus, an all-inclusive term, and the May-Thurner syndrome is a specific variant of this, capable of producing those symptoms and signs.)

Descriptive venous terms.

1. **High ligation and division:** Ligation and division of the great saphenous vein (GSV) at its confluence with the common femoral vein, including ligation and division of all upper GSV tributaries.
(Explanation: This is still the gold standard against which new endovenous and surgical methods which may preserve the upper tributaries should be compared. Partial or complete preservation of the upper GSV tributaries, when the GSV is ligated, stripped, or ablated, must be clearly stated.)
2. **Stripping:** Removal of a long vein segment, usually most of the GSV or the small saphenous vein (SSV) by means of a device.
3. **Venous ablation:** Removal or destruction of a vein by mechanical, thermal, or chemical means.
4. **Perforating vein interruption:** Disconnection of a perforating vein by mechanical, chemical, or thermal means.
5. **Perforating vein ligation:** Interruption of a perforating vein by mechanical means.
6. **Perforating vein ablation:** Disconnection or destruction of a perforating vein by mechanical, chemical, or thermal means.

(Explanation: The introduction of "standards for endovenous ablation for the treatment of venous insufficiency" in 2007,¹³ and the increased use of minimally invasive and/or endovenous procedures underscores the need for uniform nomenclature regarding such procedures. The loose application of the term "venous ablation" has been particularly problematic. For the most part, the terms "ligation" and "ablation" adequately define the range of interventions, however, it must be emphasized that ablation literally means "destruction or removal", whereas interruption implies a more localized occlusion or luminal obliteration, such as by ligation, cautery, or clipping.)

7. **Mini-phlebectomy:** Removal of a vein segment through a small skin incision.
8. **Sclerotherapy:** Obliteration of a vein by chemical introduction (liquid or foam).
9. **Endophlebectomy:** Removal of post-thrombotic residue from the venous lumen.

DISCUSSION

A compelling demand for a common scientific language in the literature on chronic venous disorders has recently led to national and international multidisciplinary efforts to refine venous nomenclature.^{3-8,13} Evidence-based medical practice requires uniform terminology in reporting clinical and basic studies of chronic venous disorders. Venous terms directly associated with acute venous disease and congenital disorders, as well as those having been comprehensively defined in previous consensus documents^{3-5,7,8} were excluded from consideration in this VEIN-TERM consensus document. This VEIN-TERM consensus document has a transatlantic interdisciplinary base and the above recommendations were arrived at as a result of open debate and free communication between venous experts from a number of countries. It is intended to provide those involved in the management of CVD around the world, who may report their experiences in the English literature, with clarifying refinements in venous terminology. Hopefully it will result in a more precise use of venous terms in English language articles on CVD in the future.

AUTHOR CONTRIBUTIONS

Conception and design: MP, BE
Analysis and interpretation: MP, BE, KD, RR, PG, VEIN-TERM FACULTY
Data collection: MP, BE, KD
Writing the article: KD
Critical revision of the article: MP, BE, KD, RR, PG, VEIN-TERM FACULTY

Final approval of the article: MP, BE, KD, RR, PG, VEIN-TERM FACULTY

Statistical analysis: Not applicable

Obtained funding: American Venous Forum Hurtigrut

Overall responsibility: MP, BE, KD, RR, PG

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MANAGEMENT OF PRIMARY VENOUS DISORDERS IN C6 PATIENTS

—Michel. R. Perrin, MD, *Lyon, France*

The highest clinical class of venous disorders in the CEAP classification is C6. To decrease venous ulcer prevalence, two steps are necessary: first, healing the ulcer, and second, preventing its recurrence. It must be kept in mind that primary etiology is not only identified in the superficial venous system, but encompasses the perforator and deep systems, which means that all of the venous system must be investigated in patients presenting with an ulcer - at least by ultrasound scan investigation.¹ Repartition and percentage of the different reflux locations have been evaluated in numerous surveys, but in most of them the etiology is not specified.¹⁻⁸ Only two studies give both information on etiology and reflux location.^{9,10} More recently, it has been pointed out that ilio-caval primary obstruction is an underestimated cause of severe chronic venous insufficiency.^{11,12} This information on etiology and pathophysiologic disorders is not only of academic interest but is crucial if operative treatment is considered. Conversely, when conservative treatment is used, the above mentioned information is not important as treatment relies mostly on symptoms and signs.

50S Abstracts

JOURNAL OF VASCULAR SURGERY
November Supplement 2010

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MANAGEMENT OF PRIMARY VENOUS DISORDERS IN C6 PATIENTS

—Michel. R. Perrin, MD, Lyon, France

The highest clinical class of venous disorders in the CEAP classification is C6. To decrease venous ulcer prevalence, two steps are necessary: first, healing the ulcer, and second, preventing its recurrence. It must be kept in mind that primary etiology is not only identified in the superficial venous system, but encompasses the perforator and deep systems, which means that all of the venous system must be investigated in patients presenting with an ulcer - at least by

ultrasound scan investigation.¹ Repartition and percentage of the different reflux locations have been evaluated in numerous surveys, but in most of them the etiology is not specified.¹⁻⁸ Only two studies give both information on etiology and reflux location.^{9,10} More recently, it has been pointed out that ilio-caval primary obstruction is an underestimated cause of severe chronic venous insufficiency.^{11,12} This information on etiology and pathophysiologic disorders is not only of academic interest but is crucial if operative treatment is considered. Conversely, when conservative treatment is used, the above mentioned information is not important as treatment relies mostly on symptoms and signs.

The purpose of this study was to get precise and complete information, which investigations are compulsory in patients with C5 to C6 disease. Level 2 investigations, as described in the CEAP classification, must be carried out in all patients.¹³ Additional investigations have to be undertaken according to various situations when operative treatment is considered. In patients with C5 to C6 disease with moderate superficial reflux and absence of primary deep reflux, primary obstruction is possible. Venography, according to Raju and Neglén,¹¹ underestimates ilio-caval vein compression and intravascular ultrasound scan should be undertaken to identify this anomaly.^{12,14} The problem is that ilio-caval vein compression and intravascular ultrasound scan is invasive and expensive. In patients with axial deep reflux and when valve reconstruction is considered, descending venography is the best investigation to determine the optimal technique to be used.¹⁵

TREATMENT

Ulcer healing. Most of the studies devoted to venous ulcer healing do not give detailed information on etiology and pathophysiologic disorders. Whatever they are, compression remains the first-line of treatment for healing venous ulcers. In a retrospective review of 113 patients with venous ulcers, complete ulcer healing occurred in 99 of 102 patients (97%) who complied with the use of stockings vs 6 of 11 patients (55%) who were not compliant ($P < .0001$).¹⁶ Another retrospective review of 99 venous ulcers confirmed this data¹⁷ and Cochrane review.¹⁸

There is a strong recommendation (grade 1B) for using compression for healing ulcers, whatever the etiology and the physiopathology.¹⁹

The question arises: does operative treatment enhance healing? Three randomized controlled studies (RCTs) comparing superficial venous surgery + compression vs compression alone are available.

