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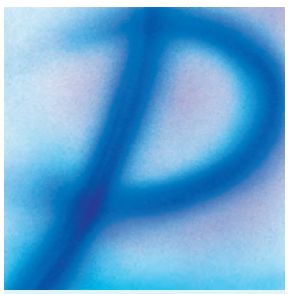

Phlebolymphology

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Aims and Scope

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

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

Phlebolymphology is scientifically supported by a prestigious editorial board.

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

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

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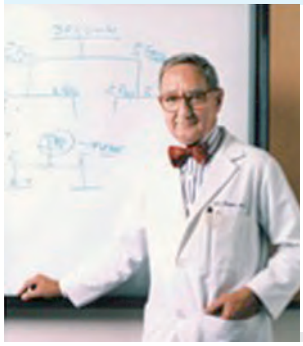
Obituary



John J. Bergan Obituary

John passed away in Chicago on June 11, 2014. He was 87-years-old.

Figure 1. ***JJ. Bergan*** *(left) and* ***B. Eklof*** *(right), members of the American Venous Forum ad hoc committee that contributed to the revised document on the CEAP classification in 2004*

The first time I met him was in 1973. At this time, he was working with James Yao at Northwestern University and Hospital, Chicago, IL as a vascular surgeon. I spent 2 full days with him at the hospital where I learned a lot. He invited me to a delicious dinner at the Chicago yacht club and he was delighted when I offered him an Hermes tie, as I knew he was very keen for this garment accessory.

At this time, John was already a world-renowned vascular surgeon; he performed the first kidney transplant in 1964. Since 1980, he specialized in venous disease when he moved to La Jolla, CA, where he was appointed as professor of surgery at the University of California, San Diego and he based his practice on vein management at Scripps Memorial Clinics.

He was the founder and first president of the American Venous Forum in New Orleans, LA in February 1989. He also served as the president of the Society of Vascular Surgery and he held leadership roles in numerous medical societies. John was a very active member in the first CEAP classification consensus meeting held in Hawaii, which was chaired by Andrew Nicolaides in February 1994. He contributed, of course, to the modification of the CEAP classification, which was initiated by Bo Eklof and published in 2004 (Figure 1).

He was also involved in the Cyprus International Consensus Meeting on the "Management of chronic venous disorders of the lower limbs: guidelines according to scientific evidence" and published in International Angiology in 2008.

In addition, he was a prolific author, publishing more than 700 scholarly papers and editing 39 books, not to mention his key role as Editor in Chief of "Venous Digest" and "International Venous Digest by Fax," the two newsletters dedicated to venous and lymphatic diseases. John also edited "The Vein Book," of which the first edition was published in 2006. He asked me to write two chapters of this book and I shared this honor with 80 contributing authors. The second edition was published a few months ago (Figure 2).

Among his numerous qualities, John was an expert at convincing everybody that they were the most qualified person to deal with a given topic.

Along his professional life, he was interested by all the new investigations and procedures, and was happy to collaborate with young people. In 1998, in a book entitled "Foam Sclerotherapy," he favored ultrasound-guided foam sclerotherapy over other procedures in varicose vein treatment, which looks surprising for a surgeon, as most of them, at this time, were reluctant to use this method until analyzed randomized controlled trials confirmed its efficacy.

To describe the man, I would say that he was a handsome, noble person who was always elegantly dressed. In the meetings, his remarks or comments were appreciated and he maintained his cool throughout a debate to disarm the opponents.

John's absence from the meetings in the last years was painfully experienced by the medical and surgical phlebologists and his death saddens us all.

Michel PERRIN

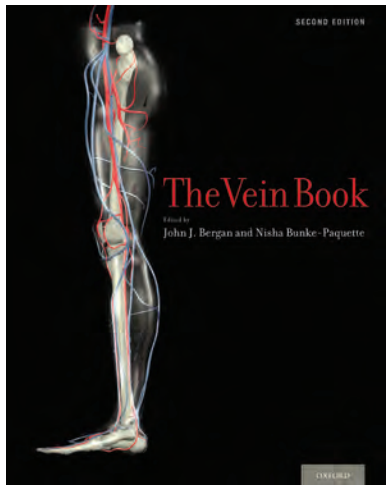


Figure 2. "The Vein Book," cover of the second edition of the book.

Editorial

Marianne DE MAESENEER

Dear Readers,

In this issue, ***Michel Perrin*** *reviews the evidence–or the lack of thereof–for treatment of recurrent or residual varicose veins after previous treatment (PREsence of VArices after operatIve Treatment [PREVAIT]). Duplex ultrasound is essential for determining an adequate therapeutic approach. Several treatment methods have been reported, of which foam sclerotherapy is becoming the most popular. Unfortunately, the vast majority of available studies on surgical treatment, thermal ablation, or chemical ablation only report short-term results up to 1 year after the procedure. More prospective studies are definitely needed.*

Giovanni Mosti *sheds light on compression after treatment of varicose veins and superficial venous reflux. At the thigh, it is particularly difficult to exert efficacious compression on the treated great saphenous vein (GSV) by means of elastic stockings. To reduce postoperative pain and bruising, additional eccentric compression devices, or even inelastic bandages, may be required. Unfortunately, the studies available, so far, are not sufficient to draw definitive conclusions, but in cases with more extensive disease, compression may certainly be beneficial.*

Tsoukanov et al *reports on a selected, small group of 26 female patients with a Clinical, Etiological, Anatomical, Pathophysiological (CEAP) classification of C0s who did not have reflux in the GSV according to duplex ultrasound investigation in the morning, but developed at least a segmental reflux in the GSV when reexamined in the evening. The effect of micronized purified flavonoid fraction (MPFF) was studied in these particular patients. Tsoukanov's interesting preliminary findings certainly warrant further investigation.*

With the increasing frequency of long-haul flights, physicians receive many questions about the risk for developing venous thromboembolism (VTE). ***Michèle Cazaubon*** *reviews the current knowledge on this subject and summarizes recommendations for clinical practice. Whereas some general rules are applicable to all air travelers, some additional measures may be required for selected travelers who are at intermediate or high risk of developing a VTE. These measures mainly consist of medical elastic compression stockings and/or pharmacologic thromboprophylaxis. Cazaubon illustrates the whole theme very well with a challenging clinical case.*

Robert Launois *explains the importance of measuring methods to evaluate quality of life (QOL) in patients with chronic venous disorders. Before being used in clinical trials, QOL tools should be constructed carefully, with a vocabulary that is understandable for most patients. The scale used should be as reliable as possible. Furthermore, these QOL tools need to be extensively validated, and revalidated, when translated into different languages. Generic QOL tools should always be used in addition to disease-specific QOL tools for scientific studies and audits.*

Enjoy reading this issue!
Marianne De Maeseneer

Presence of varices after operative treatment: a review

Part 2: This is the second part of the review article "PREsence of Varices After operatIve Treatment (PREVAIT)." The first part was published in Phlebolymphology, 2014;21(3):158-168.

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Keywords:

duplex scanning; endothermal ablation; neovaricoses; REVAS; sclerotherapy; varices recurrence; varicose vein; varicose vein surgery

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Abstract

Background: PREsence of VArices after operatIve Treatment (PREVAIT) occurs in 13% to 65% of patients and remains a debilitating and costly problem. The second part of this review aims to provide an overview of its optimal management according to published data.

Methods: A PubMed search was conducted in English and French for the years 2000-2013 by using keywords (ie, duplex scanning, endothermal ablation, neovaricoses, recurrent varicose veins after surgery [REVAS], sclerotherapy, varices recurrence, varicose vein, and varicose vein surgery).

Results: Diagnostic and operative treatment methods for managing PREVAIT were identified and their results analyzed. Indications for PREVAIT treatment are suggested according to clinical status and ultrasound information.

Conclusion: According to published data, ultrasound-guided foam sclerotherapy (UGFS) is used as a first-line treatment, yet the grade of recommendation for such a procedure is weak. It is only 1B according to European guide for sclerotherapy to improve the UGFS grade of recommendation, we suggest that larger prospective studies with a randomized controlled design be performed and supervised by an international group of experts.

Management of PREVAIT

Diagnostic

Medical history and physical examination must be completed by full duplex scanning of the three venous systems every time there is a PREsence of VArices after operatIve Treatment (PREVAIT). This investigation provides anatomic and hemodynamic data including: (i) topographical sites of recurrence that can be mapped; (ii) possible sources of reflux from the deep to the superficial venous system (*Figures 1 and 2*); (iii) intensity or degree of reflux; and (iv) nature of sources, keeping in mind that causes have to be classified differently if recurrence occurs in a site previously treated or not. In addition, duplex scanning (DS) gives information on perforator and deep venous systems.

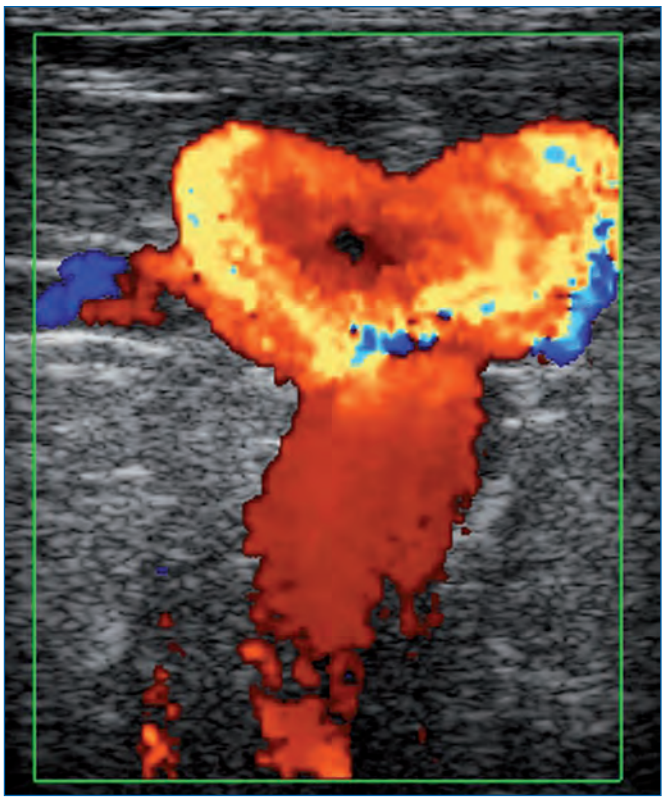

Figure 1. Presence of varices at the groin in a patient previously treated by saphenofemoral ligation.

Color duplex ultrasound. Massive reflux induced by a Valsalva maneuver.

Image courtesy of Dr Gillet.

One problem remains: a standardized DS investigation protocol was not universally used by the different investigators. Recently, a consensus document has been published on postoperative DS that provides a precise investigation methodology as well as a better and more precise description of the anatomic and hemodynamic anomalies according to the operative treatment modalities, surgery, or endovenous treatment.[1]

In a few select cases, ascending venography in 3D imaging may give complementary and valuable information. PREVAIT related to refluxing pelvic varices is investigated better by selective descending phlebography *(Figure 3)*. Other investigation such as air plethysmography may be useful, but is never performed in routine.

Patient evaluation with quality of life questionnaires

To determine whether PREVAIT affects patients' quality of life (QOL), the health-related QOL scores for patients can be used in different ways for clinical studies. Beresford et al compared patients presenting with recurrences after conventional surgery versus patients with untreated varicose

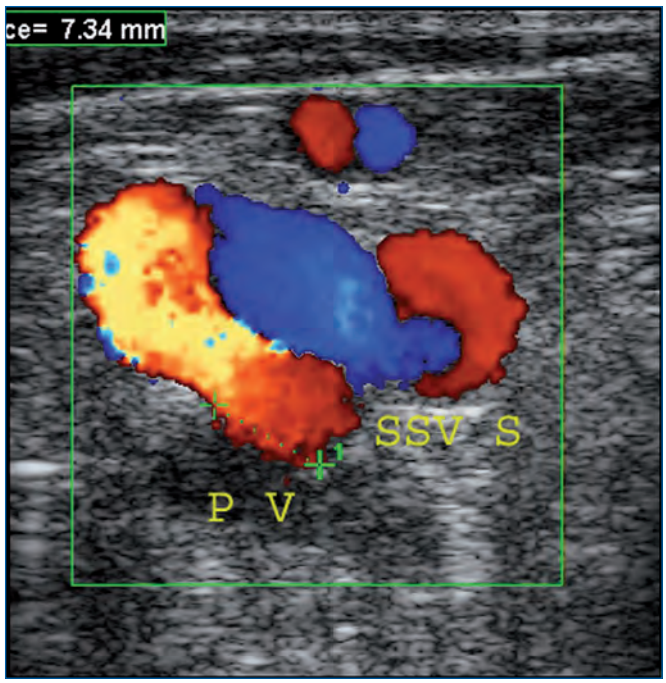

Figure 2. Presence of varices in the popliteal fossa in a patient previously treated by saphenopopliteal ligation.

Postoperative duplex scanning identified reflux in the SSVS that feeds the varicose network after the compression-decompression maneuver.

Abbreviations: PV, popliteal vein; SSVS, short saphenous vein stump.

Image courtesy of Dr Gillet.

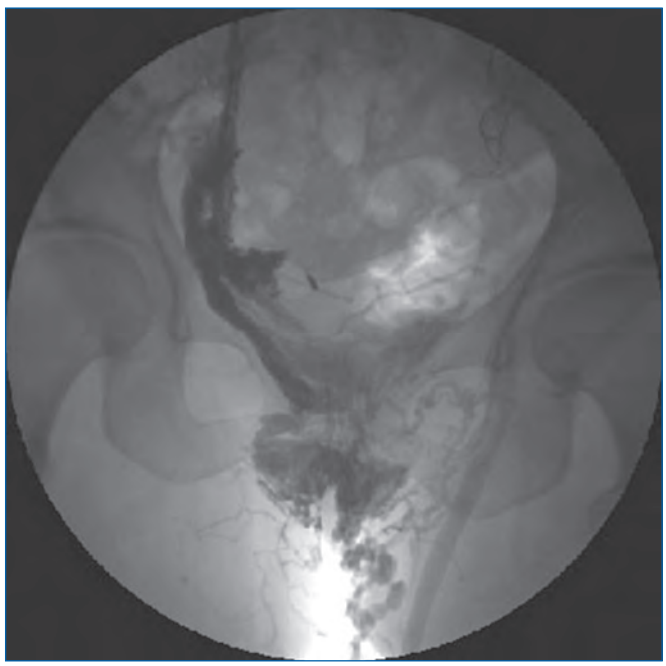

Figure 3. Selective phlebography of the right pudendal vein feeding the left GSV.

Abbreviations: GSV, great saphenous vein.

Image courtesy of Dr Monedero and Dr Zubicoa.

veins.[2] No survey has compared operated patients with or without PREVAIT.

Treatment methods

Compression therapy

Compression for improvement in both symptoms and signs of varicose veins is frequently recommended, but it does not cure the disease.

Drugs

In varicose veins, venoactive drugs are prescribed mainly to improve edema and symptoms. The most commonly used are flavonoids, more particularly, the micronized flavonoids.

Operative procedures

The final objective of any operative procedure is multiple and consists of decreasing the ambulatory venous pressure, preventing worsening of chronic venous disorders, avoiding further recurrences, and of course, relieving patients of their symptoms, signs, and any unpleasant cosmetic aspects of their legs.

Operative procedures share the same goals: (i) supress reflux from deep to superficial venous systems, when reflux exists; (ii) ablate varices; (iii) in some specific cases, to suppress deep vein abnormalities to prevent new recurrences; and (iv) suppress the reflux from pelvic and gonadal varices, when it exists, since the reflux feeds recurrent varices of the lower limbs.

Sclerotherapy. This treatment has been used for a very long time for the treatment of recurrent varicose veins after surgery (REVAS). Different protocols have been used, but no comparative study was available. Recently, ultrasound-guided foam sclerotherapy (UGFS) has entered the ring, and a minimal consensus exists on the techniques, doses, concentrations, or sclerosing agents according to the location and extent of varices.[3] One of the main advantages of UGFS is that the process is cheap, simple, less invasive than other operative procedures, and easily repeatable. UGFS can obliterate the refluxive varices and suppress most of the leak points between the deep and superficial venous systems, that is to say an incompetent saphenofemoral junction (SFJ), saphenopopliteal junction (SPJ), and perforator. For pelvic reflux, coils are used in association with a sclerosing agent.

Superficial vein surgery. Procedures can be classified into three groups according to their objective, and should be used in combination.

