



Guidelines for the diagnosis and therapy of the vein and lymphatic disorders

REVISION 2004

Evidence-based report by the Italian College of Phlebology



del Collegio Italiano di Flebologia

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INTRODUCTION

1.1 The Italian College of Phlebology (ICP) was set up in 1996, combining the Italian Society for Clinical and Experimental Phlebology, the Italian Society for Phlebo-lymphology, and the Italian Phlebology Society. The ICF represents Italy in the Union Internationale de Phlébologie.

1.2 Between 1998 and 2000 three working groups drafted guidelines for diagnosis and therapy in phlebology and lymphangiology. These were published as a supplement to the ICF Journal (1) and in International Angiology (2001, Suppl.) in english version. In 2002, in order to update the guidelines, the original teams of phlebology and lymphology specialists were enlarged to include various other experts: physiatrists, nurses, economists and lawyers, and patients' representatives.

1.3 The method drew on evidence-based medicine, applying rules of evidence to the medical literature to produce recommendations for clinical management (2,3,4). Particular consideration was given to the evidence set out in Consensus Statements in this field (5-15), giving high priority to meta-analyses and randomised trials. The Cochrane Collaboration has published two analyses in this field: venous thromboembolism, and venous ulcers (16), besides others on sclerotherapy and measures for varicose veins and edema in pregnancy, available in their database (17).

We set out to adapt the findings to the working methods and approach taken by the Italian National Health Service, taking account of the extensive experience of European phlebology (18,19), compared to more recent Anglo-Saxon scientific models. Therefore, the different levels of recommendations have been classified as A, B and C:

Grade A, recommendations based on large randomised clinical trials, or meta-analyses, with no heterogeneity.

Grade B, recommendations based on randomised clinical trials sometimes with small populations, and meta-analyses including non-randomised clinical trials, with some possible heterogeneity.

Grade C, recommendations based on observational studies and on consensus reached by the authors of the present guidelines.

This grading system is based on the US Agency for Healthcare Research and Quality method (AHRQ, formerly AHCPR), simplified without the levels of evidence for the reasons stated, but also because of objective limits (there may be strong recommendations even when only observational studies are available).

1.4 The references were obtained from widely available sources such as MEDLINE, the Cochrane Database of Systematic Reviews etc. We also took full account of the extensive experience of the various national phlebology societies that belong to the Union Internationale de Phlébologie, basing ourselves on their various scientific journals:

Acta Phlebologica (Italian College of Phlebology)

Australian & New Zealand Journal of Phlebology (The Australian College of Phlebology and Australian & New Zealand Society of Phlebology)

Dermatologic Surgery (American College of Phlebology)

Flebología (Societad Argentina de Flebología y Linfología)

International Angiology (International Union of Angiology).

Journal of Vascular Surgery (American Venous Forum)

Phlébologie - Annales Vasculaires (Société Française de Phlébologie)

Phlebologie (Deutschen Gesellschaft für Phlebologie; Societè Suisse de Phlébologie)

Phlebology (Venous Forum of the Royal Society of Medicine, UK, and Societas Phlebologica Scandinava)

1.5 We have started an economic analysis (cost/effectiveness, cost/benefit ratios) which will be developed further when larger studies become available.

1.6. The drafting of these guidelines involved no conflicts of interest, except for reimbursements for attendance at symposia, lessons and conferences, by pharmaceutical or biomedical firms (see methods for declaration in Ministry of Health, Clinical Evidence, Italian edition 2001, no. 1).

1.7. We employed various strategies for the diffusion of the guidelines: conferences and courses for continuous education in medicine (CEM), summary editions for specific uses (Guidelines on compressive therapy, published by Minerva Medica, Turin, and kindly sponsored by CIZETA Medicali; a manual of extracts from the guidelines for general practitioners, also published by Minerva Medica, Turin, and kindly sponsored by Servier Italia); an international edition in English (International Angiology, 2001, 20, Suppl. 2 to No. 2); audit and feedback at the ICF National Congress, Lecce, October 2002).

1.8. A full-text, on-line version of the Guidelines published in 2000 is available at

<http://www.flebologia.unisi.it/lineeguida>

PRINCIPLES

In this first up-date of the guidelines it is perhaps a good idea to go over recent general aspects which strongly influence physicians' decisions.

2.1 Obligatory updating courses

Since 1/4/2002 health workers in Italy are obliged to attend continuous medical education (CEM) courses. Each category is allowed full independence as regards how it updates its knowledge, but clearly it makes sense to follow the national and regional training objectives. This Italian scientific society wishes to encourage its members to give priority to the theoretical and practical training schemes organized and conducted or supervised by scientific and professional societies (20).

2.2 Conflicts of interest

Potential sources of conflicts of interest for the specialist include direct participation in biomedical, technological and pharmaceutical enterprises, conduction of clinical trials, attendance at sponsored symposia or conferences, preparing scientific articles or editorials, and lack of transparency in the choice of surgical techniques or drugs in public hospitals. Specialists must therefore look closely at even apparently harmless contacts with industry and review their participation at congresses because it has been said that "the conflict of interest is primarily a condition, more than a behavior". It is therefore advisable to follow specific guidelines, taking account of the latest positions on this question (21,22).

2.3 Ethics and code of deontology

It is worth underlining our commitment to work for the patient's interests, resisting all influence from market forces, social pressures, administrative requirements, and so forth. We must foster the most equitable use of the health system, including fair distribution of the resources. The Charter of Medical Professional Conduct drawn up in 2002 by the American and European foundations for internal medicine offers an opportunity for a new contract between medicine and society (23). The new Code of Conduct established by FNOMC&O in Italy is another basic tool for correctly establishing the relations between advertising and health information to the public (24).

Numerous other ethical considerations emerging from recent tendencies in medicine must also be taken into account, such as the ethical aspects of sending a patient of one's own to another specialist for specific problems such as skin ulcer, for instance to a dermatologist or a specialized nurse, or for surgery – for instance to a colleague with more experience of that particular kind of case (25).

2.4 Medico-legal responsibilities

“The time is over when a doctor was only answerable for his actions to his conscience and his peers.” The specialist today must always remember this, though obviously without taking a totally “defensive” attitude to protect his own interests at the expense of the patient. Guidelines have no legal force, but they can be used as a basis for assessment should legal controversy arise. They are therefore an unofficial means of medico-legal protection, though nowadays this rests on other legal points too, among which informed consent from the patient has absolute priority (26-28). The ICF has set up a commission to deal with ethico-deontological and medico-legal questions.

2.5 Essential levels of assistance

The variety of clinical presentations of venous and lymphatic diseases is reflected in the wide choice of methods for managing these diseases. This complex picture is further complicated by the fact that the rules are constantly shifting. Essential levels of assistance (ELA) and protocols for a review of hospital use in Italy (PRUO) lay down outlines that the specialist cannot ignore. The ELA establish three broad areas of assistance in which the various types of assistance are listed that the Italian State-Region Conference (in an agreement signed on 8 August 2001) recognised as “essential” – meaning they must be guaranteed to all citizens (see *Gazzetta Ufficiale* no. 26, Ord. Suppl. to GU no. 33, 8/2/2002).

The scientific societies are responsible for identifying the headings in each area under which diagnostic-therapeutic procedures, drugs or other devices employed in each specialty fall. In phlebo-lymphology, for instance, the services provided under the “District Assistance” heading do not include elastic support hose or specific massage-therapy (manual lymphatic drainage) for patients with venous and lymphatic disorders. Under this same heading, pressure therapy is not included as a part of rehabilitation medicine.

Parallel to the rules aimed at rationalizing the use of resources, measures must be identified to verify and quantify non-clinical risks, such as improper use of the various modes of assistance – normal hospital admission, day hospital, outpatient or home treatment, etc.

The PRUO, mentioned above, was developed to verify the appropriate use of hospital admissions for acute cases. This was established by the Italian Regions under the heading of national laws (national health plan 1998-2000; DL 502/92 and subsequent supplements) and has been operative since 2001. The PRUO uses a method based on explicit criteria to quantify the frequency of inappropriate hospital admissions for acute conditions. Inappropriate is taken to mean a service that would be available elsewhere, or another level of care (long-stay, outpatient, home care, sheltered accommodation, etc.). This concept of inappropriateness has no clinical connotation, so should not be taken to mean the approach is useless or ineffective. The PRUO is not intended to express any judgement on clinical appropriateness, but considers a hospital admission or day stay medically justified – i.e. appropriate – if it makes use of documented skills or resources, and if their use and organisation are intense and coordinated so as to avoid waste.

One of the scientific societies’ tasks in the near future will be to define the levels and types of care required for the services provided by each specialty, and to “stage” the various diseases according to their severity, indicating the level of care required for each; they will then have to trace out the diagnostic-therapeutic path most appropriate for each pathology, and work up dedicated PRUO models (29).

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EPIDEMIOLOGY

Chronic venous insufficiency (CVI) is an important clinical condition with substantial epidemiological implications and socio-economic repercussions. In the western world the consequences of its high prevalence, the costs of diagnosis and therapy, the significant loss of working hours and the repercussions on patients' quality of life are well known (1,2,3). Recent figures set the prevalence of CVI in the lower limbs at 10-50% of adult males and 50-55% of the adult female population. Clinical manifestations of varicose veins are seen in 10-33% of women and 10-20% of men (1,4,5,6,7)

Among the various epidemiological approaches, prospective studies are of considerable interest – though speculative – with a view to establishing figures for the pure incidence. Unfortunately only very few deal with CVI. The most widely cited is the Framingham trial, which found the incidence of varices (appearance of new cases per unit of time) was 2.6% for women and 1.9% for men, per

annum; at two years 39/1000 men and 52/1000 women had varicose veins (8). Epidemiological studies in different parts of the world report widely differing figures for the prevalence of varices (7). The correlation between the prevalence of varices and age is almost linear: 7-35% of men and 20-60% of women aged 35-40 years; 15-55% of men and 40-78% of women aged over 60. Venous pathology and varices are rare in children and adolescents. However, children with a family history of varices may present ectatic or incompetent veins in adolescence (1,7,9).

It is still debated whether venous disorders are inheritable. The incidence of varices among people with and without transmissible hereditary factors ranges from 44-65% in those with and 27-53% in those without (7). Family predisposition is seen in 85% of patients with varices but in only 22% of those without (10). Although many studies indicate “vertical heredity”, there are none so far showing a “horizontal” pattern which would explain a genetic model.

CVI mainly affects women up to the fifth or sixth decade, but after that there is little difference between the sexes. Epidemiological studies give an overall male-to-female ratio of 1:2.3, although the important study by Widmer in Basel (11) reported a ratio of 1:1. Probably the findings reflect differences in the study methods (7). There are many epidemiological studies correlating the incidence of varices with pregnancy and the number of births. The figures are 10-63% for women with children against only 4-26% in nulliparae. For 1-5 pregnancies the incidence of venous disorders is 11-42%, rising linearly with the number of births. The correlation is even more striking for women who already have varicose veins. However, some studies find no relation between the incidence of varices and the number of pregnancies (7).

Various investigations have looked into the relations between varices and body weight.

Overweight people, particularly women, and town-dwellers, are more likely than normal-weight persons to suffer CVI and varices, the figures ranging from 25 to over 70% (for both sexes) as against 16-45% (7).

Varices normally arise in both legs – in 39-76% of cases (7). Hypertension, cigarette smoking, and constipation do not appear to be significant risk factors, and are not correlated with CVI. Some occupations, particularly those involving prolonged standing, are associated with a higher prevalence of varices, although this correlation is very hard to prove in statistical terms (5,12). The incidence of varices has been studied in people doing different jobs, particularly in industry. An association has often been reported between standing and varices (7,13). The temperature of the workplace also has an influence (12).

There are so many unrelated risk factors for varices that it is difficult to suggest useful preventive measures on the basis of single epidemiological findings (14,15). However, preventive measures against CVI, or its treatment, tend nowadays to be spread over the whole year, to cover the whole range of climatic or microclimatic changes, and to follow chronobiological patterns as they come to light. Phlebologists are always busiest in the warm weather, and in English-speaking countries there has even been talk of extra staff in the vein clinics in the hot season. However, from experience in Italy (16), from an English study (17), and from the Austrian SERMO study (18), questionnaires administered to two homogeneous groups of patients at different times of the year found no difference either in the symptoms, or in the decision to ask for treatment. This may reflect climatic factors – unexpected hot periods in a normally cold season or vice versa – or microclimatic ones, such as overheated homes or workplaces in the winter, long car trips with direct heating onto the legs, or excessively cold air conditioning and long holidays in summer.

Chronobiology and chrono-epidemiology report a higher incidence of acute events, involving venous insufficiency, and more frequent venous thrombosis in the winter months – January and February – possibly related to meteorological factors such as lower atmospheric pressure (19), or more probably hemorheological ones, which are also known for the two other most frequent cardiovascular events, infarct and ictus (20).

Oedema and trophic lesions, hyperpigmentation and eczema, in cases with CVI of CEAP stages 4-6 (see next section), affect 3-11% of the population. The rates of development of new symptoms/year are around 1% for oedema and 0.8% for mild skin disorders (1). Active venous ulcers (VU) are reported in about 0.3% of adults in the Western world; the global prevalence of

active and cured ulcers is 1% but the figure reaches 3% in persons over 70 (21). VU may take longer or prove more difficult to cure in patients from medium-low social classes. The prognosis of VU is anyway poor, as they tend to take a long time to clear up and recur easily; 50-75% close in 4-6 months but 20% are still open at 24 months and 8% at five years. Among patients of working age, 12.5% take early retirement (1,2,22,23,24).

CVI poses a considerable burden on health care services and is a major source of costs for society (25,26). It is estimated that 500,000 working hours are lost yearly in England and Wales because of CVI. In the USA, where 25 million people have varices, 2,500,000 CVI and 500,000 active VU, about two million working hours are lost. The Brazilian public health service reported that among the top 50 diseases most frequently causing absenteeism from work, and eligible for reimbursement, CVI holds 14th place, and is the 32nd cause of permanent invalidity (1).

Annual costs for the management of CVI – certainly underestimated – were reported to amount to 290 million pounds in Britain, 2,241 million Euros in France, 1,237,326,000 Euros in Germany, 845,956,400 Euros in Italy, and 103,614,400 Euros in Spain. The main countries in the European Union allocate 1.5-2% of their whole health care budget in 1992, without counting the indirect costs arising from invalidity (2,25).

Yearly costs for care of VU in the UK amounted to 400-600 million pounds (40 million only for materials for medication), more than a billion dollars in the USA (300 million for home care), 204,520,000 Euros in Germany and 32,940,000 Euros in Sweden. France counts the average cost of treatment for an ulcer at 36,000 Euros/year (1).

In Italy about 291,000 visits/year involve ulcers, with prescriptions in 95% of these cases, the total expenditure amounting to 243 thousand million lire (1997) (27). As a whole the direct and indirect costs of CVI add up to about one billion dollars for each European state for which the figures are available (UK, France, Germany) (1,23).