The ESCHAR study concluded that correction of superficial venous reflux in addition to compression bandaging did not improve the ulcer healing rate whether the etiology was primary or secondary.^{20,21}

In another RCT including 76 patients of primary and secondary etiology presenting with superficial venous reflux +/- deep venous reflux +/- perforator incompetence were randomized into two arms: compression alone and varicose vein surgery + compression. Superficial venous

surgery gave no additional benefit to compression therapy from the point of view of healing rate and quality of life.²²

In the third RCT, 200 ulcerated legs (C6) were randomized and treated by varicose vein surgery +/- perforator ligation + compression vs compression alone, knowing that primary and secondary patients with segmental and axial deep reflux were included. Healing rate was not statistically different whatever the etiology, pathophysiologic disorder, or treatment.²³

Conversely, in an Italian series of isolated primary reflux, 80 patients (87 extremities) were treated by minimally invasive surgery (CHIVA technique) vs compression. The healing rate was better in the surgical group $P < .02$, but ulcers <12 cm were excluded; there is no information on postoperative compression in the surgical group and in both groups the healing time was abnormally short.²⁴

Many observational studies support various operative treatments in primary varices to improve ulcer healing, but none of them includes a control group. In conclusion, there is no recommendation for using operative treatment to improve ulcer healing rate.

The effectiveness of a venoactive drug in improving ulcer healing has been assessed in a meta-analysis including five large European studies ($n = 723$). Its administration to patients had a statistically significant effect on the healing of medium size trophic ulcers (5-10 cm²) that had persisted for 6 to 12 months. In addition, healing time was shortened by 5 weeks. The authors concluded that venoactive drugs might be an appropriate and valuable addition to standard therapy of venous leg ulcers.²⁵ In the *Handbook of Venous Disorders*, two venoactive drugs in combination with compression are given a grade 1B recommendation whatever the etiology in long-standing or large venous ulcers.²⁶

Several observational studies pointed out that the healing rate is improved when patients are managed by specialized centers on an ambulatory basis.²⁷⁻²⁹

The types of compression (stocking and bandages) will not be broached in this review nor will local treatment.

Ulcer recurrence prevention. Usually, effectiveness and value of operative treatments are compared with conservative treatments, in other words, compression. The problem is that compliance with compression is very difficult to assess in a long-term follow-up. According to a survey including a large cohort of patients under the care of primary care physicians and specialists, 63% of patients did not use the stockings prescribed and there was no difference between the C0s to C2 and the C3 to C6 group.³⁰ Long-term compliance in the Milwaukee's group was also poor, 67.7% vs 32.3%.¹⁷

It is regrettable that most articles on compression treatment outcome do not make a difference between primary and secondary etiology and the venous system involved or the pathophysiologic disorder anomaly responsible for the venous ulcer. Conversely, operative treatment must take into account the venous systems involved and the pathophysiologic anomaly, which is to say to the A and P CEAP headings.

52S Abstracts

JOURNAL OF VASCULAR SURGERY
November Supplement 2010

In the presence of superficial venous reflux (primary varices), the three RCTs already quoted are reliable. In the ESCHAR study, rates of ulcer recurrence at 4 years were 56% for the compression group (group 1) and 31% for the compression + surgery group (group 2; $P < .01$). What is particularly interesting in this prospective study is the fact that isolated superficial reflux, or combined with deep reflux, was evaluated separately.²¹

For patients with isolated superficial reflux, recurrence rates were respectively 27% in group 2 vs 51% in group 1, $P < .01$. For patients who had superficial with segmental deep reflux, recurrence rates at 3 years were 52% for group 1 and 24% for group 2, $P = .04$. In the last subgroup, combining deep axial reflux as defined in the vein-term consensus,³¹ recurrence rates at 3 years were 46% for group 1 and 32% for group 2, $P = .33$.

In the Dutch RCT already mentioned, the conclusion was that only patients with medial and/or recurrent ulcer had better results with superficial surgery +/- superficial endoscopic perforator vein surgery whatever the etiology and the presence or absence of deep reflux, but this information is not clear because the CEAP classification was not used in describing the patients.

In the Italian series, the recurrence rate was 9% in the surgical group vs 36% in the compression group at 3-year follow-up, $P < .05$.²⁴

There is no RCT available both for thermal ablation or chemical ablation, but their outcome in patients without healed or active ulcer is as good as conventional surgery.

In conclusion, in patients with isolated primary varices, treatment by open surgery to prevent venous ulcer recurrence is a strong recommendation (1A); as far as other operative treatments (thermal and chemical ablation) are concerned, data have not been reported.

At the present time, there is no RCT comparing outcome in patients treated by surgery and wearing or not wearing long-term postoperative compression stockings.

In patients combining superficial and deep reflux, the boundary is the extension of the reflux; when it is segmental, operative treatment of superficial reflux remains a strong recommendation (1C). Nevertheless, to determine if patients would be really improved by operative treatment of their superficial reflux, Marston et al³² has suggested taking into account the preoperative value of maximum reflux velocity measured in the femoral and popliteal vein. If the velocity is more than 10 cm/second, the effectiveness of operative treatment is doubtful.

When axial deep reflux is also present, it is known that about 50% of patients will not be improved by superficial venous surgery.³³ Their optimal management will be discussed later and in the combination of primary obstruction with superficial reflux.

Another unsolved question is related to perforator insufficiency combined with superficial reflux. Again, there is no RCT comparing the outcome of C5 to C6 disease in patients treated operatively by isolated superficial venous surgery vs suppression of incompetent perforators in combination. Nevertheless, re-ulceration has been cured by complementary perforator ablation in observational series.

Isolated primary perforator insufficiency is a rare condition, but in the presence of venous ulceration, there is a weak recommendation (grade 2B) for treating them operatively as there is no RCT comparing operative treatment including sclerotherapy³⁴ with compression.