Procedures suppressing reflux from deep to superficial venous systems

Persistent reflux at the SFJ or SPJ. According to the extent of postoperative fibrosis, redo surgery may be difficult. Complications following reexploration of the groin are common.[4]

Patch interposition at the SFJ has been recommended for avoiding new recurrences,[5] as well as closure of the cribiform fascia[6] or reflected pectineal flap.[7] No data are available concerning redo surgery outcomes at the SPJ.

Incompetent perforator ablation. When severe cutaneous and subcutaneous changes are present, subfascial endoscopic perforator surgery (SEPS) was the favored surgical technique, but chemical or thermal endovenous procedures can be used.

Procedures ablating refluxing varices. According to the location and type of varicose vein, various techniques can be used: stab avulsion and phlebectomy are the most used techniques, while stripping, thermal ablation, and chemical ablation are used for treating the residual saphenous trunk.

Correction of deep reflux. Various procedures whose goal is to suppress deep vein reflux should be used as valvuloplasty or valve transfer, legitimated by several studies demonstrating that primary deep axial reflux is frequently associated with REVAS.[8,9]

Embolization using coils and foam of the pelvic and gonadic veins. In patients whose varices are fed by pelvic or gonadic reflux, this procedure is less invasive than direct ligation.[10]

Results

Compression therapy and drugs

We have no specific data on the efficacy of compression treatment and drugs in patients presenting with PREVAIT.

Chemical ablation

The efficacy of liquid sclerotherapy using one protocol–the compass technique–has been reported on a large series (253 legs) with a follow-up of 3.1±1.7 years (range, 1.5-5.7 years). The cumulative obliteration rate was sustained at >90% and there was a significant decrease in the venous dysfunction score. Unfortunately, the end point of sclerotherapy sessions was not given.[11] UGFS has been reported in 4 studies.

In a series by Kakkos et al, 45 lower limbs presenting REVAS were treated by UGFS (3% sodium tetradecyl sulfate foam). After the UGFS sessions they were assessed by DS.[12] In 28 legs, a reflux appeared at the level of the groin, in 5 legs at the perforator vein level, and isolated GSV in the rest of legs. Despite further sclerotherapy (single session with an injection of 6 mL in 58% of legs; ≥3 treatment sessions in 11%), complete occlusion at the end of treatment was achieved in only 39 of the 45 retreated lower limbs (87%).[12]

Darke and Baker treated recurrent GSV varices in 18 legs with UGFS (3% polidocanol foam). Persistent or reconstituted GSV trunks were seen in all legs. In the 6 weeks following treatment, clinical examination of re-treated legs and DS were performed. One treatment was sufficient to reach a complete occlusion in 10 legs, while 2 treatments had to be done in a further 5 legs. The 3 remaining legs had partial occlusion after 1, 2, or 3 treatments.[13]

Coleridge Smith reported the outcome of a series of 267 recurrent varices due to incompetence of the GSV managed by UGFS (mostly 3% STS foam). A total of 106 legs (40%) were reviewed at a mean follow-up interval of 11 months after treatment. The GSV had remained obliterated in 98/106 (92%); better than the 86% occlusion rate seen in primary incompetence.[14]

O'Hare et al reviewed 32 recurrent veins at 6 months after UGFS (3% STS foam). Occlusion rate on DS was 72% (23/32), and 88% (28/32) of the patients were satisfied with the results. There was no significant difference in occlusion rates between primary (45/60, 75%) and recurrent (23/32, 72%) veins. Unfortunately, information regarding the type of recurrence treated is missing.[15]

The most convincing data was the Birmingham' series. A total of 91 patients presenting with symptomatic recurrent great saphenous varicose veins were treated by 1 or 2 UGFS sessions. At a 1-year follow-up, above the knee reflux was eradicated in 81/88 lower limbs and below the knee reflux in 72/80 legs. Unfortunately, no data were provided concerning the presence or absence of symptoms and varices.[16]

Surgery

Surprisingly, very few data are available on the results provided by redo surgery in patients investigated preoperatively with DS. We reported a series of 145 limbs with a follow-up of 5 to 6 years. All had major reflux from the deep system at the SFJ or SPJ feeding recurrent varices that were treated by surgery. Postoperative sclerotherapy was performed in all patients during the first 2 years. An external audit revealed a global objective improvement of 85%, but there was better improvement in signs and symptoms than cosmetic appearance.[17]

The results of 2 studies using an interposition patch for treating recurrence at the SFJ have been published. Creton used this procedure without resection of the groin cavernoma, but with combined resection of varices (saphenous trunks and/or tributaries) had only 4.2% of recurrences at the SFJ at a mean 4.9-year follow-up (range, 3-7 years) in 119 extremities. Nevertheless, 22.6% of patients had diffuse varices, with a new site of incompetence between the deep and femoral systems.[18]

De Maeseneer et al compared the results at 5 years of 2 nonrandomized groups with and without a patch, respectively, group 1 and 2 in a prospective study. All patients had recurrent SFJ incompetence. At 5 years, thigh varicosity recurrences were observed in 58% of group 2 versus 26% of group 1.[19]

Thermal ablation

Fassiadis et al described his clinical experience on the use of radiofrequency ablation (RFA) in 18 treated legs for recurrent GSV. Recurrences were due to neovascularization at the SFJ in 15 legs, a persisting midthigh perforator in 2 legs, and a refluxing anterior thigh branch reconnecting with the GSV in 1 leg. None of the 18 legs had recanalization of the GSV at 1 month, and all patients returned to daily activities within 3 days. At 12 months, the occlusion rate was also 100% in the 16 follow-up patients. The only complication was a temporary sensory disturbance at the inner thigh in one-third of patients.[20]

Hinchliffe et al reported a randomized control trial in 16 patients with recurrent varices initially treated by isolated SFJ ligation.[21] For each patient, 1 leg was selected at random to receive redo high ligation (HL) + conventional stripping and the other RFA. RFA treatment was faster than traditional redo groin surgery (25.5 min vs 40 min; P=0.02), and caused less pain and bruising. On DS examination at a 12-month follow-up, 15 lower limbs in the group treated by RFA had complete GSV occlusion, 3 had partial occlusion. In the group treated by surgery, complete GSV stripping was reported in 14/16 lower limbs. The authors were in favor of RFA this was justified by shorter operative time and lesser postoperative bruising and pain.[21]

van Groenendael et al[22] retrospectively compared outcomes of 2 different procedures in 216 patients with a recurrent varicosity of the GSV. A total of 149 underwent conventional surgery consisting of redo HL+incompetent GSV or tributary phlebectomy and 67 patients were treated with endovenous laser ablation (EVLA).[17] All patients had previously been treated at least once with a saphenofemoral disconnection (SFD) with or without stripping of the GSV. Of the surgically treated legs, 87% had previously been stripped, while there were 57% who underwent EVLA. The conventional surgery was performed successfully in all legs and success was achieved in 100% of the EVLA legs. All treated veins remained occluded postoperatively according to the DS made an average of 8 weeks after EVLA in 46 legs (69%).

After a follow-up period of an average of 13.5 months in the conventional surgery group and of 15.0 months in the EVLA group, clinical recurrences occurred in 26% of the surgically-treated limbs and in 12% of the EVLA-treated limbs (*P*=0.024). This was no longer significant after correction for the length of follow-up. It must be highlighted that no definition was given for "clinical recurrence" by the authors and that repeated DS investigations were not performed. The postoperative pain score was significantly lower in the surgery group than in the EVLA group (*P*=0.02), and the median duration of postoperative pain was shorter (4.5 days in the surgery group vs 7 days in the EVLA group; *P*=0.03), but the use of nonsteroidal anti-inflammatory drugs was significantly higher in the surgical group. The authors concluded that if anatomically suitable EVLA is a good treatment alternative for recurrent GSV, only 31% of patients were suitable for EVLA in their series.[22]

In a series of 42 patients presenting PREVAIT in the SSV territory, 26 were treated by EVLA and 16 by surgery including redo SPJ ligation+SSV ablation±tributary phlebectomy. After correction for the follow-up duration, the difference in terms of results did not reach statistical difference.[23]

Embolization

At a 6-month follow-up, 90% of 215 patients treated by embolization of gonadal and pelvic veins were significantly improved in both signs and symptoms.[10] Conversely, Castenmiller et al, with a mean 1.8-year follow-up (range, 1-3.5 years), 33 patients presenting PREVAIT after previous surgical treatment of lower varices disappeared only in 12% (4/33) after embolization. The explanation, as suggested by the authors, may be related to inadequate treatment of incompetent pelvic veins as only ovarian veins were treated by embolization.[24,25]

Indications for treating PREVAIT patients

Patients complaining of symptoms

They present symptoms and/or esthetic concerns, and/or signs of chronic venous disease (C_2-C_6). In all cases, these patients need to be investigated by DS.

Subjects attending a routine follow-up

The decision whether to undertake DS, or not, depends on the presenting complaint and physical findings. In practice, DS is usually done.

Asymptomatic patients

When hemodynamic or anatomic abnormalities are found in asymptomatic patients without severe signs, who are not concerned by their minor varices as cosmetic problems, the decision to treat depends of the severity of the noninvasive findings. In all cases, follow-up is required knowing that abnormal DS findings precede symptoms and signs.

Symptomatic patients

In these patients presenting PREVAIT and hemodynamic anomalies, operative treatment must be considered. Although there is no RCT comparing redo surgery with chemical ablation, there is a consensus for treating them with UGFS as a first-line treatment for reasons exposed in the methods evaluation.[16,24] The European guidelines for sclerotherapy in chronic venous disorders gives a recommendation grade 1B in PREVAIT.[3] In very few cases, when DS reveals an intact and large incompetent saphenous stump at the SFJ or SPJ with a massive reflux filling the varicose network (*Figure 1*), redo surgery at the junction should be considered in combination with UGFS.

Patients in CEAP class C_{4b}-C_6, with PREVAIT and primary deep vein axial reflux

UGFS and valvuloplasty, in association, must be considered in active patients reluctant to wear lifelong compression or with a recurrent ulcer.

Guidelines for prospective studies

In order to know the prevalence and annual incidence of PREVAIT after nonconservative treatment, we need prospective, detailed, and well-documented studies from the outset of surgical treatment as was done in the series by Kostas.[26] These studies may give information on: (i) the value of routine postoperative scanning in the early detection of persisting reflux; (ii) the relationship between

hemodynamics and clinical recurrence; and (iii) the possible role of compression therapy and/or complementary postoperative sclerotherapy in preventing recurrences.

These studies may use both the updated CEAP and REVAS classification and a QOL questionnaire. Regarding the choice of the procedure, UGFS should be the first-line treatment for PREVAIT according to its satisfying outcomes. This method was assigned a 1B recommendation in the European Guidelines,[2] despite the lack of RCTs comparing UGFS versus other methods–such studies are difficult to implement.

Conclusion

PREVAIT is a frequent condition frustrating both patients and physicians and has been poorly evaluated. In order to build a scientifically convincing evidence base and to achieve a greater degree of comparability between studies, an international consensus on conformity is required.

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Postinterventional compression in phlebology: evidence and empirical observations

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Keywords:

elastic stocking; endovascular procedure; inelastic bandage; low pressure; strong pressure; surgical procedures

Abstract

There is almost a general agreement on the effectiveness of compression therapy in preventing unwanted side effects after procedures to remove superficial venous reflux. However, there is still a great debate on which material and compression pressure to use. In order to exert its effects, compression must occlude the vein segments ruptured by surgical or endovenous procedures. At the thigh, the critical segment in every venous intervention, the intravenous pressure is about 40 mm Hg and a higher compression pressure is necessary in order to narrow and occlude the veins. Despite this, intravenous pressure compression is infrequently applied with inelastic bandages (IB) or elastic stockings (ES), on top of eccentric compression devices, which are able to overcome the intravenous pressure and compress the vein. More often, compression is applied with simple ES exerting a 20 to 40 mm Hg pressure at the ankle, which will exert about 10 to 15 mm Hg at the thigh. This pressure is not enough to interfere with the vein diameter and occlude the vein; however, ES are claimed to be as effective as, if not better than, IB. In most studies, interface pressure exerted by compression devices is not measured, raising the suspicion that a good ES was compared with a poorly applied IB. In fact, in the few studies where compression pressure was measured, compression devices exerting a strong pressure were always more effective than ES exerting a low pressure.

When ES exerting strong pressure is compared with ES of milder pressure, or when ES is compared with no compression, the compression pressure exerted at ankle level is so light that it is as if "nothing" were to be compared with "nothing." Good results achieved when a low compression was applied post-procedure are maybe explained by painless procedures in small veins without tributaries or avoiding tributaries avulsion.

Introduction

There is an almost general agreement that leg compression after any kind of vein procedure (surgery, endovascular laser treatment, foam sclerotherapy) is effective in preventing thrombosis of the superficial and deep vein; reducing bruising, hematoma, and hemorrhage; minimizing inflammation and pain; preventing

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recanalization and neovascularization; and compression therapy seems to shorten recovery time and sick leave.[1-10]

Despite these generally accepted benefits, there are not many well-designed, randomized, clinical trials comparing different compression devices and resulting in clear outcomes. In some clinical trials, unfortunately often with major methodological flaws, different compression devices exerting mild to very strong compression pressure were reported to be effective in preventing unwanted effects and minimizing pain, and as a consequence, there is no agreement on which kind of compression should be used.

The following will give an overview on what we currently know about compression after vein procedures. As the crucial area when dealing with vein procedures is the thigh, this paper will be focused on thigh compression.

Compression pressure to occlude the thigh veins

The main purpose of postoperative compression is to narrow or occlude the vein segments that might have been traumatized by endovenous procedures (or the segments surrounding the removed vein in open surgery) in order to keep the treated veins or the vein track free from clots. To narrow/occlude the venous lumen, the compression pressure must overcome, or at least, be very close to the intravenous pressure. Ideally, the compression pressure should increase in the standing position and during muscle contraction, and should narrow/occlude the vein lumen.[11]

Venous pressure in the lower leg equals the weight of the blood column by the measuring point from the right heart to the lower leg. Assuming that the specific weight of blood corresponds to that of water, a blood column of 100 cm (eg, between the calf and the right heart) would exert an intravenous pressure of 73.5 mm Hg at the midcalf. Considering a distance between the midthigh and the heart of 50 cm, pressure in the midthigh femoral vein would be about 37 mm Hg in the standing position.

Duplex examination confirms that a compression pressure higher than 70 mm Hg is necessary to occlude the calf veins and 40 mm Hg is required to occlude the thigh veins.[12-15] A thigh-length elastic stocking exerting a pressure of 20 to 30 mm Hg on the lower leg will provide a pressure of 10 to 15 mm Hg at thigh level. These stockings will produce some vein lumen reduction in the supine position, but will not be able to reduce the vein diameter at thigh level in the upright position.

Clinical reports on postprocedural compression

Some authors measured the pressure exerted by compression devices applied after flush ligation and stripping of the great saphenous vein.[7,16,17] They reported a significant improvement in prevention of hematoma, hemorrhage, and pain when comparing strong pressure with mild pressure–superficial and deep vein thrombosis never occurred. Travers et al[7] compared strong compression using a short-stretch, adhesive bandage on one leg with low compression using a nonadhesive crevic-crepe bandage on the other leg in ten patients who underwent bilateral high ligation and stripping. The primary outcome was postsurgical bleeding measured by using 99 m Tc-labeled red blood cells. He concluded that bleeding was significantly reduced in the strong compression group.

In the paper by Benigni et al,[16] 53 patients underwent great saphenous vein ligation and stripping and received an elastic stocking postoperatively with or without a stiff pad applied along the vein track. The pressure exerted by compression increased in the supine position from about 14 mm Hg without the pad to about 49 mm Hg when the pad was added. Pain, the primary outcome in this study, was decreased by half in the patients where the stiff pad was added.

In our experience,[17] 54 patients who underwent flush ligation and stripping were randomly divided into three groups to postsurgically receive one elastic stocking exerting a very light pressure (≈10 mm Hg) on the thigh; the same stocking on top of a stiff rubber foam pad firmly stuck to the skin over the vein track by means of plasters to locally increase the pressure (exerting a pressure >60 mm Hg); or a stiff inelastic adhesive bandage exerting a pressure of about 40 mm Hg. Pain, bleeding, hematoma, superficial and deep vein thrombosis were the primary outcomes. The patients treated with a stocking on top of the stiff device or an inelastic adhesive bandage had significantly better outcomes regarding pain, hemorrhage, and bleeding when compared with elastic stockings alone.