CLASSIFICATION

The field of chronic venous disease has suffered from a lack of diagnostic precision; this has led to conflicting findings in studies of specific venous pathologies (28). These differences would probably not arise if the disorders of each limb were diagnosed and classified precisely before treatment started. Clearly, a single, universally acknowledged classification system would make for clearer communication on CVI and permit more scientific, exact analysis of the therapeutic alternatives (29).

In February 1994, at a meeting organized by the Straub Foundation in Maui, Hawaii, USA, the American Venous Forum set up an international committee with the precise task of looking into this possibility. Chaired by Andrew Nicolaidis, the committee drafted a Consensus Document for the classification and staging of CVI. Known as the CEAP classification, it was based on clinical manifestations (C), etiological factors (E), anatomical distribution (A), and pathophysiological conditions (P). Its aim was to provide a full, objective classification, for use throughout the world (30,31,32,33). The CEAP classification was published in 25 journals, in eight languages, and today it is used in most publications in phlebology. (Table I).

Table I: CEAP Classification

Clinical

Clinical signs, C0 - C6

a – asymptomatic; s - symptomatic

Etiology

Ep, primary; Es, secondary; Ec, congenital

Anatomic

As, superficial veins; Ad, deep veins; Ap, perforating veins

Pathophysiology

Po, obstruction; Pr, reflux; Po+r obstruction and reflux

Clinical classification C0 - C6

C0 no visible or palpable signs of venous disease,

C1 teleangectasia or reticular veins

C2 varicose veins

C3 oedema

C4 skin changes due to venous disorders (pigmentation, eczema, dermatosclerosis, white atrophy)

C5 as C4 but with healed ulcers

C6 skin changes with active ulcers

Etiologic classification (Ec, Ep, Es)

Ec, congenital (from birth)

Ep, primary (cause not identifiable)

Es, secondary (post-thrombotic, post-traumatic, etc.)

Pathophysiologic classification (Pr,Po, Pr+o)

Pr, reflux

Po, obstruction

Pr+o, both

Anatomic classification

As, involving the superficial venous system

Ad, involving the deep system

Ap, involving perforator veins

Superficial venous system: As

1. teleangectasias, reticular veins, long saphenous vein:

2 above the knee;

3 below the knee

4 short saphenous vein

5 non-saphenous districts

Deep venous system, Ad

6 inferior vena cava, iliac vein:

- 7 common;
- 8 internal;
- 9 external
- 10 pelvic veins: genital, large ligament, others femoral vein
- 11 common;
- 12 deep;
- 13 superficial
- 14 popliteal vein
- 15. veins of the leg: posterior tibial, anterior tibial, peroneal
- 16. muscular veins: gastrocnemius, soleal, others

Perforating veins: Ap

- 17. in the thigh
- 18. in the leg.

The original drafters subsequently decided the classification needed extending and modifying in the light of recent findings. In 2000 two revisions of the CEAP classification appeared. One came from an American Venous Forum committee, presenting a new method for assessing venous disease according to severity (34) and the other was from an international Consensus Conference in Paris that proposed a new classification for varices recurring after surgery (35).

The French group set up a European Phlebological Data Bank, starting with complete information on 872 patients supplied by 49 angiologists from nine European countries. Statistical analysis showed that the external consistency of the clinical classification, "C", was good but its internal consistency less so (36). The French group also studied the reproducibility of the C classes and found good intra-observer reproducibility - 85% - but the inter-observer figure was lower - 47% (37). This led to a consensus conference on the redefinition of the C in CEAP, during the 14th World Congress of the Union Internationale de Phlébologie, held in Rome on 8-14 September 2001 (38). This working group assessed the original CEAP definitions, and after much consideration decided that a better, extended definition was needed (39).

NEW CEAP CLASSIFICATION

The table below explains how some clinical terms are used in the CEAP definitions (39). These must be employed correctly to ensure uniformity in "phlebological" language.(Table II).

TABLE II

Definition of clinical items

Telangiectasia

A confluence of permanently dilated intradermal venules of less than 1 mm in caliber.

Explanations: These would normally be visible from a distance of 2 meters under good lighting conditions.

Synonyms: spider veins, hyphen webs, thread veins.

Reticular veins

Permanently dilated bluish intradermal veins usually from 1 mm in diameter and less than 3 mm in diameter.

Explanations: They are usually tortuous. This excludes “normal” visible veins in people with transparent skin.

Synonyms: blue veins, intra-dermal varices, venulectasies

Varicose veins

Subcutaneous permanently dilated veins equal to or more than 3 mm in diameter, in the upright position.

Explanations: varicose veins are usually tortuous but refluxing tubular veins may be classified as varicose veins. These may be truncal varicose veins, tributaries, or non saphenous.

Synonyms: varix, varices, varicosities.

Corona phlebectasica

Fan shaped intradermal telangiectasias on the medial and or lateral aspects of the foot.

The place of corona in “C” is controversial and requires more consideration. Sometimes it could be the starting sign of advanced venous disease.

Explanations: This may occur in limbs with simple telangiectasias elsewhere in the limb.

Synonyms: malleolar flare, ankle flare.

Edema

Perceptible increase in volume of fluid in subcutaneous tissue characterized by indentation under pressure.

Explanations: This definition includes only edema attributable to venous disease. Venous edema usually occurs in the ankle region, but it may extend to leg and foot.

Pigmentation

Brownish pigmentary darkening of the skin usually occurs in the ankle region, but may extend to leg and foot.

Explanations: This is an early skin change.

Eczema

Erythematous, blistering, weeping or scaling eruption of the skin of the leg.

Explanations: It is often located near varicose veins, but may be located anywhere in the leg. Sometime may spread to the entire body. Eczema is usually due to chronic venous disease, and/or to sensitization to local therapy.

Synonyms: Stasis dermatitis.

Lipodermatosclerosis

Localized chronic induration of the skin sometimes associated with scarring and/or contracture.

Explanation: this is a sign of severe venous disease, characterized by fibrosis and chronic inflammation of the skin, subcutaneous tissues, and sometimes the fascia.

Hypodermatitis

An acute form of lipodermatosclerosis is referred to as hypodermatitis. This is characterized by

diffuse reddening of the skin due to acute inflammation and by tenderness.

Explanation: The absence of lymphadenitis and fever differentiates this condition from erysipelas or cellulitis.

Atrophie blanche or white atrophy

Circumscribed, often circular whitish and atrophic skin areas surrounded by dilated capillary spots and sometimes hyperpigmentation.

Explanation: This is a sign of severe venous disease. Scars of healed ulceration are excluded in this definition.

Venous ulcer

Chronic defect of skin which fails to heal spontaneously, caused by chronic venous disease.

CEAP class 4 is divided into two parts: C4a comprises pigmentation and edema, C4b lipodermatosclerosis and white atrophy. The aim is to establish more precisely the severity of the trophic changes, bearing in mind that the signs of class C4b are predictive of progression to ulcer (39)

NON-INVASIVE DIAGNOSIS

Non-invasive diagnostic methods for venous disease were developed for screening, for quantifying lesions, and for hemodynamic studies. Both the general practitioner and the specialist must, at their different levels, know the significance of the various vascular tests, their indications and limitations, so they can avoid having to prescribe unnecessarily invasive and costly tests (40,41,42).

Venous disease is more difficult to evaluate than arterial disease and requires experience and closer evaluation. This means venous tests are much more operator-dependent and require specific clinical skills, particularly in the evaluation of CVI. CVI can be the result of obstruction to venous outflow or reflux, or to a combination of the two. Clinical examination and diagnostic techniques therefore aim to establish which conditions are present. The anatomical location of the alterations must be found and the reflux and/or obstruction must be identified.

There are many simple, rapid and efficient tests available, with good cost-benefit ratios. The diagnostic procedures listed summarily below reflect those set out in the Procedure Operative per Indagini Diagnostiche Vascolari (Operating Procedures for Vascular Diagnostic Investigations) published by the Italian Society for Vascular Investigation, and accepted by the Italian College of Phlebology (43).

MAIN INVESTIGATIONAL TECHNIQUES

Ultrasound

- Continuous-wave (CW) Doppler
- Duplex scan
- Echo(color)Doppler (ECD)

Radiographic imaging

- angio-CT scans
- angio-MR scans

Plethysmography

- quantitative photoplethysmography
- phlebography (venography).

DIAGNOSTIC PROCESS

The aim of the investigation is to check whether there is venous reflux or superficial and/or deep venous thrombosis. Depending on the findings, the diagnostic pathways divide. The deep venous circulation should always be examined.

EVALUATION OF VENOUS REFLUX

Reflux is usually assessed with the patient standing. The examiner holds the probe which is placed at the origin of the short or long saphena. The left hand makes swift compressing motions, releasing the vein distally. These maneuvers are essential, especially for CW Doppler, which does not visualize the vein being probed. Once the probe is centered on the vein the patient executes a prolonged standard Valsava maneuver during which reflux is assessed. The following are usually taken as normal and pathological limits (Table III):

Table III

Normal saphenus veins:	reflux up to 0.5 sec
Dilated but competent saphenous vein: 1.0 sec	reflux more than 0.5 sec but less than 1.0 sec
Saphenous valves incompetent :	reflux more than 1.0 sec.

The vein can be followed distally, identifying the axis of the reflux and establishing whether the valves are incompetent throughout the vein or only in parts. This is important as a basis for establishing how far distally the saphena needs stripping.

ECD is easier to interpret than CW Doppler, and provides more information on the morphology of the greater saphena, such as its diameter, caliber and the competence of valves in the ostial collaterals and any accessory saphenous veins. It gives an excellent view of the ostial and preostial valve (44,45). When examining reflux in the short saphenous vein ECD is useful to study the vascular anatomy of the popliteal area, helping establish the exact origin of the popliteal vein, rather than a high start of the long saphenous vein from the superficial femoral vein; it also confirms competence of Giacomini's vein, and whether reflux comes from a popliteal perforating vein.

Briefly, therefore, the procedure is similar for ECD and CW Doppler examinations. Both provide the information needed, i.e. the duration of reflux, in seconds, during the Valsava maneuver, which should always be clear from the documentation supplied by these techniques. ECD provides morphological data, so one can "reconstruct" the vascular anatomy and establish the diameter of vessels, giving a useful preoperative hemodynamic map and serving to assess post-surgical or post-sclerotherapy recurrences. ECD shows accurately when reflux comes from an incontinent perforating vein, but CW Doppler cannot give this information clearly and should therefore not be used for this assessment.

Ultrasonography serves to study a single superficial or deep axis, identifying it on the basis of the anatomical location. The origin and axis of the reflux can be established completely. This examination also gives a repeatable, reliable quantitative finding (the duration of reflux during a standard Valsava maneuver). As US selectively evaluates one district at a time, it cannot be used for an overall functional investigation of damage due to a single venous reflux (46,47).

Photoplethysmography (PPG) is a computerized quantitative technique for assessing the venous pump. For example by dorsal extension of the tibio-tarsal joint, it can evaluate the overall functional efficiency of the muscle pump and valvular competence of the venous axes (48,49).

Venous plethysmography measures changes in venous blood volume in the legs, to evaluate overall venous function. Three plethysmography techniques are currently in use: photo-pulse-plethysmography/reflected light rheography (PPG/RLR), strain gauge plethysmography (SGP), and air plethysmography (APG) (1,50,51).

PPG/RLR uses photo sensors attached to the skin to measure filling of the cutaneous vein network (41). SGP uses extensimetric sensors (elastic sensor straps) to measure changes in the circumference of the leg at the point where they are applied (42). The APG sensors are inflatable leg cuffs which measure changes in the total venous volume of the leg (40). By taking measurements in various positions and during various maneuvers it is possible to evaluate the following:

- 1) venous outflow (slowed if there is occlusion)
- 2) total venous reflux (degree of valvular incontinence)
- 3) the efficiency of the muscle pump in the calf (venous drainage during exercise and the speed of refilling after exercise).

These measurements can be done in baseline conditions, or using a tourniquet to exclude the superficial veins, to give separate evaluations of the superficial and deep veins and forecast how removal of the saphena might affect venous return. A 3-cm cuff is recommended, inflated to 100 mmHg. PPG offers the advantage of a quantitative result, in seconds – indicating the venous refilling time – that gives an overall picture of the functional impairment of venous return due to reflux.

Instruments and procedure: quantitative computerized PPG

For this quantitative investigation the baseline signal is automatically adjusted and a precise evaluation can be made of the parameters connected with refilling time after the muscle pump test, and with the signal amplitude. The probe is fixed about 8 cm above the internal malleolus, with a bi-adhesive ring. The patient sits comfortably with his feet firmly on the ground. There should be an angle of about 110° between the patient's trunk and his thighs/legs. The muscle pump test is the most widely used and involves eight dorsal extensions of the tibio-tarsal joint in 16 seconds. At the end of the test the patient sits still for 30 seconds.

Modern equipment is programmed to emit sound signals for the dorsal extension of the foot and to mark the filling period. The venous refilling time (To) is expressed in seconds, and classified as follows (Table IV):

Table IV

1) normal	more than 24 seconds
2) pump inadequate grade 1, mild	24-20 seconds
3) pump inadequate grade 2, moderate	19-10 seconds
4) pump inadequate grade 3, severe	less than 10 seconds

These computerized instruments also assess the power of the venous pump (Vo) but this findings is not yet sufficiently standardized for use in diagnosis.

Venous plethysmography has the following applications in clinical practice:

- a) to measure and document the degree of impairment of the various venous functions (obstruction, reverse flow) and follow them over time;
- b) to quantify the involvement of the superficial and deep veins and predict the hemodynamic effects of superficial vein surgery;
- c) to study and document the hemodynamic effects of different surgical options and validate new technics.

One limitation of PPG is that it may be difficult to distinguish superficial and deep venous reflux, or reflux from incompetent perforating vessels.

Phlebography using injection into a vein of the foot is no longer used to assess venous reflex, as ECD is preferred. Phlebography should be kept for patients with a history of venous thrombosis, those who have undergone surgery, and have unexplained recurrences (surgical technic not known), and cases where US gives unclear results. Some centers still use “varicography” to investigate recurrences after surgery or sclerotherapy, especially in the popliteal cavity or for incompetent veins, particularly if there are several.

Radiographic imaging is the second level requested by a specialist, and completes the US examination, helping establish the site and nature of the lesion, and evaluate the pathology, especially in cases involving the deep circulation. It is indicated for angiodysplasia, where angio-MR is preferred. It cannot yet replace phlebography (52,53).