Deep venous reconstructive surgery remains the most debated topic. Both its long-term effectiveness and superiority, if compared with compression, are still controversial, essentially because precise information on compression

Table. Valvuloplasty results

Author year	Surgical technique	Number of limbs (number of valves repaired)	Etiology PVI/total	Follow-up mos (mean)	Ulcer recurrence or nonhealed ulcer (%)	Results	Competent AVP valve (%) VRT ■
Masuda 1994	I	32	27/32	48-252 (127)	(28)	24/31 (77)	□ ↗ 81% (av) ■ ↗ 50% (av)
Lehtola 2008	I TMEV I+TMEV	12 7 1	5/12 3/7 0/1	24-78 (54)	—	(55)	—
Perrin 2000	I	85 (94)	65/85	12-96 (58)	10/35 (29)	72/94 (77)	■ Normalized 63% (av)
Raju 1996	I	68 (71)	—	12-144	16/68 (26)	30/71 (42)	—
Raju 1996	TMEV	47 (111)	—	12-70	14/47 (30)	72/111	—
Raju 2000	TCEV	141(179)	98/141	1-42	(37)	(59)	□ ↗ 15% (av) ■ Normalized 100%
Rosales 2006	TMEV	17 (40)	17/17	3-122 (60)	3/7 (43)	(52)	□ ↗ 50% (av)
Sottiurai 1988	I	143	—	9-168 (81)	9/42 (21)	107/143 (75)	—
Tripathi 2004	I	90 (144)	118	(24)	(32)	(79.8)	—
	TMEV	12 (19)			(50)	(31.5)	—
Wang 2006	TMEV	(40)	40/40	(36)	—	(91)	■ ↗ 50% (av)

I, Internal valvuloplasty; PVI, primary venous insufficiency; TMEV, transmural external valvuloplasty; TCEV, transcommissural external valvuloplasty; □ AVP, ambulatory venous pressure; ■ VRT, venous refill time; av, average; ↗, improved.

compliance is lacking in patients with primary ilio caval obstruction C5 to C6 and in patients with primary deep axial reflux.

Observational studies are available both for obstruction and reflux. Furthermore, most patients with axial deep reflux were failures of conservative treatment and/or superficial and perforator operative treatment. Outcomes after valvuloplasty are presented in the Table. It is worth noting that, in all studies, there was a good correlation between absence of ulcer recurrence, repaired valve competence, and hemodynamic results. Valve reconstruction is recommended in primary axial deep reflux after less invasive therapies have failed or in young and active patients reluctant to wear permanent compression (recommendation 1A).

In primary ilio caval obstruction, only one large series has been reported.³⁵ Among 982 chronic nonmalignant obstructive lesions of the femoroilio caval vein which were stented, 517 were of primary etiology. Seventeen percent of the extremities treated had an open ulcer. Healing of leg ulcers was followed-up in 148 of 158 limbs for a mean 23 months (range, 1-99 months). In 47 limbs (31.7%), the ulcer did not heal. In the remaining 101 limbs, the ulcer healed and recurred in only 8 limbs during the follow-up period. Thus, if healing of the ulcer was achieved after this intervention, ulcer recurrence was rare within the study period. The cumulative rate of ulcer healing at 5 years was 58% overall: 62% for nonthrombotic iliac vein lesion, in other words primary etiology, and 55% for thrombotic limbs ($P = .2819$). In a few cases, superficial venous insufficiency was treated in combination. The authors concluded that the beneficial clinical outcome occurred regardless of the presence of remaining reflux, adjunct saphenous procedures, or etiology. However, almost one-third of the patients did not heal. It is not known whether they had a combination of superficial or deep reflux that was not treated. This point might explain the high percentage of non-healing ulcers.

In primary chronic iliac vein obstruction in patients with C6 disease, stenting is recommended (recommendation 1A). Nevertheless, when extended reflux is also present and if the ulcer does not heal after stenting, correction of the reflux must be considered.

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54S Abstracts

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**SUMMARY OF EVIDENCE OF EFFECTIVENESS
OF PRIMARY CHRONIC VENOUS DISEASE
TREATMENT**

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**COMPRESSION AFTER DEEP VENOUS
THROMBOSIS TO PREVENT POST-
THROMBOTIC SYNDROME AND
ULCERATION**

A Cochrane review of non-pharmaceutical measures for prevention of postthrombotic syndrome identified three randomized controlled trials (RCTs) evaluating compression stockings to no compression or sham compression in patients after an episode of deep vein thrombosis (DVT).¹ The use of compression stockings in each study was associated with a significant reduction of the development of postthrombotic syndrome (PTS; odds ratio 0.39). Because the incidence of venous ulceration after DVT is low (<10%) and may not present for more than 10 years after the initial event, randomized studies on the prevention of ulceration after DVT are unlikely to be performed.

The use of compression hosiery to prevent PTS after DVT can be given a 1A recommendation based on the clear benefit and low-risk of complications, but for prevention of ulceration, a 1C grade is recommended as a prevention of PTS is only a surrogate for ulcer prevention. It may also be argued that a treatment modality that suffers from poor patient compliance (fewer than 50% of DVT patients are estimated to routinely wear compression stockings long-term) should not be assigned a 1 grade because patients frequently decide that the therapy is not worth the supposed treatment benefit.

**COMPRESSION FOR VENOUS ULCER
HEALING AND PREVENTION OF
RECURRENCE**

The Cochrane Collaboration recently (January 2009) updated their extensive review of the literature on the use of compression for venous leg ulcers.² After a review of 39 RCTs examining various forms of compression in venous leg ulcers, they concluded that compression clearly increases ulcer healing rates compared to no compression. Multi-component systems are more effective than single-component systems, and most studies found that multi-component systems with an elastic bandage were more effective than those composed mainly of inelastic components.

An RCT of 153 patients compared the effectiveness of compression hosiery in reducing the incidence of ulcer recurrence after healing.³ Significantly fewer patients using compression routinely developed ulcer recurrence at 6 months of follow-up (21%) than did those not using compression hosiery (46%; $P < .05$). Another RCT compared the relative benefit of class 2 compression stockings compared to class 3 stockings in preventing ulcer recurrence.⁴ Whereas no significant difference in the incidence of ulcer recurrence was found (32% recurred using class 3 and 39% recurred using class 2), 42% of patients randomized to class 3 hosiery were unable to comply with their use, potentially masking the ability to prevent recurrence in this group. In the class 2 group, 28% of patients were noncompliant with routine use.

Based on this analysis, it seems appropriate to assign a 1A grade to the use of compression bandaging for the healing of venous leg ulcers. A grade of 1B seems reasonable for the recommendation of compression hosiery to prevent recurrent ulceration. There is little risk to compression bandaging and hosiery as long as patients with arterial insufficiency are identified and appropriate stocking sizing and training is performed. However, it must be acknowledged that compliance with high-grade compression hosiery is poor, and in many cases lower amounts of compression may be preferable to achieve compliance.

**MEDICAL THERAPIES FOR TREATMENT OF
PRIMARY CHRONIC VENOUS DISEASE AND
ACCELERATION OF ULCER HEALING:
PHLEBOTONIC AGENTS**

The category of phlebotonic agents contains a variety of natural and synthetic compounds believed to have "venoactive properties" that will reduce the symptoms of venous disease. These properties include a reduction of capillary permeability, improvement of venous tone, inhibition of inflammation or leukocyte activation, and others. Flavonoids, natural extracts from plants such as grape seed and French maritime pine bark, are included in this category, as are horse chestnut seed extract (HCSE) and rutosides.