In the paper by Lugli et al,[18] where compression pressure was not measured, 200 patients treated by endovenous laser ablation were randomly assigned to receive one

elastic stocking exerting a pressure of 35 mm Hg at the ankle or the same stocking on top of a self-made cotton roll firmly stuck to the skin over the vein track by means of plasters to locally increase the pressure. Even if the compression pressure was not measured, it is conceivable that, when the cotton roll was added, the local pressure along the great saphenous vein was increased under the same stocking. The primary outcome in this paper was postprocedure pain. The primary outcome was significantly lower in the group treated with stronger compression and was achieved by placing the cotton roll under the stocking.

In conclusion, strong compression pressure over the treated segments is obviously more effective to control the side effects compared with lower compression. Strong compression is widely used after surgery, foam sclerotherapy, and other endovascular procedures.[19-22]

Bradbury et al[19] suggest minimizing pain and inflammation after sclerotherapy by applying cotton rolls over the treated veins and tributaries, fixing the rolls to the skin with crevic-crepe bandages, and finally, superimposing an elastic stocking. Biemans et al[20] and Rasmussen et al[21,22] compared endovenous laser ablation, foam sclerotherapy, and vein stripping in 861 patients, globally. Following vein procedures, they applied some dressing over the treated area and an inelastic bandage for 2 days and then moved to an elastic stocking. Therefore, at least for the first 2 days, when the greatest part of inflammatory and hemorrhagic events takes place, a strong pressure over the thigh was exerted.

This attitude of applying a strong compression pressure following vein procedures has been questioned in other publications that claim to have a greater or similar effectiveness with strong elastic stockings vs light elastic stockings, or with elastic stockings vs bandages.[2,5,23,24] Shouler et al[2] compared high vs low compression stockings (40 mm Hg vs 15 mm Hg at the ankle) after varicose vein surgery and found that both were equally effective in controlling bruising and thrombophlebitis. Scurr et al,[23] Bond et al,[5] and Mariani et al[24] compared compression exerted by elastic stockings and by different types of bandages after sclerotherapy[23] or flush ligation and stripping,[5,24] and did not find any difference between groups or a better reported outcome with elastic stockings.[24]

In other publications, postprocedure compression is considered useless.[25-27] In the paper by Pittaluga and Chastanet,[25] the authors performed a minor surgery with some small side branch avulsion under local anesthesia. After this procedure, an elastic stocking was donned by all the patients for the first 24 hours; then patients were divided into two groups and only one group continued with compression for 8 days without any additional benefit compared with the group without any compression.

In the second work, by Maurins et al, 94 patients were divided in three groups after laser ablation of the great saphenous vein with 1470 nm diode laser and 2 rings fiber.[26] The first group wore elastic compression stockings only during the day for one week, the second group wore elastic compression stockings during the day for four weeks, and the third group did not receive compression. At the end of the observation period, the outcomes were the same–in terms of both vein occlusion and pain.

In the third work, by Hamel-Desnos et al,[27] a small dose of foam polidocanol at a light concentration (4 mL at 1% on average) was injected in the great saphenous trunk. The patients were subsequently divided into two groups: (i) the "no treatment" group did not receive compression; (ii) the control group wore a light compression stocking for some hours during the day and the compliance was very poor (only 40% of patients wore the elastic compression stockings as prescribed). Therefore, it is not hard to understand that, in these conditions, no differences were found between groups.

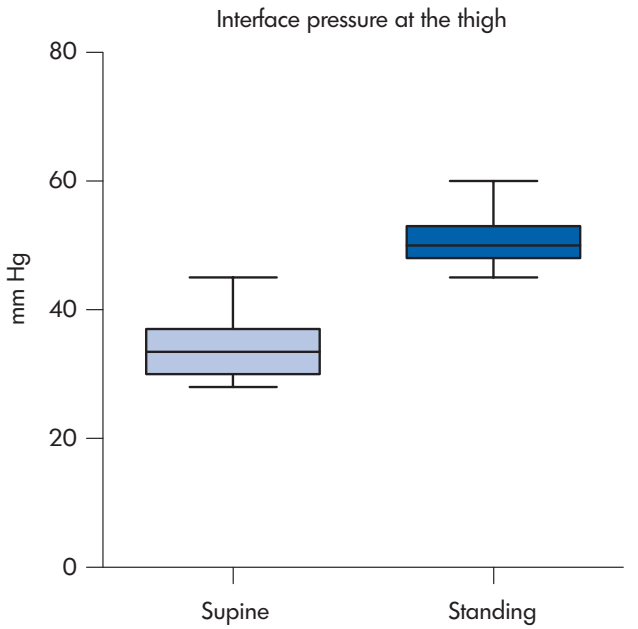
Recommendations from the guidelines

Even if it was clearly shown that thigh veins could be compressed only by exerting a strong compression, the guidelines are quite vague in giving recommendations. Reflecting the lack of proven clinical effectiveness of one compression modality compared with others, the NICE (National Institute for Health and Care Excellence) guidelines do not provide any recommendation,[28] while other guidelines indifferently suggest compression with any kind of modality (elastic stockings, elastic bandages, or inelastic bandages).[29-33]

Empirical observations

In our own clinical practice, we usually apply cotton rolls along the veins treated by flush ligation and stripping, endovenous laser ablation, or foam sclerotherapy. We fix them tightly to the skin by means of a crevic-crepe bandage and finally superimpose an elastic stocking exerting 23 to 32 mm Hg at the ankle. This kind of bandage is easy

to apply, taking only a few minutes, and is generally well tolerated. In 30 patients, we measured the pressure exerted at the thigh with this compression device and found an average compression pressure of 33.5 mm Hg (interquartile range [IQR], 30-37) in the supine position and about 50 mm Hg (IQR, 48-53) in the standing position (*Figure 1*). We ask that the patients wear all of this material for as long a time as they are able to tolerate, but at least for 3 days, and then they can remove the bandages and cotton rolls and keep on only with the elastic stockings.



	Supine	Standing
Minimum	28.00	45.00
25% Percentile	30.00	48.00
Median	33.50	50.00
75% Percentile	37.00	53.00
Maximum	45.00	60.00

Figure 1. Compression pressure measured at the thigh in the supine and standing position with a compression device made up of an elastic compression stocking plus an inelastic bandage made up of an eccentric compression device and crevic-crepe bandage.

In our experience, some patients complain about a light discomfort caused by the compression system, but never about inflammation and pain. When it happens that poorly compliant patients remove their compression device too soon, they frequently experience pain, and this pain can be strong, requiring a new consultation. By reapplying a strong compression, pain disappears within a few hours.

Discussion

It remains to be clarified why so many colleagues are satisfied with light compression or even no compression on the thigh after vein procedures and why in some comparative studies elastic stockings exerting no more than 10 to 15 mm Hg at the thigh are reported to be equivalent to, or even more effective than, bandages that should exert a much stronger pressure.

There are some possible explanations:

1. In the studies comparing different compression devices, compression pressure at the thigh was almost never measured. When stockings exerting a strong pressure, up to 40 mm Hg, were compared with stockings exerting a light pressure at the ankle,[2] they achieved about 15 mm Hg at the thigh, which is not enough to compress the thigh veins; therefore almost nothing was compared with nothing and it is not surprising that the difference between treatments was not significant.

2. In the cases where elastic stockings were compared with bandages: (i) we do not know anything about the compression pressure of the bandages because it was not measured; (ii) we do not know what kinds of bandages were applied (elastic or inelastic); and (iii) the skill of bandagers, bandage slippage, or bandage rolling are never reported. In this condition, the suspicion that an effective elastic stocking was compared with a poorly applied bandage is very strong. Another explanation suggesting that compression pressure significantly falls with inelastic bandages,[6] coming close to or lower than the compression exerted by an elastic stocking, is hard to accept. When we measured interface pressure at the thigh after vein surgery, immediately after application, and after 1 week, the pressure exerted by a correctly applied inelastic bandage, despite a massive pressure drop, was still, on average, 17 mm Hg and 31 mm Hg in supine and standing position, respectively, which was always significantly higher than that of an elastic stocking (12 and 14 mm Hg in supine and standing positions, respectively).[17]

3. When compression by an elastic stocking is compared with no compression, especially when using compression stockings classified according

to the French standard,[25,27] the pressure at thigh level is so light that practically the comparison is nothing vs nothing, which is especially true when patient compliance is poor.[27]

4. There are some important variables that are hardly considered in reported papers, but which could explain some satisfactory results also with low or no compression: (i) the diameter of the treated trunks and number of tributaries, and avulsion or no avulsion of tributaries; (ii) laser wavelength (new laser wavelength of 1470 nm is almost painless); (iii) the amount and concentration of sclerosing agent; (iv) the level of pain tolerance by patients; and (v) the level of acceptance of unwanted effects by surgeons. To make it very simple: we need to face two completely different situations when treating patients affected by huge great saphenous trunk and many varicosities by flush ligation and stripping, and multiple stab avulsion or tributary phlebectomy; or treating a patient with a small great saphenous vein without varices not needing stab avulsion or tributary phlebectomy by a 1470 nm laser. It is conceivable that the first patient will need strong compression pressure and the second maybe only an elastic stocking for a few days.

Conclusion

If the compression of calf veins is necessary to minimize the traumatized veins after procedures and prevent undesired effects, we need a strong compression pressure in order to overcome the intravenous pressure. This pressure needs to be higher than 40 mm Hg when standing, which is out of the range of a compression stocking. Only inelastic bandages firmly stretched or elastic stockings with some eccentric compression devices can exert this pressure range, and are to be used when large vein trunks and varices are treated.

It is conceivable that when using poorly traumatic procedures, such as new laser wavelengths or small amounts of sclerosing agent in small vein trunks without performing varicectomies stab avulsion or tributary phlebectomy, a light compression may be enough.

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Great saphenous vein transitory reflux in patients with symptoms related to chronic venous disorders, but without visible signs (C0s), and its correction with MPFF treatment

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Keywords:

chronic venous disorders; MPFF; diagnosis; great saphenous vein; micronized purified flavonoid fraction; quality of life; symptoms; ultrasonography; venous reflux

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Abstract

Aim: the study was aimed at investigating the frequently encountered clinical group of patients presenting with subjective leg symptoms without visible signs of chronic venous disorders. The great saphenous vein (GSV) of such patients was investigated using duplex scanning (DS) to verify whether a reflux could occur in certain circumstances, ie, at the end of the day in an orthostatic position. If there was a reflux, the possibility to eliminate it with a drug treatment, ie, MPFF, was assessed.

Material and methods: women consulting for complaints related to chronic venous disorders (CVDs) of the lower extremities, but without visible signs; therefore, with a C0s, En, An, Pn classification according to the Clinical, Etiological, Anatomical, Pathophysiological (CEAP) classification, were enrolled. Symptoms were assessed using a 10 cm visual analogue scale (VAS) and the patients' quality of life was assessed using the Chronlc Venous Insufficiency Quality of life questionnaire-20 items (CIVIQ-20). Patients underwent a DS of the lower extremities in the upright position twice a day: once in the morning (before 10 AM) and once in the evening after normal physical efforts (after 6 PM). The investigations included the following measurements: (i) reflux duration; (ii) GSV diameter in the groin area (mm); and (iii) difference in the GSV diameter between the evening and morning values (mm). Patients with evening reflux received a 2-month pharmacological treatment with MPFF (1000 mg of MPFF once a day in the morning). A DS investigation was repeated after 2 months of treatment in these patients.

Results: a total of 41 C0s women aged 21 to 57 years (mean age, 35.4±15.1 years) were enrolled in the study and then investigated with DS. A total of 15 of the patients had no reflux, either in the morning or in the evening. The remaining 26 patients had no reflux in the morning, but presented with an evening GSV

reflux. As for reflux extent, 2 had an axial reflux and 24 had a segmental reflux, of which 11 were proximal and 13 were medial. Regarding reflux type, 4 had an intervalvular reflux and 22 had a commissural reflux. The evening GSV diameter in the subgroup with reflux (n=26) was significantly larger ($P<0.05$), compared with patients without evening reflux (n=15; 6.33 mm [95% confidence interval (CI), 4.50-8.00 mm] *vs* 5.45 mm [95% CI, 4.00-6.50 mm]). This was also true for the difference in GSV diameter between the evening and morning (0.82 mm [95% CI, 0.30-1.20 mm] *vs* 0.42 mm [95% CI, 0.10-0.65 mm]). Of the 26 patients with previous baseline evening GSV reflux who were investigated after a 2-month MPFF treatment, 22 no longer had reflux at 6PM, and 4 had a nonsignificantly reduced length of reflux. In parallel, the GSV diameter decreased from 6.33 mm (95% CI, 4.50-8.00 mm) to 5.50 mm (95% CI, 1.10-7.00 mm), and the difference in GSV diameter between the evening and morning decreased from 0.82 mm (95% CI, 0.30-1.20 mm) to 0.37 mm (95% CI, 0.10-0.70 mm; $P=0.000008$). There was a parallel significant decrease in the intensity of subjective symptoms as demonstrated by the VAS score and a significant improvement in the patients' quality of life after treatment ($P=0.00001$ for both).

Conclusion. Cos, En, An, Pn patients may present with a transient reflux in the GSV that occurs at the end of day. Objective abnormalities can be detected by DS investigations and by measuring the difference in GSV diameter between the morning and the evening. Treatment with MPFF (1000 mg of MPFF once a day in the morning for 2 months) resulted in the elimination of the evening GSV reflux in most of the treated patients, decrease in vein diameter and also resulted in beneficial effects on symptom relief and quality of life improvement.

Introduction

The Cos, En, An, Pn patient according to the Clinical, Etiological, Anatomical, Pathophysiological (CEAP) classification describes a particular kind of patient with chronic venous disorder-related symptoms, such as heavy legs in the upright position, restless legs, sensation of swelling particularly in the evening, but without visible signs of chronic venous disorders (CVDs).[1,2]

Despite the fact that the condition is often encountered in daily practice, the so-called phlebopathic symptoms are scarcely broached in the literature. Although, it is hard to interpret the meaning of these symptoms when there are no objective signs of CVDs.

In the 80s', the Italian group of Andreozzi et al indicated that the prevalence of such subjects was about 20% of all people visiting their vascular lab with a suspicion of CVDs.[3] Thirty years later, the same prevalence of Cos subjects was found in the Vein Consult Program, which included more than 90 000 subjects consulting their practitioner in 23 countries.[2] However, the Italian team was able to find some objective abnormalities in the venous tone by plethysmographic investigations and by measuring the difference between the venous diameters in the supine and in the upright position using duplex scanning (DS). At that time, associated symptoms, such as leg pain and heaviness, were attributed to an increase in venous wall compliance. Therefore, the "Pn" scoring for "no pathophysiology detectable" might be disputed.

Since then, theories have evolved and it seems important to remember that venous valve incompetence is central to the venous hypertension that appears to underlie most or all of the symptoms and signs typically associated with CVDs.[4] In most cases, venous hypertension is caused by reflux through incompetent valves in the superficial venous system. Reflux and subsequent hypertension promote chronic venous inflammation, which is likely to be responsible for the disease progression toward complications. Genetic risk factors, hormonal impregnation, prolonged hydrostatic load, and abnormal fluid shear stress may serve as mechanisms that lead to a cascade associated with an aseptic inflammation.[5] Activated endothelium, leukocytes, mast cells, macrophages, and fibroblasts target the extracellular matrix as well as parenchymal cells to produce a spectrum of inflammatory mediators and metabolites, membrane adhesion molecules, prothrombotic receptors, growth factors, and chemotactic agents. The inflammatory cascade in CVDs serves as a tissue repair mechanism, but the resulting valvular incompetence may favor further inflammation, which leads, in turn, to venous stasis and clinical manifestations (from varicosities to, ultimately, the occurrence of ulcers). Evidence is accumulating that surgery aimed at preventing venous reflux can also aid healing and prevent the recurrence of venous ulcers.[6]

At the very beginning of disease, the Cos patients (named phlebopathic patients by Andreozzi et al) may also have reflux in the subcutaneous trunks revealed by DS.[7] The Italian team, on its side, did not find any reflux in such patients upon DS investigation, but they detected a localized valve dysfunction with flaps or prolapse.[8] A recent study has shown that incompetence can occur in human small superficial venous valves of C0 and C1 subjects, independently of

reflux within the great saphenous vein (GSV) and major tributaries.[9] Reflux in these micro venous valves may play a role in the appearance of venous symptoms, but we are presently unable to perform this assessment.