The microcirculation is investigated using the following techniques:

- Laser-Doppler
- Capillaroscopy
- Microlymphography
- Interstitial pressure
- O₂ and CO₂ partial pressure

Recommendations:

Ultrasound examination is useful to demonstrate reflux, identify its origin and follow its axis cranio-caudally. Grade A

After clinical examination, the main screening method for CVI should be CW Doppler. Grade B

Echo-Doppler and echo color-Doppler should be used to establish the location and the morphology of the problem., and preoperatively. Grade A

Phlebography is only needed for a small number of patients who have anatomical anomalies or malformations, or when surgery on the deep venous system is indicated. Grade B

Plethysmography should be considered as an additional quantitative test. Grade B

Investigations of the microcirculation are only indicated in selected patients, mainly for research purposes. Grade C

SURGICAL TREATMENT

Surgical treatment for superficial venous insufficiency

BACKGROUND AND INDICATIONS

Surgical treatment of varicose veins in the lower limbs started a century ago, with the work of Keller in 1905 (stripping by invagination), Mayo in 1906 (extraluminal stripping), and Babcock in 1907 (intraluminal stripping with a rigid probe). It is a procedure whose value has been confirmed by many thousands of operations and studies and validated by “common experience” and various authoritative studies (54,55,56,57,58,59).

Essentially, three innovations have improved the results of the standard surgical technique: the saphena stripping technique itself has been improved, on a new anatomical and physiopathological basis; simplified surgical procedures are now used, such as microsurgical phlebectomy (60,61) and stripping by invagination under local anesthesia (62); and pre-operative mapping is done using color echo-Doppler scans (63,64,65,66).

Many new surgical approaches have been proposed, some only used by the proposer. These may give good clinical results, but controlled multicenter trials are needed to assess them. For the time being, therefore, they cannot be considered substitutes for the standard techniques; at best they can be considered alternatives.

The importance of varicose vein surgery in Western health services is shown by the frequency of demand. Generally, the requirements are calculated at 80,000 interventions/year in the United Kingdom (67), 200 per 100,000 inhabitants in Finland (68), up to the more than 150,000/year in Italy (2000 DRG data plus a rough estimate from the private phlebology sector), and 200,000/year in France (69). Therefore, the surgical indications must be discussed in depth.

The aim of surgery is total removal of all varicose veins, and this itself must be viewed in the context of the underlying pathology - CVI - and the troublesome problem of varicose veins recurring and new ones appearing after surgery.

The main aim of treating patients with CVI is to cure or relieve the symptoms and to prevent or treat complications. The standard treatment is elevation of the lower limb to a drainage position and elastic compression hosiery to control edema, with local medication for ulcers. However, this does not treat the underlying hemodynamic disorder causing the venous disease.

Significant progress has been made in the surgical treatment of severe forms of CVI, which can now be diagnosed non-invasively with imaging and velocimetry methods. It is possible to distinguish between situations in which obstruction prevails, and others – either primary or secondary – in which reverse flow is dominant. The surgical strategy chosen will depend on the different clinical, anatomical and pathological presentations. A wide range of strategies is available, no longer restricted to extensive and indiscriminate ablation, but aimed at correcting, where possible, the venous and microcirculatory hemodynamic abnormalities in the limb (70).

Indications for surgery in CVI depend on the symptoms, and on the objective findings definitely related to varices or their complications. The symptoms and pathologies that motivate the surgical choices are:

- clinical presentation and appearance
- pain
- heaviness in the legs
- fatigue in the limb
- superficial venous thrombosis
- bleeding varices
- pigmentation at the ankle
- lipodermatosclerosis
- white atrophy

- ulcers.

However, as patients themselves may not attribute some of these signs and symptoms to CVI, a thorough, specific case history should be taken. Fifty percent of patients with telangiectasia and varices suffer from only some of the disorders listed and with suitable treatment these problems will be eliminated in 85% of cases (71).

Heaviness of the legs is the most common reason for an examination by a venous specialist, especially among younger women. It may not be caused by varices, nor is it necessarily a pre-varicose syndrome and is more likely to be the result of a combination of constitutional venous stasis, venous hypertension and lipedema (72,73).

Numerous other diseases give the same symptoms of fatigue and easy functional exhaustion: joint, neurological and peripheral arterial diseases are the most frequently cited. Similarly, oedema of the lower legs is not obligatorily correlated with CVI, and a differential diagnosis must take account of congestive cardiopathy, blood dyscrasias, metabolic disorders, etc. Finally, patients who have an unhealthy lifestyle, are overweight, do little exercise, have bad posture and are excessively sedentary may also have CVI, or it may be masked by these factors. In these cases, corrective measures may be sufficient to obviate the need for surgical intervention which may, in fact, even be contraindicated. Many symptoms are not actually caused by venous factors and the venous disorder is simply concomitant with the underlying problem; in cases such as these surgical intervention is unlikely to relieve the symptoms (74,75).

Surgery of the superficial venous system accounts for a substantial portion of the workload of a general and vascular surgical unit and is one of the main reasons why waiting lists tend to be long. There is also the suggestion that “inadequate” venous surgery is responsible for many cases of recurrent varicose veins, even if the surgical technique was error-free (76) although it is not clear what exactly was meant by adequate (or appropriate) or inadequate (or inappropriate) surgery (77).

Recommendations:

The aim of varicose vein surgery is to relieve the symptoms, and prevent or treat any complications while recognising that the varicose disorder is likely to be progressive.

Grade A

The surgical patient will require regular clinical and instrumental follow-up. Grade A

There are valid medical alternatives, and sclerotherapy, for collateral veins, which therefore do not necessarily call for a surgical approach. Grade B

SURGICAL TECHNIQUES FOR VARICOSE VEINS

Nowadays any surgical intervention for superficial venous insufficiency should be preceded by hemodynamic studies using color echo-Doppler mapping of the area (78,79,80). The surgical techniques can be classified in three main groups:

- ablative surgery
- conservative surgery
- endovascular obliteration.

1) Ablative surgery

This heading comprises surgery for stripping the saphena - “crossectomy” - at the sapheno-femoral

junction, and phlebectomy.

a) Stripping the saphena

This includes stripping the great saphenous vein (internal saphenectomy), or the small saphenous vein (external saphenectomy). In the first case the intervention may be long (removal of the great saphenous vein from the sapheno-femoral junction to the medial malleolus), medium (from the sapheno-femoral junction as far as the middle third of the leg), short (from the sapheno-femoral junction to the upper third of the leg), or ultrashort (from the sapheno-femoral junction to the lower or middle third of the thigh).

Stripping is the standard surgical treatment. It has been extensively studied over the years and comparative studies have been made with sclerotherapy and with crosssection alone or combined with sclerotherapy. In many clinical trials stripping was more effective in terms of long-term efficacy (54,55,81,82,83,84,85). Several techniques have been described: Babcock's intravenous stripping with a rigid probe, or with a flexible probe according to Myers; Mayo external stripping, and its derivations; stripping by invagination as done by Keller and Van der Strict, Ouvry, and Oesch. Often these approaches are less invasive and have a better effect on quality of life than the standard stripper (86).

Ablation of the saphenous veins may be completed by varicectomy at the thigh or leg, and by section and ligation of the incompetent perforating veins (87) so as to achieve the required hemodynamic result by excising the refluxing vessels.

b) Simple "crosssection" or combined with phlebectomy

Crosssection involves disconnecting the sapheno-femoral vein with a ligation and sectioning all the collaterals. The functional results are well documented but it is not as effective as stripping for varicose veins (88,89). Crosssection with phlebectomy can give results comparable with stripping but only when the case has been carefully investigated before surgery (90,91,92).

c) Phlebectomy

Phlebectomy with microincisions, according to Muller, may be used either alone to cure varicose veins, or complementary to other techniques. This method aims to give a good esthetic and functional result. An incision of a few millimeters is made and the incompetent branches of the superficial circulation are removed through this incision using special hook-like instruments (60,61). Muller's microincision can be used to treat superficial venous thrombosis, either to remove the thrombosed varicose branches or simply to squeeze out the thrombus.

A recent outpatient approach, still being tested, involves endoscopic resection and ablation of varicose veins using venous electrocautery and a fiber-optic hydroresector, with a solution to swell the veins (93).

Recommendations:

Before any decision is taken on which technique is indicated, a detailed echo-(color)- Doppler study should be done to avoid diagnostic errors. Grade A

The patient should be informed that the aim of the Muller intervention is to treat the symptoms, and that the method has limited indications. Grade B.

2) Conservative surgery

The aim is to treat the varicose veins, maintaining the saphenous drainage but not the reflux. Saphenous flow can be directed physiologically (sapheno-femoral external valvuloplasty and first step of the CHIVA 2 (Conservatrice Hémodynamique de l'Insuffisance Veineuse en Ambulatoire) strategy - see below) or reversed and directed towards the re-entering perforating vein (CHIVA 1). These techniques can be complemented by phlebectomy by Muller's method, but in any event an

echo-(color)-Doppler examination must be done beforehand.

a) Sapheno-femoral external valvuloplasty

The rationale for this treatment is based on the histological finding that in the initial stages the valve cusps are still healthy but are incompetent because of dilation of the vessel walls (94). It must be shown echographically that the cusps are mobile and not atrophic in the terminal and/or subterminal part of the great saphenous vein.

The aim is to bring the valve leaflets back together, closing up the dilated vessel walls (95,96). This can be done by either suturing the wall directly or by “buckling” the vessel with some sort of external prosthetic belt. Dacron or PTFE is used today, with a nitinol core (97). Competence should be tested during the operation using the milking maneuver or a Doppler scan, or both.

After more than a decade in the experimental stage, this approach can now boast encouraging results from multicenter randomized clinical trials, as long as the surgical indications are respected and external valvuloplasty is feasible (98,99,100).

Recommendations

External valvuloplasty of the terminal and/or subterminal valve of the great saphenous vein, after thorough preoperative assessment, and with careful intraoperative checks, is a good way to treat saphenous reflux in 5-8% of patients. Grade B

b) CHIVA type 1 hemodynamic correction

This one-step method to correct a hemodynamic defect is done when the perforating re-entry vein of a refluxing saphenous system is on the saphenous trunk (type 1 shunt and some type 3 subtypes). The sapheno-femoral vein is disconnected, conserving non-refluxing collaterals, and the saphenous vein is freed of any incompetent branches, with or without a phlebectomy. The perforating re-entry vein should be treated by tying it off or sectioning the saphenous vein downstream of its entry point (terminalization) (63,101). Retrograde flow indicates the hemodynamic success of the operation.

c) CHIVA type 2 hemodynamic correction

This two-step method to correct a hemodynamic defect converts a type 3 shunt to a type 1. It is done when the penetrating re-entry vein of a refluxing saphenous system is on a tributary of the saphenous vein, or on the vein itself if there are valves on the segment between the perforating vein and the origin of the varicose collateral (102). In these cases the simultaneous disconnection of the sapheno-femoral joint and the varicose collaterals sets up a non-draining saphenous system, raising the risk of venous thrombosis or later recurrence.

In the first step of CHIVA 2 the tributary/ies are disconnected flush from the saphenous wall and a phlebectomy may be carried out. In most cases this sets up an anterograde-flow system, which remains stable in the long term in varying proportions of patients. Should a perforating saphenous re-entry route develop, the second step is in fact a CHIVA 1 hemodynamic correction.

CHIVA operations now have at least three-year follow-ups in several reliable reports (103,104,105).

Recommendation:

The number of CHIVA operations is still limited and there are reproducibility difficulties. CHIVA 2 should not be used for saphenous veins with a caliber of more than 10 mm at the thigh, especially if the segment below the origin of the collaterals shows aplasia or hypoplasia, so as to limit the risk of saphenous thrombosis at the open cross. Grade C

3) Endovascular obliteration

Either chemical or physical methods can be used to obliterate the saphenous lumen. The former is in fact sclerotherapy. The latter employs fairly sophisticated techniques such as radiofrequencies and lasers. Lasers appear to give more lasting results than electrocauterization, where the thrombus may become recanalized in a very short time.

a) Radiofrequency treatment

The procedure has been used since 1999, and can be done under local, tumescent or loco-regional anesthesia (106,107). The vessel walls are treated with a heat-transmitting radio probe, which causes contraction and thickening of the adventitious collagen, so the lumen shrinks until it closes completely. The catheter's position in relation to the saphenofemoral junction is checked under echo-Doppler guidance.

Immediately after surgery, when all has gone well, the saphena feels like a solid, contracted cord. At one year in a multicenter observational study involving 232 checks, (108)) reported 83.6% of closed saphenous veins, 5.6% still open and 10.8% recanalized. At two years the percentages of 142 visits were similar.

This procedure can be combined with phlebectomy, or with endoscopic surgery on the perforating veins (109).

b) Laser therapy

Local, tumescent or trunk anesthesia is preferable for laser therapy. The saphenous vein is obliterated by contraction of the collagen fibers in the wall, due to the heat released by the laser. Complications – ecchymosis and a short-lasting burning sensation on the skin – are negligible. Leaving aside the preliminary findings of some clinical trials, published reports (110,111) indicate full occlusion of the great saphenous vein at one year in all patients.

Both these procedures still involve some unknown factors:

- Caselists are still small in absolute terms and in relation to long-term outcomes. Follow-up of these patients - ideally five years - has not yet been reached.
- Obliteration of the vena saphena must leave a safety margin from the ostium. There therefore remains a small terminal sac into which one or more collaterals of the sapheno-femoral junction drain, whereas this does not happen with crosssectomy. Supporters of the oblitative procedure maintain that this helps avoid relapses (112).
- On the topic of the cost-benefit ratio, the control unit involves considerable initial expenditure, and catheters are very expensive. A randomized trial (113) on a limited number of patients showed that the cost of radiofrequency treatment was double that of traditional stripping surgery, but laser treatment cost somewhat less, because the fibers can be sterilized, and therefore reused.

Recommendation:

Neither of these oblitative procedures is validated as yet in the literature. They must therefore be considered as still in the clinical validation stage, and as such only used in accredited, qualified phlebology centers, after the necessary learning period. Grade C

SURGERY OF THE PERFORATING VEINS

The perforating veins supply blood through the muscular aponeurosis to the superficial and deep

venous systems. These veins are numerous, from 80 to 140 per leg, their diameters not exceeding two millimeters. The valves are normally in the sub-aponeurotic area. The best way of identifying incontinent perforating veins in the leg is still undecided. Echo-Doppler scans seem the most reliable, though the examination procedure is still debated (114,115). A reflux is defined as pathological if it lasts more than one second and the caliber of the perforating vein is more than 2 mm.

The severity of the CVI in relation to incontinent perforating veins is based on the number of perforating veins involved and whether more than one system is affected (32,116).

Elimination of the incontinent perforating veins in combination with drainage of the varicose veins and restoration of the saphenous return in patients with severe CVI is an important therapeutic approach for trophic disorders of the skin (117,118).

The indication for surgical treatment is elective in patients with incompetent perforating veins of the leg and active or healed ulcers (CEAP classes C5- C6). Treatment of perforating veins due to superficial vein inadequacies is reserved for cases with symptomatic cutaneous dystrophy (CEAP class C4) (119).