In a recent review by the Cochrane Collaborative on phlebotonic agents,⁵ it was concluded that there is some evidence of a reduction in limb edema with phlebotonic agents, but overall there is not sufficient evidence to recommend their use with the exception of HCSE.

16S *Neglen*

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Neglen 17S

Prevention and treatment of venous ulcers in primary chronic venous insufficiency

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Prevention and treatment of venous ulcers in primary chronic venous insufficiency

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Primary chronic venous disease (PCVD) is a progressive degenerative condition that usually results in vein wall weakness, producing valvular incompetence. The disease most frequently occurs in the superficial veins and presents as asymptomatic cosmetic varicose veins. PCVD may also advance to symptomatic stages with pain, edema, skin changes, or venous ulcerations.

Primary venous reflux can also develop in the deep and perforating veins. PCVD may also include a symptomatic obstructive element when a nonthrombotic iliac vein lesion (NIVL) is present. PCVD is defined by the basic CEAP classification as: C₂₋₆ E_p A_{s,d,p} P_{o,r}.¹ The letter p (primary) refers to nonthrombotic, noncongenital etiology. The pathology is mainly related to deep and/or superficial valve incompetence creating an axial reflux projecting into the ulcer area.² Symptomatic NIVL has previously been described as May-Thurner syndrome, Cockett's, or "iliac vein compression" syndrome.^{3,4} The existence of marked iliac vein compressions (more than 50% obstruction) with or without intraluminal lesions has been shown to be more pathogenic than previously thought. In the past, these lesions have been considered a common finding of little clinical importance.⁵ Primary venous insufficiency should be differentiated from secondary postthrombotic venous insufficiency because the two conditions differ in pathophysiology, management, and prognosis. "Hydrostatic" leg ulcers without venous reflux and/or obstruction (eg, in morbidly obese patients [C₅₋₆ E_s A_n P_n]) are excluded in this discussion.⁶

As early as 1948, the Swedish surgeon Gunnar Bauer found a group of patients with venous leg ulceration who had no history of previous deep venous thrombosis (DVT) but a family history of varicose veins. Descending transfemoral venography showed a patent, uniformly wide, deep

vein with plentiful valve stations identified, which allowed the contrast to descend into the calf veins.⁷ No postthrombotic changes, such as irregular lumen, collaterals, or poorly identified valve stations, were noted. Bauer's interpretation was that there was a loss of elasticity in the vein wall leading to dilatation and subsequent incompetence of the valve. He termed this condition idiopathic deep vein incompetence; this condition today is defined as primary valvular incompetence. Hach et al have later suggested an additional hypothesis (ie, the deep veins will dilate secondary to massive superficial reflux because of "overloading").⁸ Treatment of the superficial reflux in these patients may correct the deep venous reflux. This normalization of venous flow is frequently seen with segmental primary deep incompetence, but rarely with axial deep reflux.⁹⁻¹² Mapping of reflux by duplex ultrasound scanning in limbs with primary or secondary reflux and leg ulceration has shown that superficial reflux is present in approximately 80% of limbs, and in half of these limbs it is combined with deep venous reflux.¹³⁻¹⁵ The prevalence of significant NIVL in these patients is not known.

Current evidence suggests that multiple factors may lead to intrinsic structural and biochemical abnormalities of the vein wall in PCVD resulting in remodeling of the venous wall and valvular incompetence in PCVD (see Critical Issue 2). This process appears to be multicentric; thus, primary valve incompetence develops simultaneously in discontinuous vein segments. Valves may not fail in a progressive descending or ascending uninterrupted order as previously thought.¹⁶

PCVD is widespread in the population and is far more prevalent than secondary (postthrombotic) disease. It is responsible for the development of chronic venous insufficiency (C3-C6) in 20% of the older population. A meta-analysis comprising 390 ulcer patients with PCVD having duplex ultrasound scanning revealed superficial incompetence alone and combination of deep and superficial reflux in 44% and 43% of ulcerated limbs, respectively.^{17,18} The clinical expression of PCVD is indistinguishable from that of postthrombotic disease in its late stages, but the medical and surgical treatment considerations are distinctly different.

We have identified four critical issues concerning primary chronic venous disease, which are central in the endeavor to decrease the prevalence of venous leg ulcers by 50% at 10 years.

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CRITICAL ISSUE 1

Standardization of diagnostic testing (especially ultrasound scanning) for chronic venous disease and criteria for interpretation of the results

Background. Studies on how to identify patients with PCVD that will progress to ulceration do not exist. It has been shown to be important to correct the underlying pathology in patients with established venous ulcer disease to prevent recurrence.¹⁹ However, there is no standard for evaluation of reflux/obstruction and changes of the microcirculation in CVD by Intersocietal Commission for Accreditation of Vascular Laboratories (ICAVL) in the United States. Standardization is vital to move forward because of its importance to direct treatment in clinical practice as well as to perform research. There is also a lack of basic information on ambulatory venous pressure and hemodynamic changes in the microcirculation.²⁰

Evidence. Many laboratories have developed protocols for evaluating reflux and obstruction in the lower limbs, but there is no standardization of method and interpretation.

Discussion highlights. Duplex ultrasound scanning (DUS) is the most common and available test, and, therefore, central in evaluation of CVD, regardless of etiology, in clinical practice. Standardizing the method of scanning and the interpretation of the results would quickly have a major impact on CVD treatment. Primary care physicians would learn when to consult a vascular specialist for assessment and possible intervention. Since DUS of the ilio-caval vein segment is frequently difficult to perform, additional imaging studies may be needed to detect iliofemoral venous outflow obstruction as per institutional preference (eg, transfemoral contrast venography, magnetic resonance venography, computed tomography venography, or intravascular ultrasonography [IVUS]). There are no standard methods of quantification of hemodynamically significant venous outflow obstruction.²¹ Methods of measuring outflow resistance also need to be developed.

There are no known hemodynamic methods to identify which patient with PCVD and limbs with C-class 2 to 4 will progress to develop leg ulcers. To achieve this goal, other hemodynamic tests in addition to ultrasound scanning should be utilized. Duplex ultrasound scanning parameters of interest would be the anatomic extent and distribution of reflux and obstruction (such as the system proposed by Hach),²² and quantification of reflux by peak volume reflux, peak reflux, etc.²³ Hemodynamic tests, such as plethysmography (air plethysmography, foot volumetry, or strain-gauge)²⁴ and laser Doppler measurements, such as veno-arterial response (VAR) and vasomotor activity (VA),^{25,26} need further evaluation. When these hemodynamic tests are used, the patients need to be followed with clinical severity scores (venous clinical severity, segmental disease, and disability scores or others), which are more sensitive than C-classification to detect symptomatic progression.