In our experience, and although the diagnosis of phlebopathy is based primarily on the patient's complaints, some objective signs such as venous hypervolemia could be identified.[10,11,12] Venous hypervolemia is typified by its occurrence at the end of day and manifests by an increase in the volume of the calves, resulting in increased tightness when putting on long boots (also known as the "tight boot" symptom).[10] The significant changes in the volume of the lower extremities, primarily the calves, are confirmed by plethysmography,[10] as well as by an increase in the diameter of veins measured by repeating DS before and after prolonged orthostatic load.[12]

Since phlebopathy is thought to be not only a problem of venous tone, but also a question of valve dysfunction paired with venous inflammation, we searched for pharmacological treatments with a comprehensive mode of action that acts on the venous wall tone[13] and is able to preserve venous valve structure.[14] The beneficial anti-inflammatory and venoprotective actions of the micronized purified flavonoid fraction (MPFF)* has been evidenced in many studies of treatment efficacy in various forms of CVDs.[13,15] Therefore, we chose MPFF for the present study that was designed to:

- Investigate the peculiarities of the GSV reflux in C0s (phlebopathic) patients after a prolonged time in a standing position (in the evening), before and after treatment with MPFF.
- Assess the associated venous symptoms and the quality of life of enrolled patients before and after treatment with MPFF.

Also registered as Daflon 500 mg, Alvenor, Ardium, Arvenum, Capiven, Detralex, Variton, Venitol

Material and Methods

This was an open-label study to analyze the efficacy of MPFF on transitory reflux and associated symptoms in phlebopathic patients assigned to the CEAP class C0s, En, An, Pn. Women complaining, at the end of the afternoon, of leg heaviness, pain, cramps and sensation of swelling in the calves, which were relieved after rest, were included in the study. The exclusion criteria were as follows: (i) history of vein surgery or sclerotherapy; (ii) history of venous thrombosis; (iii) presence of any visible venous signs on the lower extremities; and (iv) presence of concomitant diseases such as heart, lung, liver, or kidney insufficiency.

In addition to the routine clinical examination, all patients underwent DS of the lower extremities in the upright position twice a day: once in the morning (before 10 AM) and once in the evening after normal physical effort and being in an upright position (after 6 PM). The reflux was considered abnormal if its duration was longer than 0.5 seconds.[16] We also measured GSV diameter (mm) at the terminal segment in the evening and in the morning, and calculated the difference between the values for GSV diameter. The women with a detectable evening GSV reflux received MPFF (1000 mg once a day in the morning) for 2 months. Patients were not allowed to wear elastic compression stockings during the study period.

Duplex scanning was repeated after 2 months of MPFF treatment, as well as the measurement of GSV diameter, both in the morning and in the evening. Intensity of symptoms, such as heavy legs, pain, and cramps, was measured on a 10 cm visual analog scale (VAS) at baseline and at the end of MPFF treatment. The quality of life (QOL) was also assessed using the self-questionnaire ChronIc Venous Insufficiency Quality of life questionnaire-20 items (CIVIQ-20) at baseline and after 2 months of MPFF treatment. The global index score (GIS) of CIVIQ-20 ranges from 0 to 100. A GIS of 100 means the highest possible QOL, whereas a GIS of 0 means the worst possible QOL.

Statistical analysis was performed with Statistica 6.0 software. Mean values of parameters were calculated with a 95% confidence interval (95% CI). Group comparisons were done using a nonparametric Wilcoxon test.

Results

The study was performed in 2013 and included 41 women aged 21 to 57 years (mean age, 35.4±15.1 years) assigned to the CEAP class C0s, En, An, Pn. The intake of oral contraceptives and hormone replacement therapies within the past 5 years was reported in 22 women (54%). All women complained of heaviness and pain in the calves at the end of the afternoon. Night cramps and an increase in leg volume (the symptom of "tight boot") were also reported in 21 and 28 women, respectively.

Duplex scanning investigation

A total of 15 of the 41 enrolled women had no reflux, either in the morning or in the evening. The remaining 26 women had no reflux in the morning, but presented with an evening GSV reflux. As for reflux extent, 2 had an axial reflux and 24 had a segmental reflux, of which 11 were proximal and 13 were medial. Regarding reflux type, it was found to be commissural in 22 and intervalvular in 4 women (*Table I*). It is important to note that in the 26 women with an evening reflux (*Figure 1*), the morning DS investigation after a night's rest did not show any reflux.

Extent of GSV reflux at evening assessment (number of patients)			Type of GSV reflux at evening assessment (number of patients)	
Axial	2		Intervalvular	4
Segmental	Proximal	11	Commissural	22
	Medial	13		
Total		26		26

Table I. Reported reflux in the great saphenous vein (GSV) of the 26 Cos women (with phlebopathy).

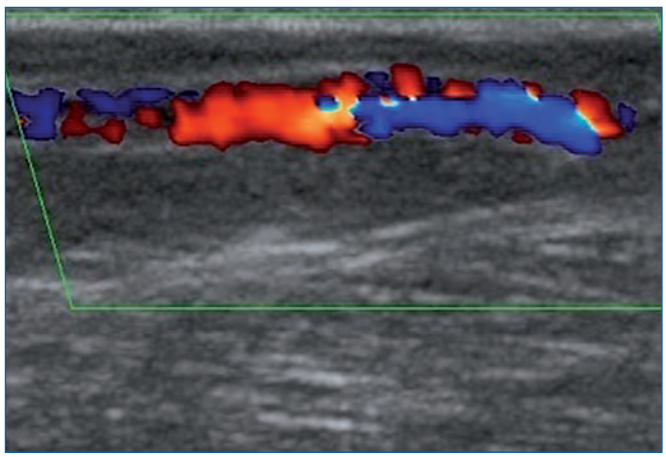

Figure 1A. Longitudinal section of the great saphenous vein at the lower third of the thigh. Segmental reflux on duplex scanning examination in the evening after being in a prolonged upright position.

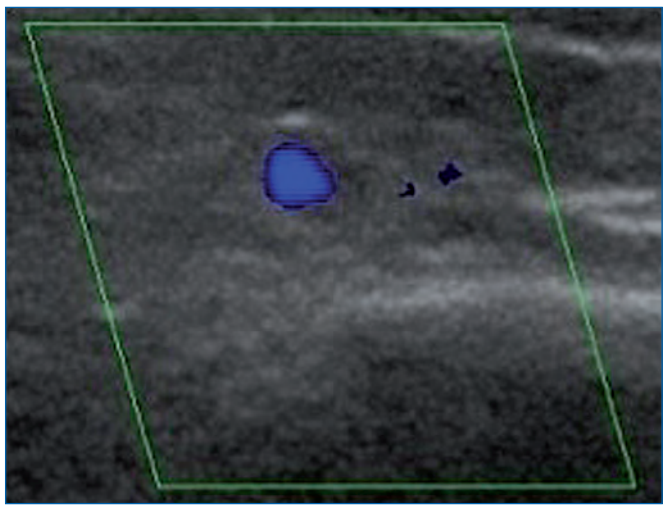

Figure 1C. Cross-section of the great saphenous vein in the valve area at the lower third of the thigh allowing assessment of vessel diameter (4.5 mm). Absence of reflux on duplex scanning examination in the morning after rest.

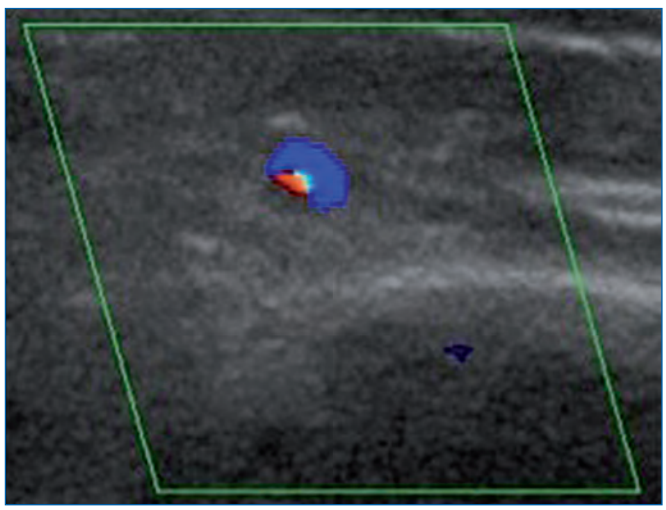

Figure 1B. Cross-section of the great saphenous vein at the lower third of the thigh allowing an assessment of vessel diameter (4.8 mm). Commissural reflux on duplex scanning examination in the evening after being in a prolonged upright position.

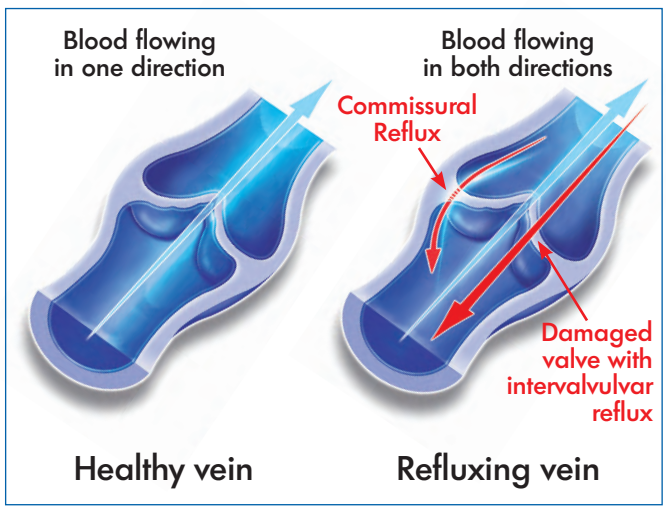

Figure 1D. Illustration of a commissural reflux.

Assessment of the great saphenous vein diameter

We compared the GSV parameters in the GSV terminal segment between women presenting with evening reflux and those without evening reflux. The evening GSV diameters and the difference in GSV diameter between evening and morning in the subgroup with reflux were higher ($P<0.05$) than in the subgroup without reflux (*Table II*).

Mean GSV diameter in mm (95% confidence interval)	Evening diameter	Difference between evening and morning
Patients with evening GSV relux (n=26)	6.33 (4.50-8.00)	0.82 (0.30-1.20)
Patients without evening GSV relux (n=15)	5.45 (4.00-6.50)	0.42 (0.10-0.65)
P value	0.044554	0.00065

Table II. Parameters related to the great saphenous vein (GSV) diameter at the GSV terminal segment in patients with and without reflux (n=41).

Effect of MPFF treatment on evening reflux and on vein diameter

The evening reflux was eliminated in 22 of the 26 women. The 22 women with no longer evening reflux presented with a commissural reflux at baseline. In the 4 women who had intervalvular reflux, the extent of reflux slightly decreased, but this was not statistically significant. The evening vein diameter decreased to normal valves after MPFF treatment (*Table III*).

Effect of MPFF treatment on symptom relief and quality of life

The change in the intensity of associated venous complaints, such as heaviness, pain, and night cramps, in patients before and after treatment is shown in *Figure 2*. Interestingly, evening leg heaviness, pain, and cramps significantly decreased after 2 months of MFPP treatment. A parallel improvement in their QOL was seen with CIVIQ-20: from 57.97±7.63 at baseline, the GIS increased to 69.64±8.65 after a 2-month treatment with MPFF ($P=0.000001$).

Mean GSV diameter in mm (95% confidence interval)	Evening diameter	Difference between evening and morning
At baseline	6.33 (4.50-8.00)	0.82 (0.30-1.20)
At month 2 after MPFF treatment	5.50 (1.10-7.00)	0.37 (0.10-0.70)
P value	0.000008	0.000008

Table III. Parameters related to the great saphenous vein (GSV) diameter in the terminal segment in women with evening reflux (n=26) at baseline and after a 2-month therapy with MPFF.

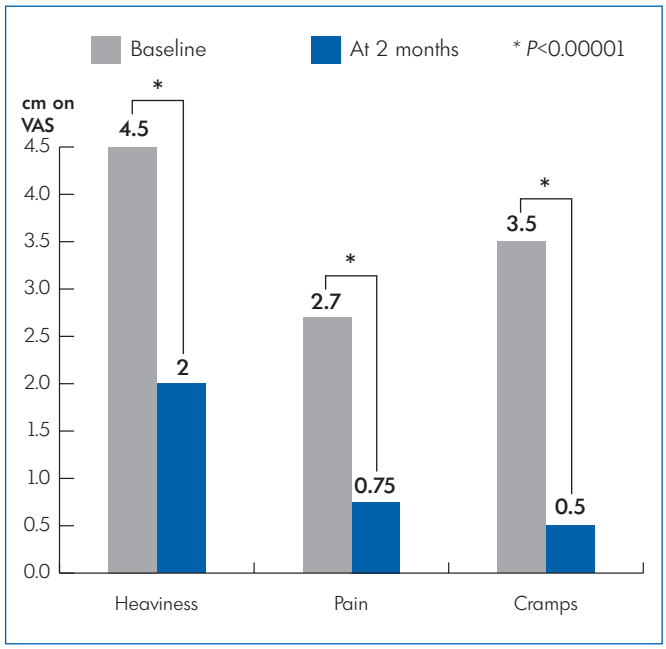

Figure 2. Symptom intensity on the 10 cm visual analog scale (VAS) before (baseline) and after MPFF treatment (at 2 months).

Discussion

Transitory segmental incompetence occurred in almost half of the Cos patients of the present study. Such reflux was not present in the morning after a night's rest because it is not related to destruction of valves. In addition, the majority had a transitory reflux of the commissural type. Commissural reflux, through one or both spaces between the valve leaflets of the lower third of the thigh in young patients in the standing position, has previously been demonstrated by Shadeck.[17] Although it hemodynamically mimics pathological reflux as the duration greatly exceeds 0.5 seconds, it remains localized to the valve with no distal extension and fully meets the definition of reflux through a healthy valve demonstrated in the GSV terminal segment. Shadeck considers that this might reflect no more than slow closure of the commissural space. For Van Cleef, such transitory incompetence affecting valves with a normal appearance is the reflection of a dilatation of the perivalvular venous ring without significant damage to the valve apparatus itself.[18]

Two of the enrolled women presented with intervalvular reflux, which is usually associated with incompetent valve leaflets that are damaged and no longer function. Such reflux is considered pathologic. The MPFF treatment slightly decreased reflux length in these 2 patients even though this improvement was not statistically significant.

In our study, transitory reflux was associated with an increased GSV diameter in the evening compared with the morning. Increased GSV diameter participates to the occurrence of a reflux because it prevents valve leaflets from closing properly. Previous studies have correlated increasing GSV diameter with increasing CEAP clinical classification, but failed to demonstrate that decreasing GSV diameter improves QOL.[19] On the other hand, the presence of venous symptoms greatly worsens the QOL of CVDs patients.[20] In our study, improvement in QOL might not be related to a decrease in GSV diameter by MPFF, but rather to symptom improvement.

MPFF significantly decreased GSV dilatation, thereby facilitating valve closure. The improvement in the viscoelastic properties of GSV by MPFF was evidenced in earlier works.[21] In the case of MPFF, venous tone is reinforced by modulation of noradrenergic signaling through reduced norepinephrine metabolism.[21,22]

The mechanism that triggers dilatation of the perivalvular area is currently unknown. For Shadeck, there is no demonstrated evidence that transitory reflux heralds irreversible valve incompetence,[17] and yet, Schultz-Ehrenburg has previously shown that a preclinical venous reflux in children not only precedes the occurrence of truncal varicose veins (W), but also that such reflux represents a 30% risk (95% CI, 13% to 53%) of developing W disease within 4 years.[23] It can be speculated that, in predisposed subjects, such as the Cos ones, a prolonged standing position and subsequent prolonged pooling of blood causes distortion of the venous valves and leads to reverse venous flow. Such flow disturbances can initiate and maintain an inflammatory reaction, which is responsible for the associated venous symptoms seen in the Cos subjects. Inflammatory events occur largely in response to abnormal venous flow and are important in causing the adverse changes in both the venous valves and vein wall that, in turn, become irreversible with time.[4] One of the most peculiar features of the mode of action of oral MPFF is its ability to protect valve morphology in models of venous hypertension. Such protection is related to attenuation, by MPFF, of various elements of the inflammatory cascade, notably the endothelium-leukocyte interaction.[13,14] This could explain the results found in the present study.