There are two main surgical procedures for perforating veins:

- the traditional supra- and subfascial approaches
- subfascial, by endoscopy.

The traditional methods (according to Linton, Cockett, Felder, De Palma) give broadly similar results, with 9-16.7% of patients having recurring ulcers when followed up for 5-10 years (120,121). The more recent endoscopic approach for perforating veins may employ a single access (one trochar) or two (operating and optical trochars). A number of studies report 0-10% of recurrent ulcers at five-year follow-up (55,119,122).

Endoscopic surgery is often combined with venous bypass (123,124) and the percentage of relapsing ulcers at five years seems similar. However, in one multicenter trial comparing endoscopic surgery alone with endoscopy plus superficial venous bypass the proportion of relapsing ulcers at two years was smaller in the combination group (125).

Since it is less invasive, involves fewer post-operative complications, and permits access far from the ulcer itself, the endoscopic technique is currently preferred to traditional surgery for perforating veins (126).

Recommendations:

In patients with post-thrombotic syndrome it is important to treat the incontinent perforating veins, with sclerotherapy, traditional surgical techniques or endoscopy.

Grade B

For varicose veins with no specific cause it is essential to distinguish the hemodynamic role of the perforating veins of the thigh (Dodd perforating veins) and the Boyd perforating veins. When these are incontinent they must always be closed or removed. For any other perforating veins in the leg, the clinical aspects and the radiological findings must be taken into account. Grade C.

RECURRENT VARICOSE VEINS

These are varicose veins that appear after surgical treatment, not the remains of the treated veins (35). Although surgery for varicose veins in the lower limbs appears to be a simple procedure, there are a number of traps. The high percentages of recurrences reported in the international literature confirm this (127,128,129,130,131,132,133). However, it is difficult to interpret these findings, as

the patient populations differ and the diagnostic and therapeutic protocols vary.

The most frequent causes of recurrences are:

1. Errors of diagnostic strategy and treatment

The long-term results of surgical treatment of varicose veins depend on correct diagnosis. If the hemodynamic causes of the varicose veins are properly identified an appropriate treatment plan can be chosen (134). “Radical surgery”, defined as physical extraction of the saphenous vein with all its collaterals and all the enlarged varices, which has been the surgical procedure of choice for varicose veins for almost a century, has been replaced by a “radical hemodynamic approach”, meaning elimination of the hemodynamic defects at the root of the formation of the varices (the reflux).

Mapping was started more than a decade ago to ensure reproducibility over time (63). A “map” of the varicose veins and circulation defects of the lower limbs is used in CHIVA interventions and “traditional” surgical procedures. Incorrect application of these concepts – especially on an anatomical basis - can leave the way open to recurrences.

2. Technical errors

Evidence abounds of the impact of errors, frequently serious, made during operations, not only in the older series (127,135,136,137,138). Among the reasons leading to errors during surgery for varices in the legs, certainly the most important is the wide anatomical variety of the sapheno-femoral junction, which can lead to the surgeon sometimes inadvertently leaving collaterals in place.

Recurrent veins can be treated by re-operation, using a subfascial lateral inguinal approach, to avoid the difficulties of cicatricial sclerosis (128,139,140 when echo-(color)-Doppler scan shows a long saphenous stump with one or more collaterals (141). In cases where surgery is not indicated, pharmacological therapy, compression or sclerotherapy are all useful alternatives, especially in view of the limited benefit of surgery for recurrent veins in relation to QoL (67).

Recommendation:

The likelihood of varicose veins recurring as the disease progresses remains. To limit the risk correct diagnosis is essential. This is routinely done by ultrasound (levels I and II), leaving selective phlebography for special cases (level III) in order to minimize the risk of error. Grade B

DAY SURGERY

A proposal for regulations is currently being drafted for the Essential levels of assistance - ELA - (G.U. Repubblica Italiana, February 2002), to cover the clinical, organisational and administrative possibilities for surgical interventions, invasive and semi-invasive diagnostic and/or therapeutic procedures, without hospital admission and without the need for post-operative observation. Such procedures can be done in the consulting room, in out-patient or other qualified centers, using local or locoregional anesthetics. Three possible regimens for surgical treatment of varicose veins are given: walk-in (ambulatory – A), day surgery (DS), or ordinary admission (OA).

Appropriateness Evaluation Protocols (AEP), developed by Geertman and Restuccia (142) are the forerunners of the protocols used today. These are the most widely verified protocols, and have been used in North American hospitals since the early 1980s. A working group from seven European countries (Austria, France, Italy, Portugal, Spain, Switzerland, UK), verified, updated and validated the AEP, producing a European version (143). An Italian version, the PRUO (Protocol for Hospital Use Review) is employed in various regions of Italy (144,145). The PRUO has specific additional sections intended to identify the reasons for inappropriate hospital admissions and stays.

Special forms must be used to establish the appropriateness of OA, DS or A.

There are four categories of criteria to establish the level of assistance required:

- a) comorbidity (concurrent medical problems that put the patient at special risk, regardless of the type of surgery planned);
- b) complications (arising postoperatively, considering surgery lasting 60 min or longer; social factors such as patients who live alone, cannot reach public transport, live a long way from a health care structure, etc.);
- c) intensive care (if needed postoperatively);
- d) extraordinary criteria (override).

DS is probably suitable for the majority of surgical interventions for varicose veins as long as specific selection criteria are used:

- I) DS procedures should preferably last less than one hour
- II) patients scheduled for this treatment must be carefully selected and should be informed prior to the procedure about the type of intervention and/or treatment. They should signed a personalised informed consent form. Patients seem mostly highly satisfied with DS, with about 25% of complaints (146,147,148,149);
- III) selection must take into account the patient's general condition and pertinent family and logistic factors;
- IV) patients who are entered in DS programmes must be in good general health. The ideal candidates are ASA classes 1 and 2. Emergencies cannot be dealt with on this basis;
- V) age and weight selection criteria apply. With few exceptions, the upper age limit is 75 years. Obesity is a very important risk factor and must be carefully evaluated.
- VI) as regards logistics, the patient's home should not be too far from the place where the operation will be done. The patient should be reachable in a short time, if necessary, so the travelling time should preferably be less than one hour. Phone contact with the center must be possible;
- VII) patients must have a family member or reliable person with them during the recovery period. This person should be given detailed instructions and should be able to accompany the patient home and give any assistance needed, particularly in the first 24 hours;
- VIII) the decision to enroll a patient in a particular regimen is the exclusive responsibility of the doctor, who, after obtaining the patient's informed consent, must be at liberty to select the most suitable regimen, on the grounds of the sound scientific and ethical principles always underlying health care;
- IX) the choice of the most suitable regimen will be guided by the patient's clinical and psychological condition. Many of the pathologies that would normally lend themselves to treatment under a walk-in regimen should, if they are more extensive or complicated, be treated in the DS or actually in hospital (OA);
- X) finally, even if a pathology or surgical procedure appears on the official list of services available in DS, this does not oblige a doctor to carry out the treatment under that regimen (150).
- XI) surgery for varices must move gradually and adaptably from OA to DS. The latest figures based on analysis of DRG 119 for the year 2000 in the Ministry of Health website give 106,158 surgical operations for varicose veins throughout the whole country, 78,521 of them (74%) in OA, with a mean hospital stay of 2.79 days, and 27,637 (26%) in DS, with a mean stay of 1.6 days.

SURGICAL TREATMENT OF DEEP VENOUS REFLUX

Candidates for deep venous surgery suffer from severe CVI, with significant venous reflux and ambulatory venous hypertension. Conservative therapy has failed for these patients and the venous disease reduces their quality of life. When the deep vein reflux is slight, stripping the saphenous vein can bring considerable benefit and eradicate the reflux in the femoral vein (151). However, if there is strong, fast reflux, the deep venous system may often require direct surgery, considering the high percentage of recurring ulcers after conservative treatment and the excellent, lasting results in centers that opt for the direct approach.

Valve reconstruction surgery includes direct methods, which aim to restore the competence of the valve, and indirect methods, which aim to improve the venous hemodynamics of the limb (152,153,154,155). Direct surgical methods are indicated in primary deep venous insufficiency (PDVI) when the valve cusps are dilated or prolapsed but still present and functioning. In the post-thrombotic syndrome or cases of valvular agenesis, when the valves are damaged or absent, an indirect technique is the better therapeutic choice.

In a review of 423 valve reconstructions, Raju (156) listed the duration of success of the surgical methods, verified by echo-Doppler, in the following order:

1. internal valvoplasty;
2. external valvoplasty with a prosthetic cuff;
3. external valvoplasty with direct sutures;
4. venous transplant.

There were no significant differences in the recurrence of ulcers with these various methods.

The time is ripe for standardisation of pathology reports, clinical findings and hemodynamic parameters, so that the different surgical techniques can be compared in randomized prospective trials.

Recommendation:

These surgical approaches are not recommended for routine use. They should be reserved for cases with specific indications, and done by surgeons with the necessary skills, in well-equipped facilities.
Grade C

SCLEROTHERAPY

Definition

Sclerotherapy is the chemical obliteration of varicose veins. The veins are injected with a histoleptive substance (sclerosing liquid) which damages the endothelium, producing spasm, thrombosis and an inflammatory reaction which are intended to produce stenosis, fibrosis and the permanent obliteration of the vein.

Efficacy

The initial obliteration of the vein is obtained in more than 80% of cases; however, part of the sclerosed veins will subsequently open again.

Instrumental study of individual veins

In studies monitored using Doppler or ultrasound scans the great saphenous vein was obliterated in 81-91% of cases (157,158,159), but after 4-6 months it was open again in 14% to 33% of cases (157,160), in between 17% and 35% after one year (161,162), in 33%, 60% and 80% of cases after

two years (114,163,164), in 48% after three years (161), and in 22% at five years (165).

Similar results are reported with the small saphenous vein, which was initially closed in 87-90% of cases (158,160) but after two years there was blood flowing again in 33% of cases (164), while after five years 27% were recanalized when the popliteal vein was competent (primary varicose veins) and 77% when the popliteal vein was incompetent (secondary varicose veins) (166). In the single trial covering collateral veins, at two years 26% were patent again (164).

Recanalized saphenous veins require retreatment at an interval that can range from a month to a year (160,167). However, this did leave the great saphenous vein closed in 86% of patients at two years (167), in 98% at three years (160), and in 80% at five years (168, retrospective study). The small saphenous vein was obliterated in 90% of cases at two years (167), and in 100% at three (160).

Clinical trials

Between 1966 and 1984 four prospective randomised clinical trials with clinical monitoring were conducted. At the beginning sclerotherapy gave results comparable with those of surgical extirpation but, over time, the recurrence of varicose veins was definitely more frequent after sclerotherapy. In Doran's trial (169), after two years the results of sclerotherapy and surgery were the same. Chant (171) and Beresford (170) found that after three and five years recurrence with sclerotherapy was respectively 22% and 40%, in contrast to 14% and 24% with surgery. In Hobb's trial (172), one, five and ten years after sclerotherapy recurrences were seen in 8%, 57% and 90%, compared with 6%, 25% and 34% after surgery. Jacobson (82) found 63% of recurrences after three years, as opposed to 10% after surgery.

Trials with clinical and instrumental monitoring

In Einarsson's trial (173), after five years the recurrence rate was 74%, in contrast to 10% with surgery. These results were checked by measuring hemodynamic parameters (volumetric measurements of the feet), confirming that the results of surgery were better.

Combined therapy

Three unsigned editorials in the British Medical Journal and the Lancet (174,175,176) proposed that the best option, as regards both the results and the cost/efficacy ratio, was a combination of surgery at the sapheno-femoral junction and sclerotherapy for the remaining varicose veins. However, though combined therapy proved more effective than sclerotherapy alone, it was always less effective than surgical removal of the varicose veins.

Lofgren (177) had already reported this in the Fifties, on the basis of a retrospective study: at five years, there was 70 % recurrence with combined therapy but only 30% with surgery. In Jacobson's prospective trial (82) recurrence at three years was 35% with combined therapy, 63% with sclerotherapy alone and 10% with surgery alone.

In Neglén's trial (178) 21% of patients had residual varices after combined therapy, and after five years the recurrence rate was 84%. Volumetric measurements of the feet, which were normal after treatment, had already deteriorated after one year and after five years had returned to the pre-treatment values.

In Rutger's trial (84), after three years the recurrence rate was 61% with ligation and sclerotherapy and 39% with stripping and phlebectomy. Doppler scanning showed saphenous reflux in 46% of patients in the first group and 15% in the second. This is the only study in which there were more clinical failures with sclerotherapy (61%) than saphenous recanalizations detected on Doppler scanning (46%). In all the other studies, about half the cases of recanalisation detected instrumentally showed clinical improvement. However, these failures with sclerotherapy were partially mitigated by the patients' subjective evaluations which were invariably better than the surgeon's objective opinion.

Evaluating the evidence

Despite some criticisms, all the trials published so far – seven prospective and randomised (82,84,169,170,171,172,173), one retrospective (177) and one prospective controlled (178) – have given unanimous results, definitively showing the superiority of surgical excision over sclerotherapy and combined therapy, at least for varicose veins with incompetence of the greater saphenous vein.

Recommendation:

Surgical removal is more effective than sclerotherapy for varicose veins due to incompetence of the greater saphenous vein. Grade A.

Indications

The high rates of recanalisation and recurrence mean that sclerotherapy is a secondary choice, not an alternative to surgery. It becomes the treatment of choice only in cases in which surgery is inadvisable (because it is difficult, with uncertain results or high risk), or is specifically requested by the patient, who must be fully informed of the likely results, complications, advantages and disadvantages of sclerotherapy in comparison with surgery.

Sclerotherapy was introduced in France in 1853, but the first attempts at producing guidelines were only made in 1996, by the International Consensus Conference, the American Academy of Dermatology (179) and the American Venous Forum (180). However, only the AVF specifically formulated the indications for sclerotherapy, which are the same as the ones the Collegio Italiano di Flebologia is proposing here. These include:

1. telangiectasias;
2. small varices (diameter 1-3 mm);
3. residual veins after surgery (purposely left by the surgeon)
4. varicose veins recurring after surgery (if originating from a perforating vein smaller than 4 mm in diameter)
5. varices from venous malformations (Klippel-Trenaunay type) for which surgery is not advisable
6. emergency treatment for bleeding ruptured varicose veins
7. perforating veins smaller than 4 mm in diameter
8. varicose veins around an ulcer.

As this list shows, sclerotherapy is an important and indispensable method for the optimal treatment of a wide range of varicose veins, from spider veins, which are not just an esthetic problem but can cause skin pathologies and even serious haemorrhage, to the serious, disabling forms of CVI such as lipodermatosclerosis, venous stasis ulcers and congenital venous malformations.

Recommendation:

The AVF indications apply. There is an open verdict on the indications for sclerotherapy of the perforating veins of any diameter and of the small saphenous vein. Grade B.