Conclusion. It is necessary to develop first a protocol for CVD investigation for clinical practice, and then introduce a more sophisticated protocol for longitudinal research of CVD.

Recommendations. Standardize venous duplex studies for clinical practice and reimbursement in the U.S. by:

1. Establishing a protocol for DUS to detect venous reflux and obstruction in CVD, regardless of etiology. The scanning should include the inferior vena cava and iliac veins as able.
2. Achieving ICAVL approval: For research purposes, it is important to develop ultrasound measurements, which identify not only presence but also provide quantification of reflux and obstruction. The ultimate goal will be to assess the contribution of reflux/obstruction in each system (superficial/deep/perforator) and at various levels (axial/segmental; ilio-femoral/femoro-popliteal) to the global hemodynamics of the lower limb. This would enable directed treatment. Additional methods of studying venous hemodynamics and the microcirculation should also be used in longitudinal studies. With regards to PCVD, it is essential to identify measurements that would predict progression of limbs of C-class 2-4 to active leg ulcers.

Action. The American Venous Forum (AVF) is well positioned to take the lead and to coordinate with other societies the development of a clinical protocol for ultrasound scanning. Members can be identified with contacts in ICAVL, and societies of interest could shoulder this responsibility. This goal should be possible to achieve in a relatively short time frame (1 year) and reached with ICAVL approval. This would impact on the overall goal to achieve reduction of leg ulcer prevalence by 50% in 10 years.

Protocols for research will be performed by individual institutions or cooperation between interested institutions. Central to this would be cooperation between members of AVF and other societies with special interest in evaluation of the hemodynamics of CVD and vascular laboratories in general. This task is more challenging. First, the hemodynamic parameters have to be identified and then applied in longitudinal studies. The time span is at least 5 years. It is doubtful that, by this stage, this will have an impact on the overall goal of the present endeavor.

CRITICAL ISSUE 2

Identification of factors (other than hemodynamic) that identify patients with PCVD and C-class 2, 3, and 4 limbs, who are at risk for progression to C-class 6

Background. There is a lack of information on the natural history of PCVD. If factors for disease progression in patients with primary chronic venous disease could be identified, a modification of these factors, if feasible, may prevent development of venous ulcer.

Evidence. Evidence is lacking as most studies on risk factors look at risk of ulceration regardless of etiology and not the risk of progression between C-classes in limbs with PCVD. No validation of risk factors in class progression exists. However, risk factors for ulcer recurrence (other than presence of postthrombotic disease) have been identified and some may be helpful (eg, residual iliofemoral vein obstruction; residual deep incompetence, particularly axial deep reflux; residual or recurrent superficial reflux; and persistent venous hypertension).²⁷⁻³⁰

Discussion highlights. There are many proposed clinical risk factors, which need clarification of their role in progression of the disease.³¹ Some of these are age, obesity, smoking, pregnancy, gender, hypertension, use of hormones, "feeling of swelling," and occupation. In addition, clinical signs (eg, swelling phlebectatica and other skin changes) may warrant early intervention to prevent later ulcer formation. In the Bonn Vein Study I, conducted in 2000, 3072 participants of the general population of the city of Bonn and two rural townships, aged 18 to 79 years took part (1350 men, 1722 women).³² Participants were selected via simple random sampling from the registries of residents. In a follow-up study (Bonn Vein Study II) 6.6 years later, the same population was investigated again. The incidence of progress to chronic venous insufficiency (C3-C6) was approximately 2.0% per year. In a multivariate analysis, the main risk factors for developing severe stages (C4-C6) were age, arterial hypertension, and obesity. Further, does development of symptoms in limbs with C2 to C4 signal a risk of progression to ulcer formation? Databases with some of this information are available, but as yet not published (www.heonline.nhs.uk).²⁴ In the Bonn Vein Study II, the "feeling of swelling" increased the risk for the development of CVI significantly (unpublished data).

There are studies showing that mechanical dysfunction of the calf muscle pump may enhance the development of leg ulceration.³³ It will be important to investigate ankle range of motion,³⁴ calf muscle pump function, and patient activity in relation to progression of disease. The data that are presently available need to be correlated to progression of the disease.

Genetic factors may also play a role in progression to advanced chronic venous disease. A relationship between the C282Y polymorphism in hemochromatosis (HFE gene) and venous ulceration has been described.³⁵ Gene polymorphisms and biomarkers that may identify high-risk patients for progression to ulceration should be investigated (some studies are in progress). Bio-banks for subsequent analysis in longitudinal studies need to be established. Patients with ulcers have a 2- to 30-times higher prevalence rate of thrombophilia than the general population, despite no previous DVT. Presence of certain thrombophilias, such as antithrombin deficiency, may be a risk factor for ulcer development.³⁶

It would be of value to identify biomarkers signaling an increased risk of ulcer formation. Most agree that universal markers such as IL-6 are elevated, but it is uncertain

whether or not they may indicate progression of the disease.^{37,38}

Most would agree that wall dilation and valve incompetence in PCVD is related to venous endothelial dysfunction. Endothelial cellular injury and activation increase the expression of inflammatory markers and leukocyte recruitment in varicosities, and venous wall changes are thought to contribute to the weakening, dilatation, and valve reflux. Varicose vein patients demonstrate imbalances in the humoral mediators of vasoconstriction and venous dilatation. Plasma levels of endothelin-1 are increased in those with varicose veins and rise disproportionately in the response to venous stasis. Plasma levels of nitric oxide, a potent mediator of vascular relaxation, may also be modulated. Matrix metalloproteinase (MMP) 2 may also lead to alterations in the extracellular matrix as well as venous relaxation. Most of the studies are observational.^{16,39} The understanding of the natural history and progression of PCVD remains incomplete. Current evidence suggests the multifactorial origin of PCVD, leading to tissue remodeling of the venous wall with changes in the microcirculation and dermis. More studies to identify markers of endothelial dysfunction of prognostic value are necessary.

Are there differences in skin type/metabolism/race that may place patients at an increased risk of ulceration? Some studies indicate this.^{24,40-42}

Do quality of life (QoL) measurements correlate with disease severity (overall, yes),^{43,44} and in turn correlate with those patients that are at increased risk for disease progression (presently no evidence)? Can QoL assessment be used as a surrogate marker for patients at risk for disease progression? Currently there is no evidence that QoL can be used to identify who will progress since QoL is not directly related to venous incompetence.