Despite the fact that hormonal influence on the occurrence of CVDs in women is disputed, sex hormones are included in the risk factors traditionally cited as contributing to venous valve failure; these also include female sex, pregnancy, obesity, a standing occupation in women,[24] and heredity.[25] Receptors to estrogen and progesterone exist in the GSV wall.[26] Progesterone is known to inhibit smooth muscle contraction, and is useful in preventing uterine contraction and spontaneous abortion. However, preventing vein wall smooth muscle contraction allows passive dilation of veins, and when a critical diameter is reached, a functioning venous valve becomes dysfunctional or incompetent.[27] As half of a woman's adult lifetime is under the influence of progesterone, which is exacerbated during pregnancy, it is no wonder that primary venous insufficiency is twice as common in women than in men.[24]

A recent study has shown that during the menstrual cycle, diameter and valve closure time of the lower limb veins increases. The authors hypothesized that such changes are mediated by the female sex hormones.[28] However, the time of the menstrual cycle was not reported in our study and was one of its limitations. Reversible transient reflux occurring after prolonged standing is not consistently reproducible.[29] Therefore, several DS evening assessments on consecutive days would have been desirable, but were not possible to perform due to limitation in study costs, reflecting another limitation of our study.

Conclusion

Our study has shown that active pharmacological treatment, such as treatment with MPFF, can protect valve structures from further damage, decrease GSV diameter, and eliminate transitory incompetence in active women who undergo prolonged periods of standing. This was significant in women with commissural transitory reflux. At the same time, MPFF relieved these women from venous symptoms and improved their quality of life.

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Deep vein thrombosis and air travel: risk management in 2015

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Abstract

Long-haul flights increase the risk of venous thromboembolism (VTE) for several weeks after the flight by 3-fold among passengers compared with the general population. The risk increases with flight duration and persists for several weeks (until week 8) after landing.

This risk is not the same for all passengers and should be determined before any long flight, especially among frequent travellers. The calculation of risk is based on simple clinical data, easily obtained by the treating physician. If the patient has a personal history of VTE and chronic venous disease, a full assessment by a vascular specialist is justified.

Risk management for any passenger taking a long flight is based on some simple advice to follow during the flight.

This article summarizes the current position and recommendations from cardiovascular physicians faced with managing the risk of VTE in patients planning long-haul flights.

Keywords:

anticoagulant, compression therapy, deep venous thrombosis, long-haul flight, recommendation, venous thromboembolism

Introduction

Cases of venous thromboembolism (VTE) following a flight are occasionally reported by the media, particularly when a celebrity is involved, and have led to the condition being nicknamed "traveller's thrombosis." This article summarizes the epidemiological data on the prevalence of VTE, as well as the current position of cardiovascular physicians faced with managing the risk of VTE in patients planning long-haul flights.

Epidemiological overview

Recent epidemiological data vary widely depending on the thromboembolic location: pulmonary embolism, proximal (including popliteal, femoral, and iliac veins) or distal deep vein thrombosis, superficial venous thrombosis, and by whether the thrombosis is symptomatic or asymptomatic (discovered by chance during a Doppler ultrasound examination).

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The prevalence of deep vein thrombosis (DVT) documented by Doppler ultrasound within 48 hours of landing is between 2% and 10%, identical to that of hospitalized patients with a medical illness (Prevention of Recurrent VENous Thromboembolism [PREVENT] study.[1]

The absolute risk of symptomatic DVT confirmed by Doppler ultrasound is 3.2 (95% confindence interval (95% CI), 1.8, 5.6) after a 4-hour flight, a rate equivalent to one event per 4656 flights according to data from the records of 8755 employees from a range of international companies who travel for business.[2] The risk of VTE was increased by exposure to more flights during a short period and to longer flights. Risk was greatest in the first 2 weeks after a flight,[3] but remained elevated for 8 weeks.[2]

Lapostolle et al reported an incidence of pulmonary embolism among passengers arriving at the Charles de Gaulle Airport of 56 per 135 million passengers.[4] When the data were analyzed by flight duration, the incidence ranged from 1 event per million passengers, if the flight was less than 6 hours, to 1 event per 700,000 passengers if the flight was longer than 6 hours.

A meta-analysis of 14 studies examining air travel and risk of VTE reported a relative risk of 2.8 (95% CI, 2.2, 3.7).[5] This is also the figure reported in the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.[6]

The risk of VTE associated with long-haul flights has also been confirmed in an approach using record linkage, which demonstrated that between 4% and 20% of patients with a VTE had travelled in the weeks prior to the acute episode.[7]

A reminder of the pathophysiological mechanisms favoring venous thromboembolism in air travellers

The pathophysiological mechanisms for VTE are based on Virchow's triad of venous stasis, vascular endothelial lesions, and hypercoagulability of circulating blood. Periods of prolonged sitting without moving the calf muscles promote venous stasis.

The pressurization of the aircraft cabin is also a factor: flights of more than 2400 meters altitude can provoke hypobaric hypoxia, a risk factor for endothelial injury. The level of oxygen saturation in healthy subjects can reach values of 90% with considerable interindividual variations. Hypercoagulability can be due to dehydration even though there is no formal proof of its role in air travel.[6]

Not only traveling in economy class, but also prolonged sitting, could cause the so-called "economy class syndrome." The risk of venous thrombosis of the lower limbs after prolonged sitting is well known, whether a result of sitting in front of a computer for several hours (there is even talk of e-thrombosis[8]) or travelling by bus or train.[9]

A hypercoagulable state has been demonstrated in marathon runners taking a plane after their race[10] and could explain the occurrence of thromboembolic events in young, high-level athletes.

The existence of genetic or acquired thrombophilia may also modify the coagulability risk.

A potential thrombotic risk for travellers exists, but it is not the same for every traveller, nor throughout the life of each traveller. The risk of VTE should be established in every subject planning a long-haul flight.

Key steps in the diagnosis of VTE following a flight

Following a flight of 4 hours or longer, the presence of calf pain and/or a swelling of the lower limbs localized at the ankle, calf or thigh, or extending to the entire lower limb, is strongly suggestive of venous thrombosis. Confirmation of the diagnosis of lower limb venous thrombosis is made with Doppler ultrasound. This allows the site of the thrombus in the deep or superficial veins to be specified, how far it extends, and possible associations between deep and superficial thrombosis.

It is particularly important to meticulously examine the popliteal hollow with the patient in a sitting, standing, and supine position. The trunk of the gastrocnemius veins or saphenopopliteal junction (termination of the small saphenous vein in the popliteal vein) are areas particularly susceptible to venous stasis after prolonged sitting, as is the case with long-haul flights (*Figures 1 and 2*).

Measuring plasma levels of D-dimer complements Doppler ultrasound, but a negative test does not formally eliminate distal vein thrombosis or superficial venous thrombosis.

The use of ultrasound for diagnosis can be problematic in a symptomatic patient who presented with DVT of the

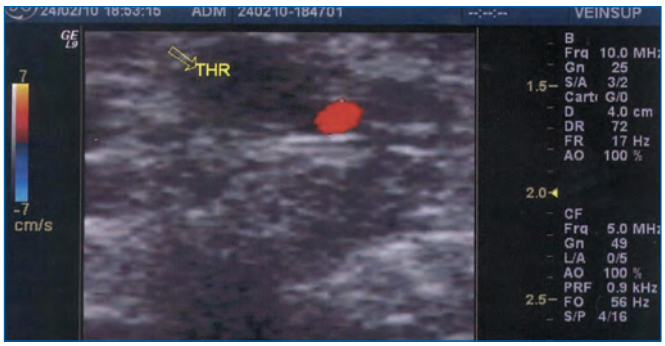


Figure 1. Thrombosis in a twin vein 4 hours after a flight.

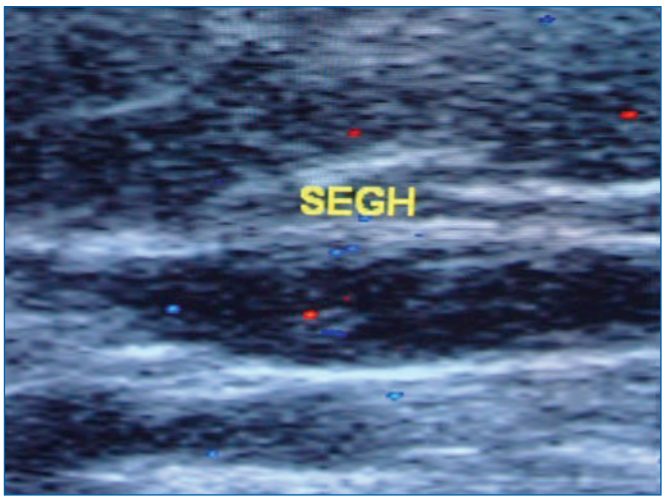


Figure 2. Thrombosis in the small saphenous vein 6 hours after a flight.

lower limbs in the weeks or months preceding the flight. In the absence of previous records, it is sometimes difficult to differentiate recurrent venous thrombosis or simply postthrombotic disease with obstructive sequelae and/or deep valvular reflux. In this case, D-dimers may be normal or increased, and provide little help with confirming–or rejecting–a diagnosis of a new thrombotic episode. In these patients, it is important to estimate the venous risk based on spontaneous, provoked, or previous thrombotic episodes, the presence of any risk factors, and to weigh the benefit/risk of a new anticoagulant treatment. If the Doppler ultrasound confirms the existence of a recent thrombus (eg, nonadherent to the vein wall) anticoagulation therapy must be resumed.

The rupture of a fluid-filled cyst in the popliteal hollow can also occur after travel in a prolonged sitting position, but is easily confirmed by ultrasound.

If symptoms suggest migration of a pulmonary embolism (dyspnea, chest pain, hemoptysis), angiography is urgently required and hospitalization is preferred for at least 24 to 48 hours.

Risk factors for VTE in travellers

A study by Kuipers et al, on nearly 9000 passengers with a total follow-up time of around 40,000 patient-years, identified a number of VTE risk factors for individual travellers including: female sex, especially if using oral contraceptives; a height <165 cm or >185 cm; and a body mass index >25 kg/m^2.[2] However, the small number of patients with VTE in this study (n=53) did not allow further statistical analysis.

The majority of studies in the American College of Chest Physicians Clinical Practice Guidelines[6] confirm the existence of risk factors in patients with VTE after a long-haul flight and also help to define patients at high risk of VTE. These factors include: prior history of VTE, recent surgery (1 month), recent trauma of the lower limbs, cancer, pregnancy, estrogen-progestin treatment, reduced mobility, congestive heart failure, severe obesity, known thrombophilia, and age >65 years.

In a set of UK guidelines published in 2010, experts defined three risk groups: low, intermediate, and high according to the presence of VTE risk factors (*Table I*).[11]

Risk group	Risk factors
Low	None
Intermediate	Postpartum (6 weeks) Prior history of VTE without triggering factor and no longer on anticoagulant treatment Prior history of post-flight VTE More than 1 of the above risk factors
High	Major surgery in the previous 4 weeks Cancer requiring chemotherapy in the previous 6 months or awaiting chemoradiotherapy

Table I: Venous thromboembolism risk groups according to reference 10.

Preventive measures adapted to the number of risk factors, could certainly reduce the incidence of VTE associated with long-haul flights.

The key to preventing VTE among passengers on long-haul flights

Information provided to travellers by airlines concerning the risk of VTE after a long flight is still inadequate.[12,13] Therefore, it falls first to the treating physician and/or cardiovascular specialist to provide advice, which should be accompanied by prevention tips based on findings from randomized controlled trials and adapted to an individual traveller's thromboembolic risk. A study by the French Society of Angiology in 2011 confirmed travellers' lack of knowledge concerning these VTE prevention tips and the information disseminated by the airlines companies (*Table II*).[13]

Advice	Knowledge of patients regarding prevention of venous thromboembolism	Learned society *(French Society of Angiology)*	Airlines
Drink water	57%	100%	34%
Walk	54%	100%	42%
Wear loose clothing	54%	100%	No recommendation
Move ankles	47%	100%	42%
Medical compression	77%	100% for the duration of the flight. Grade of compression	**13%** **Additional medical advice before flight 20%**
Aspirin	15%	Not recommended	<1%
Venotonic agents	33%	Recommended for symptoms	No recommendation

Table II. Lack of knowledge by patients of VTE prevention, and comparison of advice and recommendations from the French Society of Angiology versus Airlines companies.

Patient profile / flight duration	Global advice to passengers	Venoactive drug	Medical compression <20 mm Hg	Medical compression 20 to 30 mm Hg	LWMH	Mandatory advice from venous Specialist
No RF/ <3 hours	X					
No RF/ >3 hours	X		X			
Varicose veins	X	X		X		X
Edema	X	X	X ...	or X		X
CVI	X	X		X C++		X (ABI)
History of DVT	X			X C++	X	X (ABI)

Table III. Recommendations of the French Society of Angiology according to the risk of venous thromboembolism (VTE).

Abbreviations: ABI, ankle brachial index (indispensable for verifying the presence of arteriopathy in the lower limbs before deciding on the class of medical compression); C++, increase the class of compression before the flight in individuals habitually wearing compression; CVI, chronic venous insufficiency (from C3 to C6 of the CEAP classification); DVT, deep venous thrombosis; LMWH, low-molecular-weight heparin; RF, risk factor for VTE.

1. General rules

Choose a seat next to the corridor rather than the window to be able to stand easily, wear loose clothing and loose-fitting shoes, do not place bags beneath legs as this further limits the space available, practice regular flexion/extension movements of the feet and ankles during the flight. These venous "anti-stasis" measures benefit from a Grade 2 recommendation in the American College of Chest Physicians Guidelines.[6]

Travellers are also advised to drink plenty of water and no alcohol,[6] even if this has not been shown to have a prophylactic effect in relation to VTE.

2. Medical compression

According to the results of a meta-analysis, compression socks ensuring a compression of 15 to 30 mm Hg at the ankle (ie, Class 2 and 3 according to French standards) reduce the percentage of DVT detected by Doppler ultrasound (i.e. asymptomatic DVT): 0.2% with compression socks versus 3.6% without.[14]

Moreover, medical compression has proven efficacy for the prevention of edema, well known to passengers during landing and sometimes so important that they can no longer get their shoes back on. However, randomized, double-blind, controlled trials are lacking. Even passengers with varicose veins have a limited knowledge of the benefits of medical compression during a flight (*Figure 3*).

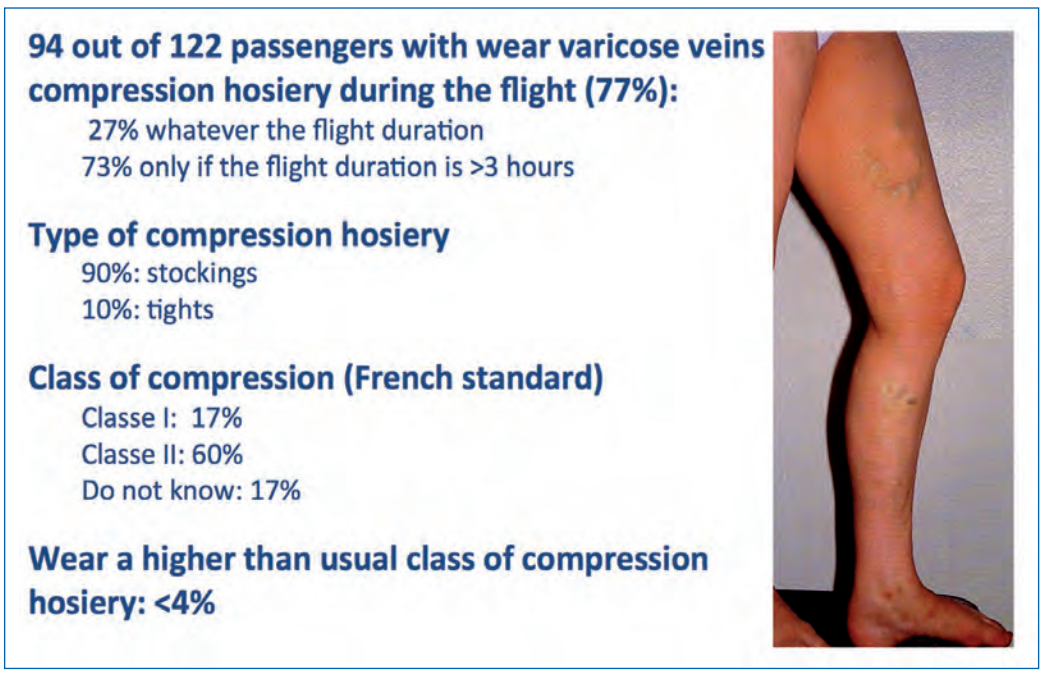


Figure 3. Knowledge of passengers with varicose veins of the benefits of medical compression. Report from 122 passengers with varicose veins.