Contraindications

The contraindications to sclerotherapy include allergy to the sclerosing solution, serious decompensated systemic disease, recent DVT, local or systemic infection, non-reducible oedema of the lower limb, immobilisation and critical ischemia of the lower limb. Caution is needed in patients with a history of recurring DVT, with confirmed thrombophilia, women taking estrogen/progestogen preparations, or who are pregnant.

Techniques

Like any manual technique, sclerotherapy has to be learned. The various techniques currently in use are derived from three European schools, Tournay (181), Sigg (182) and Fegan (183), and are described in Italian in two publications (184,185).

The types and concentrations of sclerosing fluid vary according to the type of varicose vein and are shown in the table V below. Injections are given in more than one session, a few days or a few weeks apart, depending on the individual technique. Better results are obtained, with fewer adverse effects, if the injected vein and the leg are immediately compressed with either adhesive or mobile bandages or with elastic-compression stockings (186). Compression is all the more important, and needs to be more prolonged (from three to six weeks or more) if the varicose veins are particularly large and diffuse. It is indispensable in some cases – e.g. large varicose veins or legs with a tendency to oedema.

Sclerosing fluids can be injected under ultrasound guidance (“echosclerotherapy”), but this approach has not yet been confirmed more efficient. Also requiring confirmation is the utility of injecting detergent-based sclerosing compounds (polydocanol or sodium tetradecyl sulphate) in microfoam rather than liquid (165,168,187).

The Cochrane Collaboration has made a systematic review of the various methods (Tisi 2002), but the findings do not affect the recommendations proposed as guidelines here. It appears that the type of sclerosing substance has little influence on the outcome of sclerotherapy, and this confirms histological and electron microscope findings indicating that the various different products all induce the same type of lesion to the vessel wall (189).

Recommendation:

There is no standardisation of the technique, or of the concentrations and amounts of sclerosing agents. Compression improves the results of sclerotherapy. Grade B.

Table V – The most widely used sclerosing substances: indications and concentrations

Drug	Type of varicose vein and recommended concentration				
	Telangiectasias	Reticulated varices (spider veins)	Small-medium varices	Large varices	Saphenous trunk
Chromated glycerin	72%	-	-	-	-
Sodium salicylate	8%	12%	20%	-	-
Polydocanol	0.25-0.5%	1%	1-2%	3-4%	3-4%

Sodium tetradecyl sulphate	0.1-0.2%	0.2-0.3%	1-2%	3%	3%
Iodine/sodium iodide	-	-	2%	2-4%	4-8-12%

COMPRESSION

Definition

Compression is the pressure applied to a limb, using a variety of materials, elastic or rigid, to prevent and treat diseases of the venous or lymphatic systems.

Historical outline

Elastic compression treatment has been used throughout the history of medicine. Traces of the use of bandages have been found among the Ancient Egyptians and the tribes living along the River Tigris. The prophet Isaiah in the 8th century B.C. wrote about the utility and purposes of bandaging the legs, as did Hippocrates and his school of medicine. The Roman legionnaires in 20 B.C. bandaged their legs tightly during long marches to prevent them swelling. Aurelio Cornelius Celso, a Roman author, recommended occlusive and compressive linen bandages for treating *ulcus cruris*. And throughout the medieval period, under the influence of Arabic medicine, compressive dressings were widely employed.

Physiopathology

The venous system, assisted by the lymph vessels, returns the blood from the tissues to the heart. Every time the venous flow is slowed or impeded a sort of "traffic jam" builds up: ischemia occurs in the cells, as the stasis prevents oxygen and nutrients leaving the arterial capillaries to enter the interstitial space and get into the cells where they are absorbed. This is because of an inversion of the local pressure ratios: the slowing of the blood flow causes an increase in interstitial pressure which counterbalances the residual arterial hydrostatic pressure. The lack of outflow leads to an increase in perivascular oncotic and osmotic pressures, causing water retention and edema, a self-sustaining cycle (190).

Physical and technical rationale

In phlebo-lymphology compression is achieved with bandages, elastic and inelastic hose (191,192)

Bandages

Bandages are generally applied like "knee-socks" on the lower leg. Their most important property is that they can stretch width-ways and length-ways (191,193). In relation to the initial length (191,192) they may offer:

- short extension (<70%);
- medium extension (70-140%);
- long extension (>140%).

An unstretchable or barely elastic bandage produces a considerable amount of "working" pressure when walking, as it prevents the increase in the circumference of the leg caused by contraction of the calf muscles (193), whilst the pressure at rest is minimal. In contrast, an elastic bandage exerts a moderate amount of "working" pressure and high "resting" pressure, the difference between the two being inversely proportional to the elasticity (193). An elastic bandage maintains continuous

pressure on the superficial venous system which is relatively independent of muscular activity (194,195). Elastic bandages made of fibers with a long extension factor act in a similar way. Unstretchable or barely elastic bandages can therefore be worn day and night whereas bandages that stretch more than 70% and support stockings should be taken off at night, as they are not designed to be worn when the patient is lying down (196,197).

Taking into account the various types of bandage, the pressure exercised is always found by using the Laplace law (191,193):

$$P = t/r$$

modified as follows for a bandage:

$$P = tn/ra$$

where t is the tension, n the number of turns of the bandage, r the radius of the part requiring compression, and a the width of the bandage (192,193). Compression can thus be “dosed” to meet treatment requirements (193).

There is no fixed rule about how long the bandages should be worn. Some studies show equal efficacy with bandages worn for a few hours or for up to six weeks, but there is always a significant drop in the amount of compression exerted by a bandage 6-8 hours after application (198,199).

Elastic support hose

Elastic support hose for prevention or therapy (193,195,200,201) are manufactured in various sizes, either standard or to measure, and are classified according to their length as:

- knee-socks
- mid-thigh-length stockings
- stockings
- single leg tights
- tights.
- There are also “cuffs” for the arms.

When pressure on the ankle is less than 18 mm Hg the support is defined as preventive or resting. There is controversy over whether this is effective, just as debate continues on the utility of hosiery whose pressure is expressed in “deniers” (den) (191,193,195). When the pressure on the ankle is greater than 18 mm Hg the support is defined as therapeutic. Graduated, defined compression is achieved on the lower limb, decreasing from the bottom towards the top, from 100% at the ankle, 70% at the calf, to 40% at the thigh (195,201).

Depending on the compression at the ankle, expressed in mm Hg, therapeutic support hose are grouped in four classes, which differ according to the German or the French standards.

Manufacturers of therapeutic elastic support stockings that use the German RAL GZ 387 standards give the following four classes of compression Table VI:

Table VI

Class	Compression in mm Hg
1a	18.7-21.7

2a	25.5-32.5
3a	36.7-46.5
4a	> 58.5

Based on the French NFG 30-102 B standards therapeutic elastic support stockings are also grouped into four compression classes but the values are lower (Table VII):

Table VII

Class	Compression in mm Hg
1a	10 -15
2a	16 - 20
3a	21 – 36
4a	> 36

Besides these stockings for prevention and therapy there are also support hose for the prophylaxis of thromboembolism (191,192,195). These differ from the other models as they give a standard compression of 18 mm Hg at the ankle and 8 mm Hg at the thigh and can be worn comfortably even when resting.

Manufacturing standards

The manufacturing standards for elastic support hose were drawn up at the request of the German authorities, as they are eligible for national health system reimbursement, and appear in the official German drug formulary (202). These standards comprise:

a table establishing the four classes of compression to which all the support hose for compression treatment belong;

a table showing the pressure distribution for the different classes, so the hose guarantees the correct gradient all along the lower limb;

specifications for the manufacture of the hosiery, with details of both the longitudinal and transverse stretch;

specific methods for the stitching, the seams, the heel, etc.

the materials that can be used are listed, with precise limits for the weight of the yarn, so the product will be strong enough to ensure its properties remain constant over time;

finally, there is a section on the inspection methods for the finished stocking.

The RAL-GZ 387 standards, which were last revised in September 2002 (203), are the responsibility of two authorities, one in Germany and the other in Switzerland. They conduct preliminary tests (HOSY system) to certify that the support hose complies with the technical specifications, with particular attention to the visual checks, tests for transverse and longitudinal elasticity, and analysis of the materials used. There is also a sophisticated test to measure the compression and how it decreases from the foot towards the top. This test is conducted using

special equipment which can measure any type of elastic stocking and record its static and dynamic performance.

These very strict and restrictive standards have been used for over thirty years to monitor the production and distribution of elastic support hose in Germany and are proposed as the model for European Union regulations.

Non-elastic compression

There are basically two main methods: intermittent pneumatic compression (IPC) and the intermittent high-pressure non-pneumatic approach. Compression can be achieved by blowing up air or mercury in special socks or sleeves/cuffs that come in various shapes for selective use on the foot, part of a leg, or the whole leg or arm. These devices act on the rate of blood flow and on local fibrinolytic mechanisms. The market offers one-chamber systems in which the whole device is blown up in one stage, and sequential ones in which the different sections are inflated one after the other.

CLINICAL APPLICATIONS

General points

Compression is indicated for any chronic or acute venous insufficiency, either associated with other treatments or alone. The efficacy of compression for the symptomatic treatment of CVI or the prevention of complications is supported by clinical experience and by a substantial amount of scientific literature, particularly for advanced disease. However, only the most recent publications satisfy the rigorous case/control comparison criteria, with adequate sample sizes.

The type of compression used, the method of application and duration of use will vary according to the clinical context and for each patient even in groups with the same pathologies. Therefore the choice of compression hose needs to be centered on individual requirements and the severity of the disease.

In order to unify the evaluation criteria for acute and chronic venous insufficiency, and its prophylaxis and treatment, standard classification methods must be used. There is the CEAP international classification for CVI and the high/moderate/low risk classifications from the Consensus Statement on Prevention of Venous Thromboembolism.

Acute forms

Superficial thrombophlebitis

Superficial thrombophlebitis is considered benign if there are no thrombophilic risk factors, and is one of the common complications of varicose veins. However, it may progress to pulmonary embolism, which can be fatal. Combined with drug therapy (anti-inflammatory drugs and heparin), elastic compression and mobilisation are the first line of defence for both treatment and prevention (204,205).

Recommendation:

Compression and mobilisation are always indicated for patients with superficial thrombophlebitis.
Grade B

Deep vein thrombosis

Prevention

The graduated-pressure elastic stocking reduces the incidence of DVT after surgery, using an optimum pressure of 18 -20 mm Hg at the ankle and 8 mm Hg at the thigh (206,207). In general and orthopedic surgery and neurosurgery elastic compression, used either alone or with heparin, reduces the incidence of DVT (208,209,210,211). In rehabilitation medicine the efficacy of elastic compression, either alone or together with low-dose LMW heparin (LMWH), has been investigated for the long-term prophylaxis of DVT in patients at hemorrhagic risk or with recent acute hemorrhage (212). “Antithrombotic” knee-socks are proposed for the prevention of “economy class” DVT among air travelers, a rare and controversial syndrome (213,214) involving asymptomatic DVT and even “sudden death” from massive pulmonary embolism, caused by prolonged immobility in cramped aircraft seats, or even long trips in trains or buses (215,216).

Recommendations:

Low risk - In the absence of sufficient data, there is widespread agreement that graduated compression is useful. Grade C

Moderate risk - Elastic stockings in combination with, or as an alternative to, heparin prophylaxis. Grade B

High risk - As for moderate risk or combinations of several methods of prophylaxis. Grade B.

Treatment

Although evidence from controlled trials is still lacking, the current treatment for DVT remains based on heparin meaning, increasingly frequently, LMW heparin. Mobilisation and compression have long been recommended by some specialists, even in the acute phase of DVT (217,218). Early mobilisation, with class II compression, was recently found effective in reducing edema and improving patency, with no thromboembolic complications, compared to a control population (219), but there are not a strong evidence about the beginning, duration and level of compression suitable for DVT (220)

Recommendation:

Early mobilization with elastic compression seems useful to reduce edema in the acute phase of DVT, without raising the likelihood of thromboembolic complications. Grade B

Prevention of post-thrombotic syndrome

Post-thrombotic syndrome (PTS) is an aftermath of DVT in between 10 and 100% of cases; it may cause moderate to painful disabling edema, and trophic cutaneous changes leading to ulceration (221). The use of elastic knee-socks with 40 mmHg compression at the ankle for at least two years has been endorsed by a randomised controlled trial where it halved the incidence of DVT when the stocking was used regularly (222).

Recommendation:

After DVT elastic stockings should be worn for at least two years, with compression of at least 20 mm Hg. Grade A

Compression after surgery or sclerotherapy for varicose veins

Compression after surgery is indicated for the prevention of venous thromboembolism, for the

prevention of hematomas after vascular surgery – mainly for varicose veins (2-3 days) – to reduce edema and pain (2-4 weeks), and to prevent recurring varicose veins (186,223,224,225,226).

Each surgeon prescribes the compression he considers appropriate, on the basis of his own experience. This may involve uniform concentric elastic compression bandages, fixed adhesive or cohesive bandages (total or partial), various methods for local compression with or without skin dressings, or elastic compression hose, either on their own or after the previous types of compression. Compression with bandages is usually 20-25 mmHg, though it may be more than 30 mmHg. Stockings are normally considered sufficient if they provide 15-20 mmHg of compression, from day 5-15 after surgery.

The type of compression used after sclerotherapy varies even more widely, but it is generally considered an important part of the treatment (181,184,185).

Recommendation:

Patients who have had active treatment for varicose veins (surgery and sclerotherapy) require compression support hose, but there is still no consensus on the types. Grade B.

Compression therapy in pregnancy

Pregnancy causes various changes in the patterns of venous return, including dilatation of the veins due to venous hypertension caused by compression of the abdominal and pelvic veins.

Telangiectasias and varicose veins frequently appear or become more marked, though they tend to regress – usually almost completely – in the weeks after delivery.

Treatment is therefore conservative, and relies largely on elastic compression (227,228).

Intermittent pneumatic compression is of limited utility in reducing swelling at the ankles (229).

Compression with class I or II stockings does not appear to stop telangiectasias and small varicose veins appearing, but is probably useful to prevent saphenic reflux (230).

CHRONIC FORMS

Functional symptoms of mild venous insufficiency (CEAP 0 = no visible signs of venous disease)

There is no reliable data on whether “resting” or “preventive” commercial support stockings really help prevent venous disease progressing to overt CVI (231). They do, however, have some effect on subjective symptoms (232). Stockings exerting 8 or 12 mmHg pressure at the ankle, with no reduction up the leg, help reduce swelling at the ankles and heaviness and swelling in the legs in healthy women whose work involves prolonged standing. There seems to be no difference between the two levels of pressure. Stockings exerting higher pressure cause compliance problems because of difficulties in adapting them to the shape of each leg (233).

Recommendation:

There is not sufficient data to give indications for the use of resting or preventive elastic support hose in patients with clinical signs of venous disease, but there is evidence of improvement in subjective symptoms. Grade B

Telangiectasias and spider veins (CEAP class 1)

Venous ectasia accompanied by clinical symptoms of CVI are an indication to increase compression at the ankle and consequently on the calf and thigh (234).