Conclusions. There is a need for additional studies on the natural history of PCVD and factors responsible for disease progression to ulcer formation, such as clinical, mechanical, humoral, genetic, and endothelial risk factors.

Recommendations. To perform longitudinal studies evaluating factors responsible for disease progression. In addition, identify genetic and humoral mediators of endothelial dysfunction, which are present in limbs with PCVD and disease progression.

Actions. Studies on clinical risk factors and clinical signs associated with progress of the disease are already in place, and analysis needs to be finalized (see above Bonn Vein Study II). It is possible to reach this goal within 1 year. Further studies regarding other factors have to be initiated. It will probably be difficult to perform longitudinal studies on the influence of these factors on disease progression. An alternative way is to find unique features in limbs with already established ulcers (C6) as compared with limbs with lower severity venous disease, C2 to C4. Modification of some of these risk factors may, however, not be possible. It may not have an impact on ulcer prevalence in 10 years. There is a need to obtain more information on the impact of progression on quality of life by following patients in longitudinal studies.

CRITICAL ISSUE 3

Identification of treatments, which may prevent progression in patients with C2, C3, or C4 limbs to formation of leg ulcers (C6)

Background. By intervening at early stages of PCVD, and so preventing progression of the disease, would lower the prevalence of ulcers within 10 years.

Evidence. No study exists on the efficacy of compression therapy, pharmacotherapy, or endovenous/open interventions on prevention of progression of PCVD.

Discussion highlights. There are older studies giving the prevalence of venous ulceration, although most reports have deficiencies, and regional numbers are difficult to apply to the general population.^{45,46} There is a need to establish new point prevalence rates of limbs with venous ulceration, since currently patients with venous disease have generally better care reducing the rate of ulcer incidence. It is possible that even if we add nothing to current practice, the ulcer prevalence will be reduced by 50% in 10 years. It may be of value to compare snapshots of venous ulcer prevalence today with 5 years ago as a baseline.

External compression. External support will result in clinical improvement and help control swelling. There is evidence that stockings help alleviate symptoms of C2 disease in pregnant women.⁴⁷ A systematic review of 39 randomized trials concluded that ulcer healing rates are increased when compression therapy is used compared with no compression therapy.⁴⁸ There is, however, no report evaluating their effect on progression of PCVD. The main problem when studying efficacy of compression devices, including compression stockings, is how to ensure and track patient compliance of usage. In addition, it is not known whether or not all patients with C2 to C4 limbs should use compression therapy. If only symptomatic patients are to use compression, the assumption is made that only patients with symptomatic disease are at risk for progression to leg ulcer. That may not necessarily be true. The types of stocking or other devices and the adequate pressure gradient have also to be assessed to optimize compression therapy in PCVD. Compression therapy following acute DVT has been shown to reduce the incidence of subsequent postthrombotic syndrome and progression to ulcer formation.⁴⁹ The results are not transferable to PCVD, but show that prospective comparative studies with and without compression therapy should be feasible in patients with marked C2 disease.

Drug therapy. There are studies that show pentoxifylline to have a beneficial effect on ulcer healing with or without adjunctive compression therapy.^{50,51} Although there is a theoretic possibility that pentoxifylline or venoactive drugs and statins may prevent progression, no supporting studies exist.

Endovenous procedures including foam sclerotherapy or open surgery. It is important to decide in what sequence to treat primary vein obstruction and reflux and which vein segments to treat. Most agree to control superficial vein reflux first, even in the presence of deep vein

reflux. Significant outflow obstruction by NIVL should probably be treated early. There are no data to support that treating perforators in limbs with C2 or C3 disease will have an effect on progression. It would be important to assess whether or not treatment of perforators, deep valve insufficiency, or venous outflow obstruction may prevent progression in limbs with C4 disease to C6.

Conclusions. Substantial need for more information if early intervention with compression therapy, drug therapy, or surgery will prevent progression to ulcer formation.

Recommendations. Studies have to be performed. There may be substantial difficulty to perform this adequately, since it will be difficult not to intervene in symptomatic patients with clinical severity classes below C6.

Actions. With regard to current point prevalence, it may be of value to study Medicare data today and compare with data obtained from 2000 or 2005, to reveal important trends. Data from the Olmsted County epidemiology study showed that the overall incidence of venous ulcers in patients older than 45 years of age are estimated at 3.5 per thousand per year, and the incidence of venous ulcers remains unchanged over 20 years, between 1970 and 1990.⁵² This epidemiologic study continues and may soon give us an answer on current trends. Adequate longitudinal studies on impact of intervention may not be possible.

CRITICAL ISSUE 4

Calculate the number of symptomatic C2, C3, and C4 patients needed to treat to prevent an ulcer

Background. It is necessary to find out how many symptomatic or asymptomatic patients at risk to develop venous ulcer are necessary to treat to avoid one leg ulcer. This is a critical issue since it will be necessary to justify the cost of preventive treatment to payers.

Evidence. Since there is a lack of information to identify the patient at risk, there are also sparse data on prevention. No appropriate data are available since information on early intervention and progression of PCVD largely does not exist. There are some extrapolations made from a Swedish study suggesting that 100 symptomatic patients with varicose veins have to be operated on to prevent one ulcer; however, this number decreases to 10 when limbs with C4 disease are treated.⁵³

Discussion highlights. It is important to offer best treatment options for at-risk C2 to C4 patients to optimize prevention of progression. It is likely that a large number of patients may be necessary to treat to prevent one ulcer, which may be relatively costly for society. The most obvious health care saving is made by avoiding a lengthy and costly ulcer treatment owing to decreased incidence of leg ulcer formation. However, it must also be stressed that secondary gains are achieved. The patients receiving preventive treatment are also likely to experience a substantial improvement of quality of life in addition to ulcer prevention.

Conclusion. Any preventive method has to be related to the number of patients treated to prevent one leg ulcer.

The associated cost and possible additional beneficial effects on the patients need to be assessed.

Recommendations. Based on the outcome of Critical Issues 1 to 3, it may be possible to acquire the necessary information to perform cost-benefit analysis.

Actions. This issue is intimately connected with the solution of Critical Issues 1 to 3. Without having the data giving the patients at risk, it is impossible to make a cost-benefit analysis.

CONCLUSION

To summarize, regardless of etiology of venous ulcerations, it is fundamentally necessary to develop first, a protocol for CVD investigation for clinical practice, and second, a more sophisticated protocol for longitudinal research of CVD. The natural history of primary CVD and factors responsible for disease progression to ulcer formation, such as clinical, mechanical, humoral, genetic, and endothelial risk factors must be studied. There is also a lack of information as to whether or not early intervention by compression treatment, drug therapy, or ablative interventions will prevent progression to ulcer formation in primary CVD. Any preventive method has to be related to the number of patients needed to be treated to prevent one venous ulcer, owing to the potential socio-economic impact. The associated costs and additional beneficial effects on the patients' quality of life need to be assessed.