Should medical compression be recommended to all passengers undertaking a long-haul flight?

The American College of Chest Physicians suggest that medical compression should not be recommended for all passengers (Grade 2C).[6] Advice from the French Society of Angiology (www.angeiologie.fr) (*Table III*) suggests Class 2 medical compression for all passengers taking flights longer than 4 hours. We also recommend increasing the class of compression above that usually worn for all patients with chronic venous disease. Doppler ultrasound may be useful for selecting the best compression in case of chronic venous insufficiency of the lower limbs. Global advice to air travellers are systematically delivered when possible (*Figure 4*).

The study by the French Society of Angiology has confirmed the great disparity in the choice of compression prescribed before a long journey: while below knee socks are unanimously worn by men, some women prefer tights or compression stockings to socks.

The presence of varices in the region of the small saphenous vein, especially if located in the popliteal hollow, should be treated preferably with thigh compression to prevent varicose constriction during prolonged sitting.

Contrary to what some users of first-class air travel believe, the courtesy socks offered by airlines are not medical compression socks!

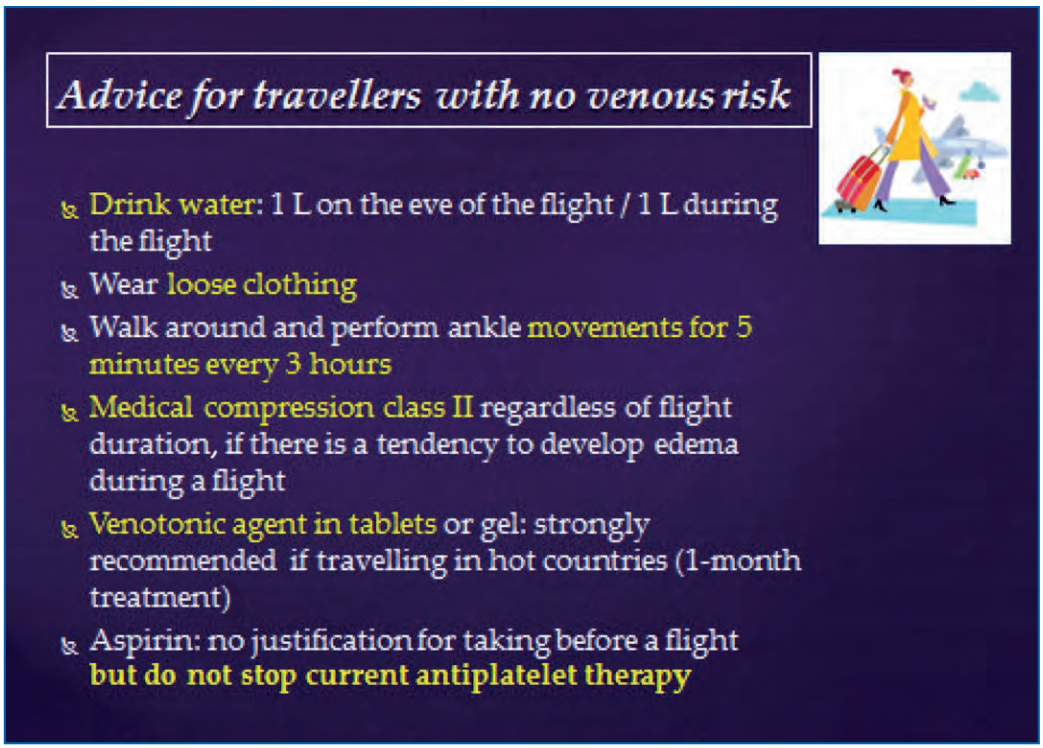


Figure 4. Advice for travellers with no venous risk. Prepared by the French Society of Angiology.

Medical compression for travellers at high risk of VTE

For long-distance travellers at increased risk of VTE, the American College of Chest Physicians suggest the use of a compression sock providing 15 to 30 mm Hg pressure at the ankle (Grade 2C).[6] This corresponds to class I compression therapy in Europe, and to class II in France. (*Table IV*) The absence of randomized, controlled, double-blind studies explains the weakness of this recommendation.

Compression class	French (mm Hg)	European (mm Hg)
I	18-21	20-30
II	23-32	30-40
III	34-46	40-50

Table IV. Relationship between European and French compression classes.

3. Aspirin

The American College of Chest Physicians recommendations concerning aspirin are clear: for travellers undertaking long-haul flights they suggest to not use aspirin to prevent VTE (Grade 2C). One of the reasons for this recommendation is because of an increased risk of bleeding with aspirin.

4. Anticoagulants

Thromboprophylaxis should be considered on a case by case basis depending on the presence of one or more thromboembolic risk factors, taking into account the benefits and risks of treatment (especially bleeding).

It is based on the use of low-molecular-weight heparins (LMWH) and fondaparinux (factor Xa inhibitor). The new oral anticoagulant therapies currently have no indication in this context. The usual contraindications for these agents should be respected.

The prescription can be made by the treating physician: travellers can perform the subcutaneous injection themselves just before their flight (outbound and return).

Reminder of LMWH prescriptions before a long-haul flight

- Enoxaparin (Lovenox) 40 mg subcutaneously, a single injection before the flight (outbound and return).
- Daltepraine (Fragmin) 5000 IU subcutaneously, a single injection before the flight (outbound and return).
- Tinzaparin (Innohep) 4500 IU subcutaneously, a single injection before the flight (outbound and return).

Clinical case

The case concerns a 40-year-old woman, a lawyer, in good health, 1.78 m in height, and weighing 80 kg. Her varicose veins appeared after her second pregnancy, 10 years ago and have gradually worsened.

She has complained of pain in the left leg for 3 days, and a clinical examination revealed an indurated cord extending the length of the great saphenous vein. Doppler ultrasound confirmed a diagnosis of superficial venous thrombosis with a relatively recent thrombus of more than 10 cm in length, not extending past the lower third of the thigh and not involving the deep veins or perforating veins.

The patient has a 5-hour flight scheduled for the next morning, and will be returning in 3 weeks.

What should be done?

Cancel the flight: probably not, although the recent superficial venous thrombosis should be considered as a risk factor for thromboembolic disease.

Prescribe medical compression: definitely

What grade and what type of compression should be prescribed knowing that she has never worn compression therapy to date?

The ideal would be a class III knee-high or thigh-high compression stocking.

Which anticoagulant treatment?

Treatment of the superficial venous thrombosis is based on guidelines from the French National Authority for Health (Haute Autorité de Santé) which recommends a prophylactic dose of low-molecular-weight heparin (LMWH) or fondaparinux for 30 to 40 days. However, given that the patient has a flight booked for the next day, is overweight, and has a history of recent thrombosis, an intermediate dose should be considered for 30 days. A check-up should be scheduled for the patients' return. The new oral anticoagulants have not been studied in superficial venous thrombosis.

In the case of a deep thrombosis, especially if proximal (*Figure 5*), it would be prudent to delay the air travel if possible.

The aim is to ensure that the patient has adequate anticoagulation treatment and that there is no major risk of bleeding.

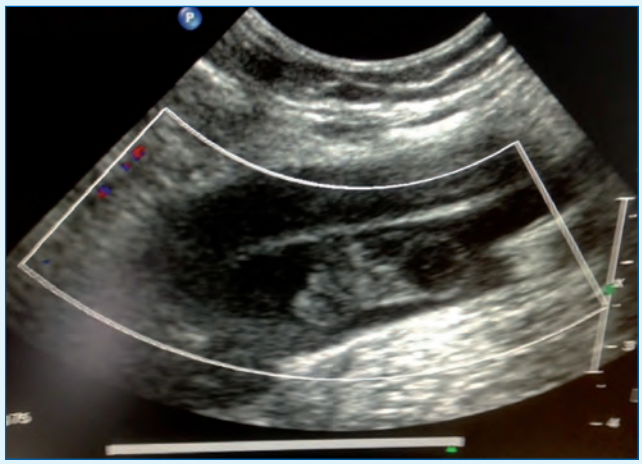


Figure 5. Thrombosis of the femoral vein–recent appearance (floating clot). Photo reproduced with permission from Dr F. Chleir.

- Fondaparinux (Arixtra) is prescribed at a dose of 2.5 mg subcutaneously, a single injection before the flight (outbound and return).

All LMWH prescriptions should be weight adjusted if there is severe renal impairment (creatinine clearance <30 mL/min).

VTE risk	Flight duration		
	<3 hours	3-8 hours	>8 hours
Low	None	None	None
Intermediate	None	None or compression	Compression
High	None	Compression	Compression ± LMWH

Table V. The American College of Chest Physicians Treatment Recommendations. Adapted from reference 6.

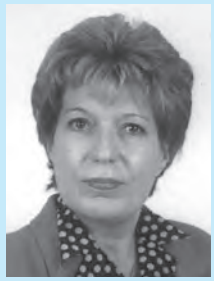
The American College of Chest Physicians recommends the use of LMWH for long-haul flights of over 8 hours, only in air travellers with high risk of VTE *(Table V)*.[6]

The French Society of Angiology recommendations differ only for flights with a duration of 3- to 8 hours where medical compression is prescribed for all passengers, adjusting the compression class to an individual's history of thromboembolism.

Conclusion

Risk management for any passenger taking a long flight is based on some simple advice to follow during the flight. We strongly recommend that all passengers wear medical compression socks. Thromboprophylaxis with LMWH is required for travellers at high risk of VTE, taking into account the risk of bleeding. Time will determine the place of oral anticoagulants in this area.

Finally, young travellers are not immune to the risk of thrombosis: in particular, young women using oral contraceptives and high-level athletes, especially when returning from a competition.



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A quality of life tool kit in chronic venous disorders

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Keywords:

Chronic venous insufficiency; generic and specific quality of life scales; utility; preference approach

Abstract

Individual preferences are now at the center of the medical decision-making process. Different experimental methods are used to determine preferences. Psychometricians use direct observation of a subject's reaction in a particular pathological situation: patients are asked to arrange the intensity of the impacts on numerical ordinal scales, but an actual metrical measure is not yet available. Traditionally, economists believe that in a market, only the consumer's choices enable us to estimate his or her level of satisfaction. In the health care field, where market mechanisms are not fully operational, they tend to extract patient preferences through forced choices between hypothetical health states. A real metrical measure is thus obtained. The objective of this article is to exhibit these 2 methods, psychometric and economic, and show how they have been implemented in medical research.

Introduction

Chronic venous disorders (CVDs) of the lower limbs are highly prevalent disorders and are a true problem of public health, especially in the industrialized countries due to the high costs of investigations, treatments, and complications. The impact of CVDs on the daily life of patients can be assessed by measuring their quality of life (QOL). Most studies conducted to date on patients with CVDs, both at the onset and at its most advanced stage, have shown a significant impact of the disease on QOL. However, disease-specific instruments to evaluate QOL in the context of CVDs were not developed and validated until quite recently. The use of comprehensive QOL instruments has shown greater consistency than the simple reporting of individual symptoms.

Quality-of-Life Approach

The first stage of any study examining QOL is to define the universe of the area to be studied. Once defined, the universe must be categorized to define specific domains to be quantified. In order to assess these domains, a number of criteria or indicators must be available in order to quantify them, and appropriate scaling procedures must be selected. Finally, development of a definitive indicator system

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must consider the objectives for which it has been designed, without which results are meaningless.[1]

QOL is such a unifying concept that ultimately all facets of the individual may be included: environmental factors, behavior, and lifestyle. This discussion shall be restricted to those factors that influence patient QOL as a result of disease or its treatment. Life may not, however, be assessed generally: at best, different aspects of life may be assessed. Categorization of health is a difficult stage. The specific nature of the dimensions of health is controversial. Factor analysis has supported the validity of 4 distinct areas: symptoms, functional well-being, emotional stability, and appropriate social integration.[2]

Until this point, these 4 domains are only concepts, that is, abstract principles. Measurement of these domains must be performed using solid recordable parameters. For each domain, a number of items have to be defined that will act as intermediaries between the abstract characteristics to be inferred and either objective or subjective measures. Choices depend on the approach taken to assess health problems. For some authors, the definition of health may be restricted to the absence of clinical symptoms or biological abnormalities. Others distinguish between those diseases that may be defined by the medical profession and sickness expressed in terms of behavior. A number of definitions stress the patient's perception of illness, that is, they are based primarily on a patient's individual satisfaction or lack of satisfaction with his or her well-being. The intensity of symptoms, degree of incapacity, or level of dissatisfaction depend both on the absolute severity of the phenomenon and on the degree to which it interferes with daily life. The scoring procedures, that is the conventions that govern allocation of values for different indicator positions, are a primary feature of standardization required for the measurement instrument.[3-5]

They package empirical interpretation into a unit which may be used, and dictate the method of statistical assessment of findings. The best characteristic of a scale is its invariance, that is, the degree to which it can be manipulated without distorting its structure. In an ordinal scale, all transformations that preserve the order on the scale do not change available information. Such a scale is said to be preserved following monotonic transformation. In an interval scale, all numbers on the scale may be multiplied by a constant factor, or the origin shifted by a constant number without changing the results. Such a scale is said to be preserved by affine transformation (y=mx+c). Finally, in a ratio scale, the relationship between values is not changed if they are multiplied by the same constant factor. It is preserved by linear transformation (y=mx). The more precise the information contained in the scale, the more restricted the ability becomes to modify the scale without changing the information contained therein. If scales are to be used as measurement instruments, they must be applied appropriately if they are to produce reliable results; in other words, they must measure what they were designed to assess.

A discriminative tool constructed to identify a problem is not necessarily that which allows changes to be followed, and the tool used to follow changes may not be useful to assess whether the allocation of resources is right. The choice of a method requires an initial definition of the users' needs: identification of a problem,[6] assessment of change in response to treatment, or greater and more coherent use of scarce resources. An economist needs overall results and requires a common measurement to compare the effects of decisions high up the health care system: techniques and equipment available to a statistically average population.[7] A clinician's aim is to apply techniques and equipment available and draw the maximum possible benefit for the patient. All features of the disease must be approached, explaining why assessment has remained a multidimensional problem.

These 2 different attitudes have produced 2 different approaches in the development of questionnaires. Quality of life may be globally assessed in 2 ways: (i) by examining the whole heath status to combine, but not categorize, partial observations; or (ii) by composition to construct the general from the specific. The overall approach is based on the supposition that QOL exists as a continuum from good health to death. Most often several dysfunctions appear in combination. Therefore, the entire range of QOL alterations must be situated on an interval scale by reasoning in terms of stereotypes[8] or on the basis of a health status classification system.[9-22]

The assessment involves determining values of coefficients between 0 and 1 attributable to each of these typical states. These weighting factors constitute adjustment factors of the quantity of life according to its quality, hence their name "QOL coefficients." The product of the number of years or fractions of a year spent in a particular health status and the corresponding QOL coefficient transforms the time spent in poor health into equivalent fractions of years of good health. Repetition of this operation over

time for various stages provides the number of years left to live adjusted as a function of the QOL, called QALY (quality-adjusted life years). The cost of the treatment can then be divided by the QALY result in order to compare the respective merits of 2 treatments.[23,24]

In the compositional approach, a number of items are combined either simply or by ad hoc weighting of selected variables into subscales. These scores by dimensions may or may not be aggregated to produce an overall score. When they remain as distinct entities in the final assessment mechanism they produce profiles. If they are combined into a single figure, the term index or combined indicator is used. In all cases, the method chosen will reflect the complexity of the situation. This is a method which has been used since the 19th century by psychometrists endeavoring to impose "the discipline of measurement and figures to aspects of the spirit." This concept was also put forward by Alvan Fenstein and the psychopathologists in recommending grading of clinical judgments.[25]

Utility preference approach

The methods used to record individual preferences are highly varied: "standard gamble," "time trade-off," and "category rating."[26-31] The first of these methods was traditionally used to assess key preferences in situations of uncertainty. Therefore, it is considered to be particularly appropriate in medical fields.

The protocol on which it is based is simple: 3 states of health (S1, S2, and S3) are carefully detailed and shown to a subject who must choose between the following options: either treatment A, which guarantees situation S2, or treatment B, which may have 2 possible outcomes-state S1 of probability (*P*) or state S3 of probability 1-*P*. States S1, S2, and S3 are arranged in a hierarchy with S2 occupying a position between S1 and S3. When the value of *P* varies from 0 to 1, this produces a threshold value where the patient is unable to decide between the 2 options. This value may be used to assess the utility of the first of these therapeutic possibilities.