Recommendations:

As the physiopathological data is not compatible with the indications described it is not possible to recommend the long-term use of compressive support hose in these conditions. Grade C

Varicose veins (CEAP class 2)

Compression is considered fundamental in the clinical management of patients with varicose veins, as it reduces the feeling of heaviness and pain and has hemodynamic effects, with trophic action in the tissues, either alone (235,236,237) or in combination with drug therapy (238). In one small group of 31 patients who had varices without complications, low-compression stockings exerting 20 mm Hg at the ankle were as effective clinically and hemodynamically as stockings giving 30 mm Hg compression, and compliance was better (239).

Recommendations:

Compression treatment is recommended. As only a small number of published trials have enrolled adequate numbers of patients it is not possible to give firm recommendations on the compression at the ankle, but it should be more than 18 mm Hg. Grade B

Edema (CEAP class 3)

Edema is a common complication of venous insufficiency even in the early clinical stages. There is slight swelling around the ankles towards the end of the day in CVI, which becomes more marked in diseases with skin disorders and stasis ulcers. It is caused by changes in the interstitial pressure ratios caused by venous hypertension (193). In workers with CVI who have to work standing for long periods, class II elastic compression stockings help prevent edema and reduce pain and tension in the legs (240,241). Stockings with higher "slope values" (the increase in compression exerted by the stocking with every cm increase in its circumference) seem more effective in preventing swelling (242).

Recommendations:

Given the limited literature, the few clinical trials, and considering that the indiscriminate use of compression could spoil the quality of life for patients, it is impossible to give any general indications for compression therapy. Grade C

Trophic changes of venous origin:., pigmentation, eczema, dermatosclerosis, healed ulcers (CEAP classes 4 and 5).

Skin changes in chronic venous disease are indicators of serious tissue damage caused by hypoxia from chronic stasis. A review of the literature by Moffat (243), showed ulcers recurred in two thirds of patients without compression therapy.

Recommendation:

Compression therapy is recommended for the prevention of recurring ulcers (30-40 mm Hg at the ankle). Grade B.

Venous ulcers (CEAP class 6)

Venous ulcers can be effectively treated with compressive therapy after local surgery and/or pharmacological therapy. Elastic stockings, Unna boots, multilayer bandages or IPC are all useful. A review of the literature, published in the BMJ (244), which considered all the available trials on the treatment of VU, concluded that compression improved the prognosis, preferably using high pressure. There does not seem to be any one system which is better than the others (multi-layer, short-stretch bandaging, Unna boot, elastic stockings) (245,246,247).

Recommendation:

Compression is recommended for the treatment of venous ulcers (inelastic bandaging, knee-socks with compression more than 40 mm Hg). Grade A

NON-ELASTIC COMPRESSION

Prevention of venous thromboembolism

Intermittent pneumatic compression (IPC) can prevent the development of DVT and acts on two of Virchow's "triad" of three factors. There are two key points to the mechanism: increased venous blood flow during periods of immobilization, and reduced hypercoagulability with activation of fibrinolysis (248). IPC is an additional measure during the treatment of edema of the legs, of venous ulcer (VU) or both, and in the prophylaxis of pulmonary embolism (249). A meta-analysis of 70 trials on the prophylaxis of pulmonary embolism in surgical patients showed that the use of a mechanical device for IPC reduced the percentages of post-operative DVT and pulmonary embolism (250).

IPC is indicated in patients undergoing neurosurgery, major urological or gynecological oncological surgery (251), eye or spinal surgery, and surgery on the knee (211). It is also indicated for patients with suspected or confirmed intracranial hemorrhage, and after recent brain or spinal trauma (252). It can be used with LMW heparin for pharmacological prophylaxis (253), and after stroke (254). Sequential pressure therapy seems to have greater clinical and hemodynamic efficacy, with better compliance from patients and nursing or medical staff (255,256).

Recommendations:

IPC can be recommended for routine per-operative use in patients at risk of thrombosis, in whom heparin prophylaxis is contraindicated.

IPC as coadjuvant in the treatment of venous ulcer

IPC is indicated in cases of VU, increasing the percentage of cures in a short time (257). IPC combined with elastic compression hosiery boosts the therapeutic effects on VU, shortening cure times compared to the stockings alone (258). A recent review from the Cochrane Database (259) noted with disappointment the lack of published data and called for randomized trials to confirm this difference.

Recommendation:

At the present time no recommendations can be made on the use of IPC in patients with VU, and randomized trials are awaited. Grade C

Contraindications

There are not many contraindications to compression therapy, and adverse reactions are extremely rare. The main limitation is the difficulty of putting on these stockings for patients with concomitant pathologies, or the elderly (260). In general terms, contraindications are either absolute or relative (261). Particular care is required in patients with joint diseases, who are often elderly (262,263).

Absolute contraindications include:

- lack of specific indication (non-venous pathology)
- immobility (except for antithrombotic stockings)
- severe skin diseases
- concomitant peripheral arterial obstructive disease (thresholds: BP at the ankle less than 80 mmHg, ankle/arm ratio less than 0.50).

Relative contraindications are:

- Bandages: weeping ulcers
- Hosiery: allergy or intolerance, dermatosclerosis, anatomical abnormalities, difficulty in putting on hose.

Recommendation:

Concomitant advanced joint disease must absolutely be excluded before a patient starts compression therapy. Grade A

DRUG THERAPY

Pharmacotherapy for CVI has greatly developed over the last 40 years. It was therefore surprising that there were no clinical or experimental studies of the tone and contractility of the veins or venous pressure in relation to treatment. Drugs for the venous system were initially called phlebotonics as they were believed to act on venous tone. They are still largely used in the symptomatic treatment of CVI and to make patients more comfortable (264).

Phlebotrophic drugs in their modern form are aimed at a wide range of processes (Table VIII). They are naturally occurring, semi-natural or synthetic substances, some of them combining two or more active principles to improve the efficacy. Most of these belong to the flavonoid family; 600-800 have been identified and were grouped by Geissman and Hinreiner under the name of flavonoids, which are plant polyphenols containing a flavone chemical structure. In 1955 the New York Academy of Sciences gave them the name "bioflavonoids" (265). Their mechanisms of action vary, but their main property is activation of venous and lymphatic return.

Phlebotrophic drugs appear to be the therapeutic strategy of choice for CVI patients who are unsuitable or not indicated for surgery, or in whom surgery is coadjuted by drug therapy (266,267,268,269,270,271,272).

Table VIII – Venous physiopathological processes affected by drug therapy

Reduced venous tone
Hemoconcentration
Depressed venous-arteriolar reflux
Vasomotor disorders
Increased capillary permeability
Edema
Pericapillary fibrin cuff
Reduced fibrinolysis
Increased plasma plasminogen
Altered leucocyte and erythrocyte rheology
Leucocyte activation
Capillary microthrombi
Stasis of the microcirculation
Reduced lymph drainage

Phlebotropic drugs are widely prescribed and marketed in Italy, France, Germany and other parts of Europe but are less used in English-speaking and Scandinavian countries, presumably because of the scarcity of published data. With new research methods this is changing.

The effects of phlebotropic drugs on physiological parameters such as venous tone, venous hemodynamics, capillary permeability and lymph drainage can be evaluated with a range of diagnostic procedures, preferably non-invasive (1). However, the main tool for assessing the clinical effects of a phlebotropic drug is a well-conducted clinical trial satisfactorily meeting clinical, scientific and ethical requirements (273). The trial must be randomized, if possible double-blind, and have enough power to attempt at least to answer firm questions about the disease. The CEAP classification now means that the same scoring system can be used for the clinical picture before and after treatment. The symptoms, signs and quality of life should all be taken into consideration.

Efficacy on the different outcomes can be obtained using drugs with different chemical structures but the same clinical indications. The ATC classifications define phlebotropic drugs as “vasoprotectors”, and make a distinction between topical treatments for varicose veins and “capillary protective substances”, mainly bioflavonoids (Table IX).

Table IX

CO5 vasoprotectors

CO5 B Anti-varicose treatment

C05BA heparin heparinoids or for topical use

Epharansulphate

Sulphomucopolisaccarides + troxerutine

Sodium heparin

Sodium heparin + escine+phosphatidil choline

Sodium pentosane poliphosphate
heparansulphate
sulphopoliglicane
glicuroseglicane sulphate
glucopolisulphate sodiumbetametasone + dextrane sulphate
oxerutine+calcium methyl galattopolisulphate

CO5 C Capillary protecting substances

CO5 CA Bioflavonoids

Diosmine
troxerutine
troxerutine+carbazochrome
oxerutine

CO5 CX Other capillary protecting substances

Bromeline+escine
amineftone
centella asiatica
calcium dobesilate
escine
cromocarb
sulmarine+sodium ascorbate

The clinical efficacy on the symptoms (feeling of heaviness, pain, paresthesia, heat and burning sensations, night cramps, etc.) has long been confirmed by Level III, IV and V evidence, but there are now Level I and II trials on specific drugs. For the bioflavonoids double-blind, randomised trials have used micronised diosmin-hesperidin (274,275,276), troxerutin (277,278); rutoside (279,280); escin (281); bilberry anthocyanosides (265); and synthetic calcium dobesilate (282). Phlebotropic action has been demonstrated in pharmaceutical classes other than the flavonoids, such as *Ruscus aculeatus* (283,284), *Centella asiatica* (285,286), and mesoglycan (287).

Various protective agents have clinical efficacy on the main sign, edema, acting on the microcirculation by lowering endothelial permeability, reducing the release of lysosomal enzymes and inflammatory substances, inhibiting free radicals and reducing white cell adhesion (238,288,289).

A surprising improvement in quality of life after a dose of 1g of micronised diosmin-hesperidin was observed in a study of 934 patients with CVI (290). This improvement was seen in all areas of life - physical, psychological and relational.

In the last ten years the relationship between macro- and microcirculation in the more severe forms of CVI has become clearer; it was already known that the relationship between reflux and venous hypertension was a factor in capillary damage (291,292,293).

Much basic research and studies in man have confirmed the effect of some phlebotropic drugs, particularly micronised diosmin-hesperidin, on the microcirculation impaired by CVI (266,290,294,295,296,297,298,299). In the light of these findings a series of drugs have been introduced into clinical practice; however, their usefulness has not always been confirmed in enough clinical trials of sufficient power. These drugs are used as coadjuvants in severe CVI (CEAP classes 4/5/6) and are listed in the ATC classification as B01, Anti-thrombotics, and in some cases as CO4/CO1E, Vasodilators, for their action on endothelial alterations and blood flow patterns, and on microthrombi, and their oxygen barrier effect.

The effect of the fibrinolytic enzyme, urokinase, is documented in two papers (300,301); the glycosaminoglycans such as sulodexide have profibrinolytic activity (302,303) as does heparan sulphate (304), and defibrotide (305). Among the vasodilators, the effects of pentoxifyllin have been well documented (306,307,308) and prostaglandin E1 (309) for the treatment of ulcers. The only indication for platelet anti-aggregation with aspirin in CVI is as coadjuvant treatment for ulcers (310).

Recommendations:

There is ample evidence in favor of treating CVI ulcers with phlebotropic drugs when surgery is not indicated, not possible or can be flanked by coadjuvant drug therapy. Phlebotropic drugs are indicated for subjective and functional symptoms of CVI (fatigue, night cramps, restless legs, heaviness, tension) and edema. Grade A

In the last few years the Italian market has seen the introduction of products whose labels claim a non-specific capillarotropic and/or venotropic action. Since most of these contain flavonoid extracts some confusion has arisen among physicians and over-the-counter purchasers as to which are drugs based on flavonoid extracts, and which are plant therapy products, herbals, foods or food supplements. It is perhaps worth taking a moment to look at the differences actually implied by the various terms, so set out below are the Italian Ministry of Health's definitions, with a comment on the market situation in the EU for each type of product (311).

Drug: Any substance or composition presented as having curative or prophylactic properties for human or animal diseases, or any substance or composition to be given to humans or animals with a view to establishing a medical diagnosis or to restoring, correcting or modifying organic functions in men or animals. The term substance is used to refer to any material of human, animal or vegetable origin, or a chemical, either natural or obtained by transformation or synthesis.

Phytherapeutic substances – plant or herbal medicines – if they satisfy the registration requirements and obtain marketing authorization as for drugs, have the right to call themselves drugs ((Decree Law no. 178 29-05-1991 with subsequent variations and integrations of EC Council Regulation, EEC, no. 2309/93 22 July 1993, Council regulation, EC, no. 297/95 10 February 1995, Commission regulation, EC, no. 541-542-1662/95 10 March and 7 July 1995, Commission regulation, EC, no. 2141/96 7 November 1996, Regulation no. 141/2000 of the European Parliament, 16 December 2000, Commission regulation, EC, no. 847/2000 27 April 2000).

Herbal product: To date Italy has no legally binding definition of a herbal product, which can therefore be sold as a food, a food supplement, a drug or cosmetic product. Each of these categories implies specific methods for production, marketing authorization and packaging. Currently under examination is a proposal for a law, No. 4380 on herbal products, in which article 2 section 1 establishes the packaging, nomenclature, active principles and use, in line with the EU definition of herbal and plant products (CPMP/QWP/2819/00 : “Note for guidance on quality of herbal medicinal products CPMP/CVMP July 2000).

Foods and food supplements: Here too Italy has no law defining a food. A definition of what

cannot be considered under this heading can be drawn from article 2 of Decree Law No. 109, 27 Jan. 1992, related to advertising: “labeling, presentation, and advertising of foods must not be such as to induce the buyer to attribute to the product properties involving preventing, treating or curing diseases in humans, nor should it refer to any such properties if it has none.”

Food supplements are subject to Decree Law No. 111, 27 Jan, 1992, implementing EEC Directive 89/398/CEE and European Parliament Directive 2002/46/EC, 10 June 2002. The Italian Ministry of Health therefore started in 2002 to subject to control the production and indications for “health” uses of all products without the intrinsic purposes of a medicinal product, such as therapy (Ministry of Health, G.U. circular 18 July 2002, no. 3).

This quick glance shows clearly that herbal and plant therapy products can be considered drugs if they meet the same registration requirements as drugs. This obviously excludes food supplements. Except for the substances listed in Table 3, there is no current evidence of pharmacological efficacy in CVI for any of the herbal or plant medicinal products on the market today.

PHYSIOTHERAPY

Patients with chronic venous and lymphatic insufficiency should generally be advised on appropriate lifestyle habits (312). The press offers a broad range of dietary and health advice, particularly as regards prevention. General practitioners and specialists should dedicate a part of the consultation to giving their patients advice on this subject, taking time to convince them. There is plenty of easily accessible explanatory literature and printed forms, and the doctor can personalise these to motivate the patient, by underlining important information or adding extra advice.