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Feasibility and Results of Incompetent Thigh Perforator Ablation by Coil Embolization in Recurrence of Varices After Surgery (REVAS).

Évaluation du traitement par embolisation des veines perforantes crurales responsables de récurrence de varices après chirurgie.

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Summary

Introduction: Treatment of thigh perforators connected to varicose veins remains difficult in REVAS. Surgery is often incomplete and traumatic, sclerotherapy often incomplete and endovenous thermal ablation inappropriate.

Material and method: Patients with REVAS were prospectively included in two surgical centers. The number of previous surgery, CEAP class, perforator's anatomy and its connexion with varicose veins were reported. Additional therapy was carried out simultaneously or afterwards. The main criteria were perforator obliteration and varicose vein recurrence.

Results: Forty patients (mean age 62) were presented with a REVAS after 2.1 operations over a mean period of 22 years. CEAP class distribution was essentially C2 (58,4%, 24/40 patients). In 16 cases, additional therapy was simultaneously performed. At 30 days, there were no major complications. At 11 months, one recanalization was reported. For 36 patients, the perforators were closed except for two, which were incomplete. At 51,5 months of mean follow-up, there were 13/40 cases without information because the patients did not their follow-up, 3/40 cases of recanalization, one case of partial recanalization, 11 cases of obliteration, no information for the other (12/40). No recurrences was observed when there was an obliteration.

Résumé

Introduction : Le traitement des veines perforantes (VP) responsables de varices est délicat chez les patients présentant une récurrence variqueuse après chirurgie (REVAS). Une nouvelle chirurgie est souvent incomplète et traumatique, la sclérothérapie incomplète et le traitement thermique endoveineux inapproprié.

Matériel et méthode : Des patients REVAS due à une VP incontinente ont été inclus de manière prospective dans deux centres médicaux. Le nombre de chirurgies précédentes, le score CEAP, l'anatomie des varices ont été renseignés. Un traitement complémentaire a été réalisé simultanément ou après. Les critères majeurs étaient l'oblitération de la VP et la présence d'une récurrence.

Résultats: 40 patients (moyenne d'âge de 62 ans), ont été inclus, après 2,1 chirurgies, après une période moyenne de 22 ans. Le score CEAP était essentiellement C2 (58,4 %, 24/40 patients). Un traitement complémentaire a été réalisé simultanément pour 16 patients. À 30 jours, aucune complications n'a été observé. Après une durée moyenne de 11 mois, 36 patients présentaient une oblitération totale, 2 patients une reperméabilisation partielle, 1 patient une reperméabilisation totale; pas de suivi pour un patient. Après une durée moyenne de 51,5 mois, 13 patients n'ont pas réalisé leur suivi. Il y avait 3 recanalisations, 1 recanalisation partielle, 11 cas d'oblitération et pas d'information pour les autres. Aucune récurrence n'a été observé lorsque la perforante était oblitérée.

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❖❖❖ **Conclusion:** Coil embolization of thigh perforators in REVAS appears to be a safe and effective procedure.

Keywords: Recurrence of varices, perforator vein insufficiency, embolization.

❖❖❖ **Conclusion :** L'embolisation des VP chez les patients REVAS semble être un traitement intéressant.

Mots-clés : Récidive de varices, insuffisance de veine perforante, embolisation.

Introduction

The incidence of chronic venous disease is estimated at 0.5-3% of the adult population in Europe and America [1]. Perforator vein insufficiency is the most common cause of recurrent varicose veins after treatment, often unrecognized [2, 3].

One of the complications of perforator vein insufficiency is ulcer, which has an important public health impact. The other complications of perforator vein insufficiency are the consequences of chronic venous insufficiency: lower extremity swelling, eczema, pigmentation, hemorrhage [4].

The different treatment options are surgical treatment and minimally invasive treatment, which are ultrasound guided sclerotherapy (USGS) and endovascular thermal ablation (EVTA) with either laser or radiofrequency energy sources [1].

Compression is the mainstay of treatment, but long-term compliance with this therapy is often inconsistent [8].

Pathologic perforator veins are described as having reversed flow from deep system to superficial vein greater than 500 ms, and with diameter greater than 3.5 mm.

Risk factors for incompetent perforator veins are the same as all chronic superficial venous disease, including history of deep venous thrombosis, multiple pregnancies, advanced age and genetic factors [5].

Current guidelines recommend perforator treatment in cases of clinical severity, etiology, anatomy, pathophysiology score (CEAP) 5 and 6, with treatment of the perforator at the level of previous or active venous ulceration.

Several authors also suggest treating incompetent perforator veins in cases of focal pain, focal swelling, associated varicose veins, focal skin irritation and/or discoloration in the area of the incompetent perforator vein [6, 7].

Subfascial endoscopic perforator surgery (SEPS) is the method recommended for the reduction of incompetent superficial venous system pressure and tibial ulcer treatment due to perforator vein insufficiency of the leg [1, 8].

There is no recommendation about the treatment of thigh perforator vein insufficiency.

Treatment of thigh perforators connected to varicose veins remains difficult in REVAS.

Open redo-surgery is often incomplete and traumatic, sclerotherapy is often incomplete and endovenous thermal ablation is difficult.

Therefore, coil embolization could be an interesting solution.

Van Dijk L.C. and al [9] has also studied percutaneous ultrasound-guided coil embolization but only to the lower leg.

The aim of our study is to assess feasibility and to present early results of ablation by coil embolization of incompetent thigh perforator vein in recurrence of varices after surgery (REVAS).

Material and method

We organised a prospective multicentre study.

Patients with REVAS fed by a thigh perforator were prospectively included in two surgical centers between 2004 and 2013.

The first center was in Nancy, France, with a vascular surgeon who included the patients and an interventional radiologist who did the procedure.

The second center was in Lyon, France.

A vascular surgeon included and did the procedure.

The number of previous surgery and also the number of years since surgery, CEAP class, perforator's anatomy and its connexion with varicose veins were reported.

We also reported the age, the side, the number of coil, radiation and time of fluoroscopy, the associated procedure with the delay, the complications, and the time of follow-up with successful obliteration.

Embolization was performed in a center by an interventional radiologist and in another center by a vascular surgeon.

The procedure was performed under local tumescent anaesthesia.

The access was the common femoral vein, homo or contralateral, or a residual saphenous trunk.

The presence of a reversed flow in the deep venous system during passage through the femoral valves was described.

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Perforator Ablation by Embolization.

The approach, the number of coils, radiation exposure and technical difficulties were reported.

Additional therapy (phlebectomies and/or foam sclerotherapy) was carried out simultaneously or afterwards.