The dilemma faced by patients suffering from varicose vein disease highlights the use of such a system. Mrs X who is suffering from varicose veins may be offered 2 possibilities: either long-term therapy or the risks of vein stripping. The outcome of the first choice in the short term is without doubt: she will live. The second choice is more risky, as the chances of surgical success without anesthesia-related problems have been estimated by her general practitioner to be 99.09% in this case. The patient is caught between 2 possible courses of action: she may either choose the risky situation, which includes an unavoidable risk of death, or adopt the secure option, but, by definition, give up any possibility of improving her functional and esthetic situation. A problem then arises in that, if the patient opts for the secure course, she will be better off than if the worst outcome of the risky approach were to occur, ie, death, but worse off than if the operation succeeds. In order to decide, she must assess the relative desirability of remaining in her present state with varicose veins compared with the best and worst possible outcomes following the higher-risk option. The dilemma may be solved using a standard gamble based on population statistics.

The structure of the gamble is identical to that of the initial problem. Choice is limited to a certain outcome and a risk outcome-survival without sequelae or death. Two differences exist, however, by comparison with the initial dilemma: (i) the decision rests on a hypothetical situation removing emotional overlay which played a part in the initial problem; and (ii) risk calculation is not based on personal assessment, but on an objective measurement. By varying probabilities attributable to the higher- risk situation, it is possible to assess the psychological value that the subject attributes to the certainty situation. Where the chances of success of the risky approach is 99.09%, the patient must choose between the certainty of living with varicose veins or the risk of undergoing an operation that may not succeed due to the risk associated with anesthesia.

The risk may not be worth the gamble and the patient chooses the safe option. If, in contrast, however, the anesthesia risk is very low ($P<0.01\%$), the probability of surviving the operation increases and the patient in this situation will opt for the gamble. Where the chances of success are low, the patient will favor the status quo. In the opposite situation, he or she will tend to lean toward the higher-risk approach. The only difference between these two situations is in the value *P*, the probability of success.

As this increases, the subject is less likely to choose the safe option and more likely to take the higher-risk option. Finally, there is a threshold coefficient value where the patient is unable to choose between the 2 options. This value may be used to assess the current QOL of the patient. If pain is severe or frequent, the value of the threshold coefficient is low. If the patient will undergo anything to escape his current condition, the operation proposal is accepted even where the chances of success are limited, confirming the

patient's poor state of health. If pain is mild, the critical value for the coefficient is higher, the patient's present condition approaches that of good health; the patient does not accept the operation proposal unless it is almost certain to succeed.

The utility/preference approach has a number of advantages. First, this method produces a detailed measurement that combines mortality, morbidity, resultant physical sensory effects, socioemotional and cognitive effects, symptoms of the disease, and secondary effects of treatment into one single score. It allows calculation of a weighted life expectancy as a function of QOL, which may not be done with specific profiles used to study the multiple effects of disease over time. Results and costs may be brought together when they may be related to a fundamental domain. Second, the score directly reflects patient preference and is not influenced by weighting factors defined by the healthy population or by the practitioners caring for the patient. The instrument may be specific for the disease if appropriate parameters are chosen to define the areas to be addressed. The method has an undisputed scientific basis: decision in the face of uncertainty, described by Von Neumann and Morgenstern.

Despite the indisputable applications of this mechanism, it cannot be denied that there are restrictions on its use. First, replies vary as a function of the context in which questions are set and, second, it is not always possible to identify clinical variables that form the basis of the overall score. Finally, the sensitivity of a given indicator must be demonstrated in different disease states.

Generic quality of life scales

Generic quality of scales uses a single self-completed questionnaire, which is said to apply to all diseases. The best known are the Sickness Impact Profile (SIP), the Nottingham Health Profile (NHP), and the 36-item Short Form health survey (SF-36). The SIP consists of 136 questions grouped into 2 domains, physical and psychological state, and 5 specific independent categories.[32] Taken as a whole, the questionnaire may be used to provide a global score. Each question assesses change in behavior and measures intensity of the upset. An interval scale using apparently equal gradations is used to assess the relative severity of each functional problem.

This system was presented in 1975 to 108 Seattle Health Maintenance Organization members and 25 health professionals. Each point was scored between 0 and 15. Subdomain and overall global scores were calculated by dividing the sum of individual scores into the maximum possible score.

The NHP uses a 2-part questionnaire. The first part consists of 38 questions with "Yes" or "No" responses, covering 6 domains: sleep, physical mobility, pain, effective reactions, social isolation, and emotional reaction. The second part assesses 7 independent variables: work; salary; domestic work; interpersonal relationships; social, family, and sexual life; holidays; and pastimes.[33] Results are scored either 0 or 1. Domains are not grouped together, but points assessing each domain are weighted as a function of their relative severity. The reference technique used is pair comparison: each item in a domain is compared successfully with all other points within that domain. The subjectively more severe point is noted in each case. This system was used on a pilot group of l200 laymen without medical training to assess the frequency of points deemed more severe than others. Symptoms and problems were graded in a hierarchy, comparing mean standard deviation with frequency.

The SF-36 questionnaire,[34] "SF-36," is a generic QOL scale widely used throughout the world. It consists of 36 items divided among 8 dimensions: physical functioning (10 items); physical role (4 items); bodily pain (2 items); general health (5 items); vitality (4 items), social functioning (2 items); emotional role (3 items); and mental health (5 items). The higher the score is, the better the patient's health status.

Profiles are not without merit: their reproducibility and validity have been well established. They also allow assessment of different domains of QOL in one combined scale without using multiple measurement scales. This is easier for both investigators and patients. They do have problems, however; in particular, they do not allow the specific consequences of a given disease on QOL to be assessed. In venous diseases, walking, far from being a handicap, is considered to be therapy, whereas standing upright and remaining immobile, which is not listed in the NHP or the SIP, is a real problem for patients suffering from venous disease. The failure of the parameters used to relate to specific problems inevitably leads to sensitivity failings or even validity problems as the functional defects explored may not be relevant.

The main drawback of the generic scales is their failure to identify small, but significant, clinical changes over time. Disease–specific scales seem to be better suited to

discriminate between the benefits of a particular treatment on venous insufficiency. It, therefore, appears important to develop a specific QOL indicator for venous insufficiency that takes into account the patient's point of view and provides the attending physician with a fine measurement of the functional and psychosocial consequences of the disorder.

Specific quality of life scales

Proponents of a specific QOL scale advocate initial identification of relevant domains based on information reported in the literature and interviews with experts and patients.[35-37] Signs and symptoms gathered may be combined to assess the impact of disease on the daily life of the patient. An initial questionnaire is designed to scale the indicators and to select the most relevant items. Given that the item pool is designed to provide the basis for construction of the final questionnaire, it is important to list many more parameters than will be used in the definitive version. For each item, 2 types of questions are formulated. The first concerns the presence and intensity of the impairment experienced, and the second, the importance attributed to it by the patient.

Authors diverge at this stage of the analysis: some only include in the final questionnaire those items with the highest product between frequency and importance.[38] The instrument implicitly integrates patient preferences as these constitute the foundations of its structure and are the basis of the choice of the items. However, once the questionnaire has been constructed, the items are equally weighted. The other school eliminates redundant parameters by principal component analysis and regroups items according to their contribution (loading) to different factors.

The example of the CIVIQ-20

The ChronIc Venous Insufficiency QOL Questionnaire (CIVIQ) is the first QOL questionnaire specific to chronic venous disorders (CVDs) based on those rules.[39-41] This 20-item questionnaire providing a global index and a profile on 4 QOL dimensions-psychological (9 items), pain (4 items), physical (4 items), and social (3 items)-was initially developed in French (CIVIQ-20). Items on the CIVIQ scale were scored from 1 to 5. A low score for items represented greater patient comfort. **Recall period of CIVIQ-20:** The recall period was the previous 4 weeks. **Calculation of CIVIQ-20 scores:** In order to facilitate the interpretation of the results, the scoring system was reversed: the highest figure was allocated to the lowest response option and vice versa such as to obtain a score directly proportional to the QOL. The score for each dimension was obtained by adding scores for each constituent item and the global index was obtained by summing the 20 items. Items were weighted equally. The extreme possible minimum and maximum values that the scales have is dependent on the number of items used in each of the dimensions and on the number of levels or categories for each item.

For example, the score for a scale constructed from 2 items, each of 5 levels, can range from 2 points (2X1) to 10 points (2X5). The score of a scale that includes 5 items of 5 points each range from 5 points (5X1) to 25 points (5X5). It is, therefore, not straightforward to identify different orders of magnitude when calculating mean scores for different dimensions affected. In order to compare mean scores between dimensions or scales, absolute scores were then converted into an index.

The method chosen was the one described by John E. Ware for the SF-36.[34] For each dimension, we calculated S, the sum of scores for the patients' answers to the questions; m, the minimum theoretical value if all of the answers were on the first level of the scale for all of the items belonging to the dimension; and M, the maximum theoretical value if all of the items were scored at the maximum level on the scale for all items belonging to the dimension.

The standardized score for each dimension was obtained by applying the following equation: (S-m)/(M-m)_100. For each dimension, we obtained a result from 0 to 100. According to this scoring method, improvement in QOL between day 0 and day 28 is represented by an increase in the score. The difference is therefore positive in such situation.

Cross-cultural equivalence of CIVIQ-20

CIVIQ-20 was translated into English before subsequent use in a prospective, multicenter, international study, the Reflux assEssment and quality of lIfe improvEment with micronized Flavonoids study (RELIEF), which assessed QOL in 4048 adult patients from 18 countries with CVDs (46.6% of whom had venous reflux). This process requires the identification of cross-cultural equivalence of the concepts or constructs measured so that comparisons may be made between populations of different cultures. Thus, the content of the questionnaire was first submitted for consideration by the different countries involved. The linguistic validation

was performed in 2 steps: first, confirmation of the cultural relevance of the questionnaire's content; and second, the translation process.

Cultural adaptations into English, Italian, Polish, Portuguese, and Spanish were undertaken. Additional versions were then made available in Arabic, Czech, Hungarian, Russian, and Slovak. During this process, some conceptual changes were made to refine the content validity of the social dimension of the CIVIQ. Item no. 11 "practicing sport" was translated in order to reflect a physical concept more than a social concept. This explains why it tends to fall under the physical dimension in the international sample. The same choice was made for item no. 10 "going out in the evening" with similar results. Items no. 8 "traveling (car, bus, plane)," no. 9 "doing the housework," and no. 15 "having to take precautions" faced specific translation problems which result here in a questionable cross-cultural conceptual equivalence. In all, 9 versions were used in the RELIEF study. With time, seventeen (17) linguistic versions were validated using a forward-backward methodology and 11 versions were the result of simple translation of the source questionnaire.[42] (*Table 1*)

Metrical properties to be validated in any quality of life questionnaire

Quality of life scales must be validated before being used in clinical trials. The scales must have specific metrological properties that must be confirmed in a validation study; these properties are face validity, content validity, precision, accuracy, and sensitivity.[43-48] A systematic review of the literature about quality of life scales in CVDs was conducted. It confirmed a paucity of validation studies, except for two scales: CIVIQ and VEINES.QOL.[49]

The 17 validated linguistic versions according to forward-backward methodology			*The 11 translated linguistic versions without formal methodology*	
Target country	**Language**	**Date of validation**	**Target country**	**Language**
Austria	German	1996	Brazil	Portuguese
Canada	French	2002	China	Chinese
Canada	English	2002	Czech Republic	Czech
France	French (source=questionnaire)	1995	Egypt	Arabic
Greece	Greek	2004	Hungary	Hungarian
Italy	Italian	1996	India	English
The Netherlands	Dutch	2009	Japan	Japanese
Poland	Polish	1996	Russia	Russian
Portugal	Portuguese	1996	Slovakia	Slovak
Romania	Romanian	2013	Switzerland	French
Singapore	English	1996	Turkey	Turkish
Slovenia	Slovenian	2013		
Spain	Spanish	1996		
UK	English	2002		
USA	English	2002		
USA	Spanish	2002		
Vietnam	Vietnamese	2013		

Table I. Summary of the available linguistic versions of CIVIQ-20

Face validity

The face validity of a questionnaire depends on the quality of its preparation: are the questions precise enough to specify the domains explored? Do they relate to a well-defined period of time? Is the aggregation procedure adequate? It is better to phrase sentences based directly on patients' descriptions. When the patients' own vocabulary is used to compile the questionnaire, a simple construction is obtained, without which it would be impossible for the patients to participate actively in the survey.

Content validity

Content validity requires 2 conditions to be fulfilled: the entire range of patients' complaints must be included, and the items chosen must be shown to be representative. The content validity of the CIVIQ-20 is supported by the fact that the process used to select items was based on input from direct definitions of complaints obtained from patients suffering from venous insufficiency. The use of factorial analysis enabled redundant items to be identified and excluded.

Reliability

A scale is reliable if, when measuring the same phenomenon on a number of occasions, it produces similar results. To determine reliability, the size of random measurement error must be assessed. If this is low, the instrument provides a consistent measurement of the universe assessed. A number of authors describe this criterion as fidelity; others refer to the precision of the instrument. The most common method that is used to address this problem is internal consistency reliability and stability (test-retest) reliability.[50] Different items in a dimension must be homogenous as they relate to the same concept even if they are worded differently. This "internal consistency" is tested by the Cronbach α, values of which range from 0 to 1. Coefficients above 0.70 are generally regarded as acceptable for psychometric measurements. Intraclass correlation coefficients are used to confirm that the indicator is reproducible, ie, to ensure that the answers to the same questionnaire remain unchanged in stable patients.

Construct validity

An instrument is said to be valid if it measures what it truly purports to measure. This assumes both the absence of random error and systematic bias. Reliability is, therefore, a prerequisite, but is not sufficient for validity. For perfect validity, there must be no consistent error. In the absence of an undisputed reference standard, the validity of a measurement scale is obtained by: (i) confirming that its factorial structure remains stable on different population samples (structural validity); (ii) testing if the results obtained using the scale fit the expected relationship across a group of individuals or clinical data available (known group differences); and (iii) comparing its results at a given point of time, and longitudinally either with other validated QOL scales assessing the same domain or with clinical indicators (convergent validity). Convergent validity is fulfilled when the scales score for a related concept produces a Spearman correlation coefficient >0.4.

Responsiveness

The sensitivity of an instrument is its capacity to detect clinically significant changes even if they are of low amplitude. Changes in scores must be able to be demonstrated in patients whose state of health is deteriorating (or improving). An inadequately sensitive indicator might miss differences between 2 treatments, as it may be unable to detect subtle changes in the patients' corresponding clinical states. An indicator is sensitive when it detects all changes in a given variable over and above the imprecision due to measurement error. Different statistical methods have been described to assess sensitivity in detecting change. The least contentious appears to be the standardized response mean (SRM) and the effect size (ES) as described by Liang[51] and Guyatt.[52] SRM is the ratio of the mean change to the standard deviation of the change. The ES is identical to the SRM, but uses the standard deviation of the scores on day 0 as the denominator.

Conclusion

QOL is, for the physician, a means to rise above too biological of an approach. Beyond organic disease, body spirit must be examined. The physician tries to achieve the best possible management for his patient who entrusts him with his most precious possession: his life. The objective is to control every aspect of the disease, which explains the physician's desire to remain within an objective and multidimensional framework. The scientific collection of data leaves little place for the evaluation of an individual's preferences. For the patient, it is important to express the specificity of his complaints. The evaluation instrument has to reflect the patient's central values and should integrate patient preferences in its structure and for the choice of its components.

For society, the goal of measurement is not to assess "the importance which each of us attaches to our lives," but to produce an overall morbidity indicator through which

the effects of actions influencing health may be judged. The tool to be used requires a precise initial definition of users' needs. The choice of an indicator depends on the answers to the following questions: does the user require an indicator producing discriminative or evaluative results? Does he wish to assess the overall QOL or specific facets of it? Which opinion is to be used: that of the doctor, that of the patient, or that of the population? Only too often, the available instruments are used blindly without clearly addressing these questions.

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Foreword

VEINews; a new heading

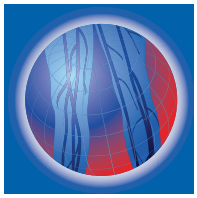
The VEINews rubric is now incorporated into Phlebolymphology and may take various forms, such as comments on a recent international publication (the most common) or on several publications on the same topic. It might also be controversial views of 2 authors on the same publication, or a state-of-the-art article on a timely topic.