The correct amount of physical exercise should be prescribed, with advice on good posture, and the contraindications outlined (313,314). Clinical and phlebodynamic testing, plethysmography, and percutaneous oxygen pressure all confirm the beneficial effects of an exercise schedule on the macro- and micro-circulation (315,316,317,318).

Strengthening the venous pump of the foot is another possibility for prevention and rehabilitation in CVI. Although there is still not enough validated data, compared to assessments of the musculo-ostearticular physiology of the foot (319), it does appear worthwhile stimulating the venous networks in the sole of the foot on the basis of classical knowledge (320) and subsequent physical and physiological findings (321). Various studies have highlighted the effects of postural malfunction on CVI, and the utility of correcting these defects with shoe inserts (322,323,324,325,326).

Manual venous-lymphatic drainage (lymph drainage)

One of the most widespread and popular massage methods for venous and lymphatic stasis, manual lymphatic drainage, was introduced by E. Vodder in 1936 (327). Current usage was codified by Leduc in 1978 (328), and the Vodder school (329). It is also indicated for CVI (330,331).

Vodder’s concept of mechanical action is based on the harmonic displacement of fluids and interstitial solutes through the lymphatic capillaries towards the ganglia or main drainage areas. The massage must be rhythmic and smooth and must not exceed the physiological drainage capacity of the tissues. It is important to evaluate the overall anatomical area as a basis for deciding the amount of strength and coordination during manual compression.

The patient should enjoy immediate relief of the symptoms if the technique is carried out properly; this will obviously depend on the experience and manual skill of the masseur. Results are confirmed by the immediate reduction in the circumference of the limb and can be checked using indirect lymphoscintigraphy.

In Germany physiotherapy for lymphedema based on lymphodrainage is termed KPE (Komplexe Physikalische Entstauungstherapie) which can be translated as “multi-factor decongesting

physiotherapy” (332).

Recommendation:

Clinical and instrumental studies confirm the utility of healthy lifestyle habits, physiotherapy and manual lymph drainage. Grade C

HYDROTHERAPY

The beneficial action of water on venous and lymphatic stasis in the limbs has always been used empirically by the patients themselves (333,334). However, the wide variety of forms of this treatment means that precise indications and “dosage” recommendations are needed to establish contraindications and avoid complications. In general, home, sea or spa treatments are based on the effects of hydrostatic pressure and the temperature of the bath, while the “medicinal” effects are provided by the salts in the water (335). The therapeutic effect is achieved through two mechanisms:

1. aspecific or hydrotherapeutic action, given by the physical properties of the water:
 - temperature
 - hydrostatic pressure
 - active and/or passive movement

2. specific action, meaning the therapeutic effect related to the chemico-physical characteristics of the water:
 - mineral salts
 - trace elements
 - heat
 - concentration

Although from the physical viewpoint any type of mineral water can be beneficial, chemically only certain types of water are specifically indicated for treatment and rehabilitation in chronic venous and lymphatic insufficiency (Table X)

Table X - Mineral waters indicated in angiology and used for prevention, treatment and rehabilitation in venous and lymphatic insufficiency.

Bromo-iodine salts	Fluid removal from edematous tissue
Sulphur	Anti-inflammatory
Ferruginous arsenicals	Tonic, stimulant and anti-stress
Calcium sulphate	Stimulates venous contractility
Radioactive	Sedative, analgesic, antispastic
Carbonic	Tonic action

Patients can have hydrotherapy at any time of the year. If possible, they should have two cycles a

year, preferably in autumn and spring, with at least three months' interval. The treatment should last at least three weeks for the patient to gain the full effect, and less than two weeks is not worth while (336,337).

Recommendation:

Controlled trials have shown that hydrotherapy for CVI, carried out in a suitable place and with suitable methods, is effective. Grade B

TREATMENT OF VENOUS ULCERS

Introduction

A venous ulcer (VU) is a chronic skin lesion that does not heal spontaneously; the epithelium does not regrow in less than six weeks, and the ulcer frequently recurs. Some definitions exclude ulcers of the foot, while others include any such lesions on the legs. Among trophic lesions of the legs, ulcers due to venous disease account for 75% (14). CVI, although it has received less attention than chronic arterial insufficiency (CAI), affects ten times as many adults (338) and its treatment is widely neglected or often completely inadequate. Many patients walk around for months, or even years, with ulcers treated only with local medication, with no effort being made to cure the venous insufficiency causing them (24).

Clinical presentation

Venous ulcers of the leg usually present as an irregular area of loss of skin, the base covered with a yellow exudate, with well-defined margins, surrounded with erythematous, hyperpigmented or liposclerotic skin. The ulcers vary in size and site, but in patients with varicose veins they are usually in the medial region of the lower third of the leg. A VU in the lateral portion of the leg is often associated with small saphenous vein insufficiency (339).

Patients with VU may suffer intense pain even though there is no infection. The pain is worse when they are upright and relieved when the leg is elevated (340).

Treatment

The treatment of VU is based on an understanding of the physiopathological mechanisms. These are not exclusively concerned with macrovascular hemodynamics, but involve the microcirculation and endothelium too (339,340).

Since the VU is a manifestation of a chronic condition with slow repair and a tendency to recur, therapy must aim not only at curing the ulcer but, above all, at preventing it recurring (341). At the same time the patient's mental attitude must be improved, so as to convince them to enter and comply with a treatment program and to improve their quality of life (3).

Treatment of a VU can involve one or more of the following:

1. basic treatment;
2. pharmacological treatment;
3. compression;
4. topical medication;
5. surgery;
6. sclerotherapy;
7. other therapies;

8. general measures.

1. Basic treatment

The basic treatment must obey the general rule of considering the patient as a whole and not just focusing on treating the ulcer (342). Patients' lifestyles are extremely important: their ability to walk, their work, whether they are obese, diabetic or have other concomitant diseases (24).

2. Pharmacological treatment

The main targets are venous tone, hemoconcentration, increased capillary permeability, edema, reduced fibrinolytic activity, increased plasma fibrinogen, anomalies in leucocyte function, pain relief, and management of superinfections and concomitant diseases. Fibrinolytic agents or substances that favor fibrinolysis, hydroxyrutosides (343,344), micronized diosmin-hesperidin (276), prostaglandin E1 (309), and pentoxifyllin (345) are widely used.

A systematic review of the literature brought to light proof of efficacy for oral pentoxifyllin for stimulating repair of VU, but it had side effects (345). There is proof of the utility of soludexide and mesoglycan (287,303), but none for acetylsalicylic acid and oral zinc supplements (346). Recent trials have confirmed the effect of bioflavonoids associated with elastocompression (296,299).

3. Compression

All patients with VU require compressive treatment. Controlled randomized trials have shown that compression hastens the healing of VU and helps prevent recurrence. Whatever treatment is given for the VU must always be combined with compression. The patient must of course be able to move about so as to obtain maximum benefit from the compression (347).

Compression stimulates the venous flow, reduces the pathological reflux when the patient is walking (24), improves the microcirculation and boosts lymphatic drainage (244). The chronic edema and the ulcer exudate are reduced and the lesion not only regresses sooner but is also less likely to recur. Current studies are still inadequate to compare the various compression methods (346).

Compressive therapy can be done with elastic bandages or stockings (348). In the acute phase, inelastic bandages, zinc oxide bandages, or multilayer bandaging provide the most effective compression. A multilayer bandage can be left in place for a week, but at the start of treatment, until the exudate and the edema have subsided, it is advisable to remove and reapply the bandaging more often. Good healing has been reported using four-layer compressive bandaging (349,350) which seems to give effective compression even when applied by unskilled personnel (351). The multilayer system was more effective than one or two layers (245).

Although no studies have actually compared the rates and numbers of patients cured when a compressive bandage is applied by skilled or non-skilled people, the literature stresses the importance of training to improve the ability to prepare and apply a bandage, especially to achieve the right pressure on the tissues (352). The bandage must give a resting pressure of at least 20-30 mm Hg (353) at the ankle and the lower third of the leg with gradually less compression towards the upper third of the leg and thigh (24).

In patients with moderate occlusive arterial disease, with an ankle-brachial index (ABI) between 0.6 and 0.8, bandaging must be done very carefully. Inelastic material must be used, so as to exert low resting pressure. If the arterial insufficiency is very severe, with an ABI below 0.6, bandaging of any type is contraindicated (24)

Compression with elastic stockings helps maintain the results gained from treating the ulcers and prevent recurrence. Generally, class II compression stockings (30-40 mm Hg at the ankle) or class III (40-50 mm Hg) are used. Elderly patients or people with joint mobility problems may find it easier to put on two Class I stockings (20-30 mm Hg at the ankle), one on top of the other (348).

For bed-ridden patients, or those who walk very little, anti-thrombus stockings should be considered. IPC may be beneficial in selected cases (258).

Recurrence still occurs after healing, in the short or longer term, in 20-75% of patients (4,354) and is linked to a variety of risk factors, but particularly to the persistence of the hemodynamic changes and inadequate or unacceptable compression (226,349,347,357). The success of compression also depends on how much the patient moves; patients must be encouraged to walk and take regular physical exercise and rehabilitation therapy (347, 357).

It is worth noting that only very few of the studies of elastocompression for VU report the complications and reasons for stopping treatment.

4. Intermittent pneumatic compression

There are very few controlled randomized trials and they have found no significant effect on healing when IPC is combined with compression bandages, although this approach does not appear to cause any harm (358). IPC is not always available, however, and, depending on how and when it is applied, it may restrict the patient's quality of life. Manual lymphatic drainage may be an alternative, although studies to confirm it are still awaited. The International Leg Ulcer Advisory Board recently proposed an algorithm for compression treatment in patients with VU (Table XI - 247).

Table XI (klik to view)

5. Topical medications

When planning topical treatment for patients with VU it is important to take account of clinical observations such as the presence and amount of dead tissue, exudates, infections and the state of the skin surrounding the ulcer (348).

Topical treatment for VU aims to keep the lesion clean, to preserve the microenvironment, protect the lesion from infectious agents and stimulate cell repair mechanisms.

The idea of wound bed preparation (359) is proposed, as the "overall, coordinated management of the lesion, aimed at accelerating endogenous healing processes while also promoting the efficacy of other therapeutic measures". This comprises debridement (autolytic, enzymatic, or mechanical) to remove necrotic tissue (reducing the "necrotic burden") and its exudative components, so as to restore a more normal microenvironment.

Ideal medications should meet the following criteria:

- they should not adhere, and should leave no residues on the ulcer
- they should keep the surface of the ulcer moist
- they should be impermeable to liquids, but allow gas exchange
- they should create a barrier against bacteria and fungi
- they should stimulate granulation tissue
- they should give some pain relief
- they should be affordable.

At the present time, despite the wide variety of medications available, none of them are ideal and it is not possible to draw up rigorous protocols valid for the treatment of all VU (342). Experience shows that any product may be effective initially, but the benefits will decrease over time and

another product may eventually heal the ulcer. Consequently, the physician's attitude must be dynamic, taking account of the different stages of natural healing: necrotic, fibrinous, exudative, infectious, cleansing, granulation, re-epithelialization.

In years past the only treatment was rigid compressive bandaging and local medication with a few cleansing and/or disinfecting products. Now, however, there are many treatments available with a variety of indications for the different stages of the disease. There are occlusive and semi-occlusive medications, absorbents, carboxymethylcellulose medications, alginates, polyurethane, collagen, fibrin glue, chitosan; they come as pastes, granules, foams and gels. Local application of growth factor has been proposed (360) and it can administered by infiltration (361).

The exudate from infected ulcers should be cultured and systemic antibiotics started. Topical antibodies are not generally indicated as they can lead to contact dermatitis (362,363). A prospective trial showed that patients with VU treated with silver sulfadiazine emulsion combined with elastocompression healed sooner than the group treated with compression alone (364).

As healing progresses and there is little secretion and the ulcer becomes superficial, the medication can be changed to a so-called "biological" treatment: a thin cellulose or hyaluronic acid-based film protects the wound and stops the ulcer getting infected, giving good support for the migration and proliferation of basal epidermal cells while maintaining a good level of moisture so the lesion does not dry out.

Sibbald et al. (365) proposed a scheme for selecting the most appropriate medication in relation to the state of the bottom of the VU (Table XII).

Table XII

Type of medication granulation tissue	Appearance of the bottom of the lesion				Appearance of	
	Black (necrotic) (granulating new epithelium)	Yellow (dry fibrinous)	Exudate (moist)	Red (infected)	Red (moist)	Purple-red (bloody)
1. Foam				++	++	++
2. Hydrofibers				+++	++	+++ +
3. NaCl gauze				+++	+++	++
4. Alginates				+	+++	+++ +++
5. Hydrocolloids ++		+	++	++		++
6. Hydrogel +++		++	+++		+	+
7. Adhesive film +++						
8. Non-adhesive film					++	
9. Enzymes +		+++	+++			

- + frequently appropriate
- ++ appropriate
- +++ highly appropriate

6. Surgery

Surgery should not be considered as the only treatment or as an alternative treatment for VU , but as a complement to conservative therapy. Surgery for ulcers has two fundamental objectives:

- a) correcting the hemodynamic changes
- b) covering the ulcer with grafted skin to reduce the healing time (323).

This procedure must be preceded by detailed morphological and hemodynamic study of the superficial and deep venous systems and by the usual diagnostic procedures (340,366).

It is commonly considered that surgery of the superficial venous system in patients with varicose ulcers achieves the best results, reducing healing time and delaying recurrences, especially if there are no changes in the deep venous system (342). Surgery for post-thrombotic ulcers is less satisfactory (367).

Surgery on perforating veins in CVI has improved recently with the development of the endoscopic technique for subfascial ligation (55). Although the early results are excellent, the failure and recurrence rates are between 2.5 and 22% (125,368,369). One technical limitation is the difficulty of access to perimalleolar perforating veins. It has been reported that 50% of incompetent perforating veins within 10 cm of the ground, identified pre-operatively with Duplex scanning, cannot be treated with the endoscopic technique (369). In addition, although, compared with the open approach in a four-year follow-up, the endoscopic technique definitely involved less morbidity, there were no significant differences in terms of cure of the ulcer (370).

Insufficiency in superficial and perforating veins must always be fully corrected before considering any interventions on the deep venous circulation (371). Valvuloplasty, valves and venous grafts should be kept as a last resort. These procedures are still in the development phase, and can only be considered in specialist centers and controlled clinical trials (24). The literature on skin grafts still does not provide sufficient proof of the stable cure of VU . Various methods are used:

meshed split skin grafting (372)

pinch grafting (373)

allograft of human keratinocytes cultured in vitro (374)

free flap grafts of venous sections with valves, preceded by ulcerectomy and ligation of the incompetent perforating veins (375).

“shave therapy”, i.e. ulcerectomy and removal of the lipodermatosclerotic tissue, then meshed grafts (376).