Patients had a one month and one-year follow-up by an ultrasound duplex scan.

A third one has been done calling each vascular doctor in order to have the most recent ultrasound scan.

The main criteria were perforator obliteration and varicose vein recurrence.

Thirty-day complications and competence of the superficial femoral vein were also reported.

Results

Inclusion

All the patients with a varicose recurrence after a saphenectomy, because of a perforator vein, were included.

Patients were included between 2004 and 2016, seventeen in Lyon, France and twenty-three in Nancy, France.

Characteristic of the population

40 patients were included and 40 thigh perforator vein were treated.

The mean age was around 62 years.

They presented with REVAS after 2,1 operations over a mean period of 22 years. CEAP class distribution was essentially C2 (58,4%, 24/40 patients).

Characteristic of the varicose recurrence

In most of the cases (n=38/40), the perforator vein was a single trunk and was mainly medial (n=38/40) from the femoral superficial vein.

In two cases, the perforator vein was lateral and in one case it was posterior.

In 22/40 patients, varicose recurrence was right and to 19/40 patients, the varicose recurrence was left.

Embolization procedure

Embolization protocol:

The procedure begins with a deep femoral ventral approach against lateral or ipsilateral with introduction of a 4F catheter.

During angiography, continence and the integrity of the deep network are visualized.

Opacification visualizes the femoral vein and localizes the perforating vein responsible for varicose recurrence.

It is then introduced a guide and a catheter into the trunk of the perforator.

The embolization of the perforating vein is carried out using metal turns of 2 to 10 mm until complete occlusion judged by angiography.

Upon removal, good femoral vein continence and good venous compressibility are verified.

The result can be appreciated remotely by phleboscans with injection on the back of the foot and withers in the calf and thigh.

In 18 cases, the approach was contralateral femoral, in 19 cases homolateral, in 2 cases through the saphenous trunk and in 1 case through the saphenous trunk and homolateral femoral (Table 1).

Femoral vein access	Number of patient	Number of patient %
Contralateral	18	45 %
Homolateral	19	47 %
Saphenous trunk	2	5 %
Saphenous trunk and homolateral femoral	1	3 %
Total	40	100 %

TABLE 1: The different femoral vein access.

In 16/40 cases, this perforator was connected to a residual saphenous trunk and in 25/41 cases, directly to tributaries.

To have a complete occlusion, the mean number of coil was 6,6, of different size.

The mean irradiation was 1993 cGycm2 and the mean time of fluoroscopy was 12,3 min.

No peri-procedural incident was reported.

Results

In 25 cases, additional therapy was simultaneously performed and in 15 cases, it was delayed.

Additional therapy consisted in 9 cases phlebectomies, 26 cases to sclerotherapies and phlebectomies, 3 cases to phlebectomies and sclerotherapies and radiofrequency, 1 case to phlebectomies and radiofrequency, 1 case to laser and phlebectomies and sclerotherapies and 1 case no data (Table 2).

Outcome and short term follow-up

At 30 days, there were no major complications.

Two superficial venous thromboses occurred, which did not allow performing complete delayed phlebectomies.

Additional therapies	Number of patient	Number of patient %
Phlebectomies	9	22 %
Phlebectomies and sclerotherapies	25	62 %
Phlebectomies, sclerotherapies and radiofrequency	3	7 %
Phlebectomies and radiofrequency	1	3 %
Laser, phlebectomies and sclerotherapy	1	3 %
No data	1	3 %
Total	40	100 %

TABLE 2: Different additional therapies.

Some minor complications were described: two coils were introduced too far into the varicose veins, resulting in pain under the skin.

At mean follow-up, 11 months, all patients had their follow-up.

One recanalization was reported. For 36 patients, the perforators were closed except for two, which were incomplete.

There was no follow-up for one patient. No deep venous incompetence was reported.

Long term follow-up

After a mean follow-up (51,5 months), one patient has presented a varicose recurrence due to a recanalization of the perforator vein.

A new coil embolization was performed and the last follow-up showed a good result with no recurrence and an obliteration of the perforator vein, after 12 months of follow-up.

There were 13/40 cases without information because the patients did not their follow-up, there were 3/40 cases of recanalization, one case of partial recanalization, 11 cases of obliteration.

Unfortunately, there were 3 patients, where there was no vascular doctor informed, no data, because of no specific ultrasound scan for one patient, and 8 vascular doctors did not respond.

No recurrence was observed, when there was an obliteration of the perforator vein.

The recanalization was associated with recurrences.

Discussion

There are a few data to compare the different treatment of perforator vein insufficiency, specially about recurrence after surgery.

Surgery is an invasive approach.

That is why some mininvasive treatment are developed for perforator vein insufficiency: ultrasound guided sclerotherapy (USGS), endovascular thermal ablation (EVTA) [1, 2] and and subfascial endoscopic perforator vein surgery in the leg.

Ultrasound guided sclerotherapy is easily used with variable success [10], but it is not evaluated in recurrence after surgery, specially long term results [11] for incompetent thigh perforator vein.

About EVTA, **J.L. Bacon and al.** [12] described a percutaneous method of treating incompetent perforator veins, using ultrasound-guided radiofrequency ablation: Transluminal Occlusion of Perforator (TRLOP).

The closure rates were comparable with the data for subfascial endoscopic perforator surgery.

But this treatment was not evaluated specially in recurrence of varices after surgery and not specially for thigh. Only some minor complications were observed.

P. Marsh and al. [11] studied radiofrequency ablation.

Truncal reflux was treated before and incompetent perforator vein of lower leg in a second time by radiofrequency ablation with a dedicated stylet.

The closure rate was good (82%) but some complications were observed (significant rate of neuropraxia, one phlebitis, one cellulitis, one chemical ulcer).

But this treatment was not evaluated specially in thigh perforator vein.

Coil embolization is a surgical technique that widespread in treatment of pelvic venous incompetence [13, 14].

It seems to be also a valid treatment to occlude thigh perforator veins.

Our study is interesting because: it is a prospective multicenter study, which assesses an original process.

In our study, there were no major complication.

Only some minor complications were described.

No reversed flow of deep venous system was described during our procedure, during passage through the femoral valves.

The feasibility is good and the process is simple. It is also efficient with almost all patients with closed perforators vein.

We, however, need a better long term follow-up to confirm these data.

Conclusion

Coil embolization of thigh perforators in REVAS appears to be a safe and effective procedure.

The feasibility is good. There is no major complications.

At short term follow-up, the rate of obliteration is good. In order to assess long term results, it would be necessary to carry out long-term follow-ups.

This process could be a treatment option in REVAS due to incompetent thigh perforator, like ultrasound guided sclerotherapy and endovascular thermal ablation.

Références

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