In this issue, Prof Michel PERRIN (Lyon, France), Dr Javier LEAL MONEDERO (Madrid, Spain), and Dr Oscar MALETI (Modena, Italy) will comment on the following publications:

- "Chronic venous disease progression and modification of predisposing factors" authored by Kostas TI, Ioannou CV, Drygiannakis I, Georgakarakos E, Kounos C, Tsetis D, Katsamouris AN. *J Vasc Surg*. 2010;51:900-907. **Commented on by Prof Michel PERRIN (Lyon, France)**

- "The role of duplex ultrasound in the workup of pelvic congestion syndrome" authored by Malgor RD, Adrahtas D, Spentzouris G, Gasparis AP, Tassiopoulos AK, Labropoulos N. *J Vasc Surg: Venous and Lym Dis*. 2014;2:34-38.. **Commented on by Javier LEAL MONEDERO (Madrid, Spain)**

- "Deep venous reflux definitions and associated clinical and physiological significance" authored by Lim KH, Hill G, Tarr G, van Rij A. *J Vasc Surg: Venous and Lym Dis*. 2013;1:325-332. **Commented on by Dr Oscar MALETI (Modena, Italy)**



Reviewed by:
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Chronic venous disease progression and modification of predisposing factors

Kostas TI, Ioannou CV, Drygiannakis I, Georgakarakos E, Kounos C, Tsetis D, Katsamouris AN. *J Vasc Surg.* 2010;51:900-907.

Aim: The aim of this study was to evaluate long-term characteristics of chronic venous disease (CVD) progression and its correlation with the modification of specific risk factors.

Methods: In this prospective, follow-up study, the contralateral limb of 73 patients (95% women; mean age, 48±12 years) undergoing varicose vein surgery were prospectively evaluated using physical and color duplex examination and were classified using the Clinical, Etiological, Anatomical, and Pathological (CEAP) classification. After 5 years of follow-up, the development of new sites of reflux in the contralateral, preoperatively asymptomatic limbs was assessed. In addition, the influence of predisposing factors including prolonged orthostasis, obesity, estrogen therapy (ET), multiparity, and elastic stocking use (ESU) were assessed.

Results: A total of 48 new sites of reflux (37 in the superficial system; 5 perforators; 6 deep veins) occurred in 38 limbs (52%). CEAP scores significantly deteriorated: clinical, 2.2±0.5 from 0.1±0.03 (P<0.01); anatomical, 3.8±1.2 from 2.6±2.5 (P<0.05); disability, 1.9±0.7 from 0 (P<0.01); and severity, 7.9±2.4 from 2.7±2.2 (P<0.01). Patient compliance to predisposing factor modification was low; no change was observed during follow-up (orthostatism, P=0.9; obesity, P=0.7; ET, P=0.9; multiparity, P=0.4; ESU, P=0.3). CVD progression was significantly lower in patients who controlled orthostatism vs those who maintained or initiated orthostatism (P<0.001), as well as in patients who controlled preoperative obesity vs those who became obese or maintained obesity (P<0.001). Patients noncompliant with ESU had a significantly higher incidence of CVD progression vs those who started ESU or continued during the study (P<0.001). By binary logistic regression analysis, orthostatism (P=0.002), obesity (P=0.009), and non-ESU compliance (P=0.037) were independent predictive factors for CVD progression, whereas multiparity (P=0.174) and ET (P=0.429) were not.

Conclusion: The authors showed that, in about half of patients with unilateral varicosities, within 5 years, CVD developed contralateraly in limbs that were initially asymptomatic. CVD progression consisted of reflux development and clinical deterioration of the affected limbs. Obesity, orthostatism, and noncompliance with ESU were independent risk factors for CVD progression.

Comment: If untreated, varicose veins are a chronic progressive disease. Obesity and orthostatism are risk factors for progression. Noncompliance with compression treatment also increases the risk of progression. However, this was not a prospective randomized interventional study.

Keywords:
chronic venous disease; progression; risk factors

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The role of duplex ultrasound in the workup of pelvic congestion syndrome

Malgor RD, Adrahtas D, Spentzouris G, Gasparis AP, Tassiopoulos AK, Labropoulos N. *J Vasc Surg: Venous and Lym Dis.* 2014;2:34-38.

Reviewed by:
Javier Leal MONEDERO
Madrid, Spain

This article reports on an evaluation of using duplex ultrasound (DU) as a diagnostic technique in the diagnosis and follow-up of pelvic congestion syndrome (PCS) due to its noninvasive nature that contrasts with other standard techniques, such as conventional venography (CV). To asses this study, the authors performed a comparative study using patients imaged with DU, computed tomography venography (CTV), and CV in order to measure the accuracy of DU in the PCS diagnosis. Their results showed that DU has a high sensitivity to identify abnormalities in the left ovarian vein, but not in the case of the right ovarian vein, reducing, in that case, both sensitivity and accuracy. They did not find significant differences between the accuracy of the different imaging modalities.

The introduction of this work is simple and straightforward. However, they should have focused more on the presentation of their purpose, giving more data on the problems concerning PCS diagnosis and workup algorithms and comparing among these algorithms. In our unit, contrary to the authors, we do not separate DU and transvaginal ultrasound (TVUS), but consider these tests complementary, performing both if necessary.

The authors did not mention the presence of varicose veins in the lower limbs, but just discussed the appearance of edema; however later on they discussed lower limb symptoms. They also do not mention vulva-perineum leaks or gluteal, which, for us, is the most frequent. Particularly, different authors have described, in detail, the functional unit of the pelvis and lower limbs, but Malgor et al mostly ignore this discussion.

In our clinic, we use a different approach. First, after a normal gynecological exam to rule out PCS signs or symptoms related to gynecological causes and after discarding causes related to any column disease, we perform a TVUS to confirm the presence of pelvic varicose veins, as well as the presence or absence of a compression syndrome (which could be identified by noncontinuous or continuous venous flow). If we suspect a compression syndrome, then a transabdominal DU is performed. We use either CTV or magnetic resonance venography for identifying gonadal vein size or reflux as routine procedures.

If PCS treatment is planned, a super selective venography by brachial access is performed. This allows us to identify LRVC or IVC, pelvic varices, and the leak point to lower limb varices, and to treat these anomalies in the same session, thereby minimizing the patient's disturbance. In addition, with a brachial approach, we obtain a better access to the ovarian veins due to the working angles for catheterization, and find no significant differences in the access to the left or right ovarian vein.

Keywords:
duplex ultrasound; ovarian vein; pelvic congestion syndrome

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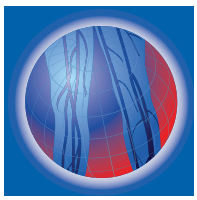

Deep venous reflux definitions and associated clinical and physiological significance

Lim KH, Hill G, Tarr G, van Rij A. *J Vasc Surg: Venous and Lym Dis.* 2013;1:325-332.

Reviewed by:
Oscar MALETI
Modena, Italy

Keywords:
chronic venous disease; classification; deep venous re1ux

Classification validation as well as physiopathological significance of deep venous reflux (DVR) remains debated knowing that DVR is frequently combined with superficial venous reflux (SVR).

Numerous key questions need to be answered. First, does segmental deep reflux have an impact on CVD or not? Second, does segmental reflux location matter? In other words, do isolated common femoral vein reflux or popliteal vein reflux have the same physiopathological importance in terms of clinical and hemodynamic anomalies? Third, does SVR suppression abolish or improve DVR segmental and/or axial reflux? Fourth, does operative treatment to restore valve competence of a single valve to improve axial reflux and hemodynamics?

Many articles referenced in the article by Lim et al that were devoted to answering the above questions and others, have been published, but, as underlined by the authors, in the absence of precise definitions, their conclusions are not clear and sometimes confusing.

To try to solve these questions, the New Zealand team suggested a new classification based on duplex ultrasound investigation determining, first, an axial level, which is slightly different from the Kistner classification, based on descending venography; second, to determine whether segmental reflux is limited to a single level or extended to multilevels without continuity with the axial vessel above the inguinal ligament.

This classification was correlated with:

- Clinical, Etiological, Anatomical, and Pathological (CEAP) classification, which the authors consider a valuable tool for evaluating clinical severity. However, even if in chronic venous insufficiency (CVI) the CEAP classification is frequently correlated with clinical severity, it seems that the use of the Venous Clinical Severity Score should have been more appropriate.[1]

- Venous filling index, measured by air plethysmography, as a tool for analyzing the severity of reflux-which is controversial.[2]

Some of their findings are in agreement with facts commonly acknowledged: DVR to knee or calf level is associated with more severe venous disease and greater hemodynamic derangement, independently of reflux in the superficial system. Others, such as the fact that segmental deep reflux over ≥2 levels is associated with more severe disease, must be confirmed.

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In conclusion, this study provides valuable information on DVR, but as the only investigation used was duplex ultrasound, some nonpostthrombotic iliac compression could have been missed.

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Instructions for authors

AIM AND SCOPE

Phlebolymphology is a quarterly peer-reviewed publication that aims to provide clinicians with updated information on every aspect of the venous and lymphatic disorders: epidemiology, pathophysiology, diagnosis, management, and basic science. Articles are usually in the form of review articles on timely topics with a broad update of recent developments and their clinical applications.

GENERAL INSTRUCTIONS

Articles

Articles should discuss a topic of current interest, outline current knowledge of the subject treated, give personal views and also analyze the different opinions regarding the topic discussed, and be up to date on the latest literature data. The article should contain:

- a **200- to 230-word abstract,**
- **2800 to 3200 words of main text** (without the references). All references should be cited in the text and numbered consecutively using superscript Arabic numerals. Please do not use the author-date system. (See § 'references' below)
- Please provide a current color portrait (head and shoulder) photograph of yourself. You can send it by e-mail as an attached jpg file provided that it has a resolution of at least 300 dpi.
- **Illustrations** are strongly encouraged (resolution of at least 300 dpi)

Comments in the *VEINEWS* rubric

The *VEINews* rubric is now incorporated in *Phlebolymphology* and may take various forms such as comments on a recent international publication (the most common) or on several publications on the same topic. It might be also controversial views of 2 authors on the same publication, or a state-of-the-art article on a timely topic. Any comment should contain:

- **A short summary of the commented publication**
- **A 300- to 500 word comment**
- References if any (no more than 5)

Text:. Abbreviations should be used sparingly and expanded at first mention. The style of titles and subtitles should be consistent throughout the text. The editorial department reserves the right to add, modify, or delete headings if necessary. *Phlebolymphology* uses SI units and generic names of drugs.

Submission: Manuscripts may be submitted by e-mail,[1], double-spaced, 8 to 16 typed . All pages should be numbered.
All texts should be submitted in English.

REFERENCES

Citation in text: All references should be cited in the text and numbered consecutively using superscript Arabic numerals.

Reference list: Presentation of the references should be based on the Uniform Requirements for Manuscripts Submitted to Biomedical Journals. *Ann Intern Med.* 1997;126:36-47 ("Vancouver style"). The author-date system of citation is not acceptable. "In press" references should be avoided. In the bibliography, titles of journals should be abbreviated according to *Index Medicus*. All authors should be listed for up to six authors; if there are more, only the first three should be listed, followed by "et al." Where necessary, references will be styled by the editorial department to *Phlebolymphology* copyediting requirements. Authors bear total responsibility for the accuracy and completeness of all references and for correct text citation.

Examples of style for references

Journal article: Sessa C, Perrin M, Porcu P, et al. Popliteal venous aneurysms. A two-center experience with 21 cases and review of the literature. *Int J Angiol.* 2000;9:164-170.
Article in a supplement: Sansilvestri-Morel P, Rupin A, Badier-Commander C, et al. Chronic venous insufficiency: dysregulation of collagen synthesis. *Angiology.* 2003;(suppl 1):S13-S18.
Chapter in a book: Coleridge Smith PD. The drug treatment of chronic venous insufficiency and venous ulceration. In: Gloviczki P, Yao JST, eds. *Handbook of Venous Disorders: Guidelines of the American Venous Forum.* 2nd ed. London, UK: Arnold; 2001:309-321.
Web-based material: Nicolaides AN. Investigation of chronic venous insufficiency: a consensus statement. American Heart Association, 2000. Available at: http://www.circulationaha.org. Accessed October 17, 2005.

Presentation at a conference: Jantet G. Epidemiological results of the RELIEF study across different continents. Paper presented at: 15th World Congress of the Union Internationale de Phlébologie; October 2-7, 2005; Rio de Janeiro, Brazil.

FIGURES AND TABLES

Figures should be of good quality or professionally prepared, with the proper orientation indicated when necessary (eg, "top" or "left"), and be identified by Arabic numerals, eg, *Figure 2*. Tables should be identified by roman numerals. Provide each table and figure on a separate sheet. Legends must be provided with all illustrations, including expansion of all abbreviations used (even if they are already defined in the text). All figures and tables should be numbered and cited in the text.

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Congress and conference calendar

DATES	CONGRESS	COUNTRY	CITY
19-21 February 2015	CONGRESS OF THE CZECH SOCIETY OF ANGIOLOGY 2014	Czech Republic	Prague
March 2015	XXXV VENOUS MEETING OF PORTUGUESE SURGICAL SOCIETY	Portugal	not confirmed yet
March 2015	THE CONFERENCE OF THE EURO-ASIAN ASSOCIATION OF PHLEBOLOGY	Russia	Chelyabinsk
3 March 2015	"OUTPATIENT PHLEBOLOGY:HOPES AND REALITIES"	Russia	Moscow
21 March 2015	5TH MASTER VENOUS ANATOMY	France	Paris
16-18 April 2015	INTERNATIONAL FORUM ON THE 50TH ANNIVERSARY OF THE STATE SCIENTIFIC CENTER OF COLOPROCTOLOGY	Russia	Moscow
22-25 April 2015	XXIII CONGRESO NACIONAL DEL CAPÍTULO ESPAÑOL DE FLEBOLOGÍA Y LINFOLOGÍA DE LA SEACV	Spain	Valencia
23-24 April 2015	VII UKRAINIAN NATIONAL CONFERENCE	Ukraine	Kiev
24-25 April 2015	ANGIOFORUM	Czech Republic	Brno
28 April-1st May 2015	CHARING CROSS INTERNATIONAL SYMPOSIUM VASCULAR AND ENDOVASCULAR CONTROVERSIES UPDATE	UK	London
May 2015	40TH DAYS OF PHLEBOLOGY	Czech Republic	Prague
7-9 May 2015	XXI CONGRESO ARGENTINO E INTERNACIONAL DE FLEBOLOGÍA Y LINFOLOGÍA	Argentina	Rosario

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8 May 2015	V CURSO ESCLEROTERAPIA HOSPITAL DE LA CRUZ ROJA	Spain	Madrid
16 May 2015	XII GEORGIAN NATIONAL CONGRESS OF ANGIOLOGISTS AND VASCULAR SURGEONS	Georgia	Tbilisi
Mid May 2015	PORTO VASCULAR CONFERENCE 2015	Portugal	Porto
21-23 May 2015	LIVE 2015 – LEADING INNOVATIVE VASCULAR EDUCATION	Greece	Heraklion - Crete
29-30 May 2015	XVI INTERNATIONAL SYMPOSIUM OF ANGIOLOGY AND VASCULAR SURGERY	Portugal	Oporto
29-30 May 2015	RÉUNION ANNUELLE DE LA SOCIÉTÉ BENELUXIENNE DE PHLÉBOLOGIE	Belgique	La Haye
30-31 May 2015	PRINTEMPS DE LA PHLÉBOLOGIE - BALARUC LES BAINS	France	Balaruc-les-Bains
2-3 June 2015	REUNIÓN NACIONAL SEACV	Spain	Castellón
11-13 June 2015	15TH CONGRESS OF THE HUNGARIAN ANGIOLOGY AND VASCULAR SURGERY SOCIETY	Hungary	Györ
12-14 June 2015	7. WACHAUER VEIN SYMPOSIUM	Austria	Melk
Mid June 2015	XV ANNUAL CONGRESS OF THE PORTUGUESE SOCIETY OF ANGIOLOGY AND VASCULAR SURGERY	Portugal	not confirmed yet
17-19 June 2015	ANGIOLOGICAL SYMPOSIUM	Czech Republic	Mikulov
1-4 July 2015	EUROPEAN VENOUS FORUM 16TH ANNUAL 2015	Russia	S.Petersburg

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