The meshed grafting technique gives the best results. Human keratinocyte allografts and human skin substitutes are under critical review, with no data as yet to show the effect on recurrence (377). Artificial skin or skin equivalents are now being used, with promising effects on tissue regeneration (378,379).

7. Sclerotherapy

Sclerotherapy combined with compression treatment is indicated in selected patients with superficial venous system insufficiency, particularly if there are only short segments with reflux from incompetent perforating veins (380), even if there is an open ulcer (381). Sclerotherapy with ultrasound guidance was proposed in one study (158).

8. *Other treatments*

These include hyperbaric oxygen, vacuum therapy, polarised light, and laser therapy.

These are experimental treatments with limited caselists, and as yet there is no full documentation for the results and follow-up.

9. *General measures*

Patients with VU must be advised to keep as close to their ideal body weight as possible. Regular walks on flat ground, 2-3 times a day for at least 30 minutes, should be encouraged. Patients should avoid standing for long periods. They should also position themselves occasionally during the day with their legs higher than the level of their heart, and sleep with their legs slightly raised.

Manual lymphatic drainage can be considered for patients with edema caused by CVI.

Physiotherapy can improve joint mobility of the ankles.

Treatment for VU is a very old problem, much discussed but not resolved, because these lesions are slow to heal and quick to return.

Recommendations:

Conservative therapy has an important role in the first instance but does not prevent long-term recurrence unless it is backed, in many cases, by surgical correction of the hemodynamic problems. Surgery gives good results only in cases with isolated insufficiency of the venous system. Grade B

Compressive therapy, when applied correctly, will cure and prevent the recurrence of ulcers. Moreover the recovery time is significantly reduced if drugs are associated.

Grade A

Many clinical trials have been published but they are too selective to be representative of the general population. They usually only report short-term cure rates, with no longer-term data on recurrences. To supply reliable clinical evidence and validate the techniques still under investigation more rigorous methods and investigation standards are needed. The international literature calls for the establishment of special units dedicated to the study and care of leg ulcers. These would be responsible for home care and rehabilitation services, with a view to improving the quality of the services offered, keeping down costs, and - last but not least – ensuring a better quality of life for the patient.

Finally, on the topic of VU, one general principle has particular weight: guidelines are never totally binding; they must always be interpreted simply as important signposts, to be critically appraised and followed as appropriate to ensure the best possible results (382).

PELVIC VARICOCELE OR PELVIC CONGESTION SYNDROME

About 20% of men have a varicocele. Women may have a pelvic or ovarian form, causing the pelvic congestion syndrome. This is found in 15% of women between the ages of 18 and 50 (383), but is often overlooked in the differential diagnosis of abdominal pain. It is, however, a sign of venous insufficiency and stasis, with its own particular hemodynamics, pathogenesis and clinical presentation, and the phlebologist must bear it in mind, especially with today's non-invasive diagnostic procedures, and new therapeutic possibilities (384,385).

Ovarian varicocele was first described by Richet in 1857; Taylor in 1949 outlined a syndrome of pelvic congestion; Chidekel in 1968 reported the selective renal phlebographic picture, in which the left ovarian system and some or all of the pelvic veins were clearly visible on retrograde

examination in about 60% of the women, with findings similar to varicocele in men. But it was Hobbs (386) who actually defined the pelvic congestion syndrome (PCS), and related it to chronic venous insufficiency.

Varicose veins appearing around the utero-vaginal complex and the broad ligament of the uterus should be assessed in relation to the patient's anatomical and functional status and any concomitant venous pathology. In the first instance, the anatomy of the venous return is important since these veins have no valves (on the right towards the vena cava, and on the left to the renal vein); the vasoconstrictor tone, intraabdominal and intrathoracic pressures must all be checked – bearing in mind that this area has no muscle pump like the legs. In the second case, dilated pelvic veins may be compensating some deep venous return problem, possibly from a peripheral post-thrombotic syndrome. In this case they may have no clinical significance, although they may have repercussions mainly in the legs, for example by making varices refractory to therapy (387).

Many women with PCS complain of pelvic pain at various times – for example, during ovulation, menstruation, or pregnancy. The syndrome may go unidentified for a long time, causing pain that gets stronger before menstruation and increases during effort or exercise, and when the patient remains standing at length.

Varices can also occur on the pelvic floor, in the vulvar and perianal areas, and atypical varices on the back of the thigh may explain why the pain can spread from the pelvis to the back and legs.

It is therefore essential to exclude other causes such as pelvic inflammation, urinary tract infection, or intestinal inflammatory disorders such as Crohn's disease, diverticulitis, neoplasms and irritable bowel syndrome. A check must also be made for orthopedic problems such as stenosis of the sacral canal, spondylolisthesis, or intervertebral disc lesions, and reproductive system diseases such as ovarian cysts, endometriosis, fibroma or polyps. Unfortunately gynecologists often do little more than prescribe analgesics or – worse – refer the patient to a neurologist or psychiatrist for suspected psychosomatic problems.

A correct diagnosis can be made non-invasively by ultrasound examination or phlebography (388). Transvaginal echo-color-Doppler scan is useful for detecting dilated ovarian veins and venous reflux, indicative of incompetence. Angio-MRI and CT scans are often valuable too (389).

Phlebography is no longer merely a diagnostic tool, but also serves for therapy, by percutaneous endovascular embolization (390).

Surgery must always be considered as a therapeutic option. Alternatives are retroperitoneal ligation of the left ovarian vein (where varicocele is most frequent), 10-15 cm downstream of its origin, or sclerotherapy under video-laparoscopic control. These, however, should be reserved for selected cases. A recent review concluded that moderate cases could be dealt with by removal of the vulvar veins and sclerotherapy; excision of the ovarian varices is better than embolization which, however, remains the first choice for high reflux (391). Pharmacological therapy should be considered in all cases, besides hormones, using phlebotropic drugs as first choice (392).

An infrequent form of pelvic congestion, often with concomitant varices in the legs, is caused by compression of the left renal vein, and is sometimes known as the “nutcracker syndrome”. It should be borne in mind when women present with symptoms of pelvic congestion and hematuria, and can be confirmed by angio-MRI or CT scan, and investigation of the reno-caval gradient. An intravascular approach, with a stent, has been suggested (393).

Recommendations:

There is no standard therapy for pelvic congestion and in each case the therapeutic approach must be tailored individually. No randomized trials have been published.

This disorder causes troublesome symptoms and must be taken seriously. The patient should be

seen by a gynecologist aware of this kind of problem. Ultrasound is the first-level examination, but angio-MRI and CT scans are essential for investigating high reflux. Grade C

VENOUS MALFORMATIONS

Venous malformations (VM) are the most widespread vascular anomalies in the general population ((394,395,396,397). These congenital malformations involve various morphological and functional alterations in the central or peripheral venous system (398,399,400). Their pathogenesis appears to be linked to genetic anomalies in various biochemical mediators (e.g. angiopoietin) and the membrane receptors that regulate the interactions between endothelial and smooth muscle cells in the end stages of angiogenesis. The resulting maturation defect leads to the formation of anomalous veins with a monolayer of flat endothelial cells on the walls, but no real smooth muscular tunic (401).

VM mostly presents in the sporadic form in subjects with no family history, but there are also descriptions of hereditary and familial forms. In the majority of cases there is an isolated malformation, though multifocal and even systemic disseminated forms are also seen.

VM are usually located in the skin and mucous membranes, but they are often intramuscular or even intra-articular, and bone or any organ may be involved (402,403,404).

Distribution by site shows a marked prevalence of peripheral VM, particularly in the lower limbs, and cranio-facial VM, particularly in the temporo-masseteric, fronto-palpebral and lingual and labial regions. Other, less common, locations are the chest, abdomen and genitals.

VM can lead to multiple secondary effects or complications. The most obvious are esthetic and psychological, though these are far from the only ones, and certainly not the most important. VM in the cranio-facial area can cause serious functional disorders, with problems in swallowing, speech, respiration, sight or hearing); in peripheral regions they can cause problems disorders in grasping, posture and walking), sometimes with disabling effects (394,396,403,405).

Circulation complications take the form of venous stasis, peripheral forms leading to CVI, and loco-regional hypercoagulation with localised thrombosis and the possible depletion of coagulation factors (Table XIII).

Table XIII

Physiopathological effects of venous malformations

Esthetic	Superficial blemishes Skeletal deformations	
Psychological	Patient Family	
Functional	Motor deficiencies:	swallowing speech respiration grasping walking
	Sensory disorders:	sight

Hemodynamic	Chronic venous stasis
Coagulation	Localised thrombosis
	Consumption coagulopathy

The natural history of VM tends to vary. Generally, these malformations are evident from birth though sometimes they only become detectable later, during childhood or adolescence. In most cases, the maximum development is during puberty, with a marked increase in size, while later the malformation expands much more slowly, linked to the progressive slackening of surrounding tissues. The hemodynamic repercussions of the venous anomalies can become clinically evident and get progressively worse over the years, even if there is no real increase in the malformation.

Table XIV gives a schematic classification of simple and complex VM, based on anatomical and pathological criteria (400, 406, 405).

Table XIV

Anatomical and clinical classification of venous malformations (VM)

Simple VM	Subcutaneous
	Intramuscular
	Intra-articular
Complex VM	Venous hypo/aplasia
	Congenital valvular incompetence
	Persistent embryonal veins

In simple forms the anomalous veins may be abnormally dilated, with very thin walls consisting of a single layer of endothelial cells, and marked hypoplasia of the smooth muscular coat (lacunar veins).

Subcutaneous VM are the most frequent and usually involve lacunar or reticular veins in the subcutaneous adipose tissue, at variable depth but normally over the fascial layer.

Intramuscular VM are more rare but are now being seen increasingly frequently. Generally these look like lacunar veins; they may be large and wide-reaching, and lie between the large muscle bundles, for instance in the quadriceps femoris muscle or the brachial biceps.

The intra-articular form is the least frequent and the hardest to diagnose clinically; large venous lacunae may be located inside a joint, causing gradual synovial erosion with degenerative lesions in the joint head as is typically observed in the femoral-tibial joint.

Complex VM involve a combination of congenital venous anomalies such as hypoplasia or agenesis of the superficial and/or deep venous systems, primary valvular incontinence, and persistence of embryonal venous trunks such as the marginal vein.

In the hypo/aplastic form there may be complete agenesis, or varying degrees of hypoplasia and reduction in caliber in one or more segments of the superficial and/or deep venous systems of a limb. One of the most frequent complex VM is agenesis of the popliteo-femoral and/or the femoral-iliac tract, with compensatory hypertrophy of the greater saphenous vein which continues, in some

cases, typically in a large suprapubic vein cross-over confluent with the contralateral iliac axis.

In congenital valvular incontinence there is primary deep vein insufficiency, caused by complete atresia of the cusps of one of the venous valves or by dysplastic changes producing a mechanical defect in valve flap closure. These anomalies are mostly found in the superficial femoral vein, but can also involve the deep femoral vein, the common femoral vein and the internal iliac vein.

In the form with persisting embryonal veins there are anomalous, large-caliber venous trunks which develop in the early stages of vasculogenesis and normally regress during the late phases of modeling of the vascular tree. The most common embryonal veins are the ischiatic and marginal veins. The ischiatic vein presents as a large trunk continuous with the popliteal vein which runs posteriorly in the thigh and terminates in the pelvis, meeting the ipsilateral iliac. The marginal vein is a large-caliber venous collector originating in the external malleolar region and running along the lateral surface of the lower limb for varying distances, draining into the deep venous system. This has been illustrated in a classification of the multiple variants of this vein's course (Table XV) (407).

Table XV

Outlets of the marginal vein

Superficial femoral vein

Deep femoral vein

Common femoral vein

External iliac vein

Inferior gluteal vein

Internal iliac vein

Common iliac vein

Multiple confluences

Clinical picture

The signs and symptoms of VM widely: differences are seen in the site, the depth, the extension and the extent of anatomical and hemodynamic changes. Malformed veins on the surface are visible as a subcutaneous swelling of variable size and form, soft and elastic in consistency, collapsing easily with pressure, covered with bluish or purplish skin of normal temperature. They have no intrinsic pulse but typically expand in the anti-gravity position; this sign is very useful for diagnosis and must be checked carefully. On palpation there are small hard nodules: these are "phleboliths" – venous stones - caused by local thrombosis.

Intramuscular or intra-articular VM are less evident on objective examination, particularly if they are small, as they are deep and are often covered by healthy skin. However, careful clinical observation will generally show a typical asymmetry of the anatomical region compared to the contralateral area. This is accentuated when the patient is lying down.

Embryonal veins present as twisted and irregular ectatic venous trunks which extend into the acral regions for varying distances in the direction of the root of the limb. In hypo/aplasia of the deep venous circulation or congenital valvular incontinence, there will be clinical signs of chronic venous hypertension: edema, secondary varicose veins, lipodermatosclerosis and VU .

Skeletal and soft tissue changes, with hypertrophy or hypotrophy, are less frequent than with

arterio-venous malformations, but may be present, particularly in the peripheral forms (395,403,408).

VM are frequently associated with anomalies in the lymph system, and signs of lymphostasis are frequent. In the mixed venous-capillary form subcutaneous VM are often associated with flat superficial angiomas.

The triad of a complex peripheral VM, cutaneous capillary malformation and skeletal and soft tissue hypertrophy in a limb is known as the Klippel-Trenaunay syndrome (409,410,411). The Proteo syndrome has multifocal capillary-venous and lymph system malformations with anomalies of the muscles and skeleton and the peripheral nerves. It causes extreme hypertrophy and deformation of the limb.

Maffucci syndrome is the combination of a superficial VM and multiple enchondromatosis of the upper or lower extremities, leading to marked skeletal deformations with shortening of the limb and possible later chondrosarcoma (412). The presence of multiple subcutaneous VM may in rare cases be an element in the Bean syndrome, in which there are also disseminated VM of the gastrointestinal tract.

Diagnosis

Venous malformations are generally diagnosed by clinical examination. However, every patient should also have a thorough preoperative clinical and instrumental diagnostic evaluation, as the treatment indications depend very much on the morphological and functional characteristics of the VM. The elements investigated will include the site and the anatomical relationships, the extension and size, hemodynamic effects, patency and competence of the superficial and deep venous systems (413,414).

A rigorously standardised diagnostic protocol must be employed based on the following instrumental examinations: standard X-ray, color echoDoppler, computerised tomography (CT), magnetic resonance imaging (MRI) and phlebography (Table XVI).

Table XVI

Diagnostic approach to patients with venous malformations

Cranio-facial venous malformations	Cranial X-ray Color echoDoppler Direct phlebography Cranio-facial MR
Peripheral venous malformations	Comparative limb X-ray Color echoDoppler Ascending phlebography scending phlebography Direct phlebography MRI or CT scan of the limb

Standard X-rays show the indirect signs of VM such as phleboliths and any skeletal dysplasia and

size abnormalities. Color echoDoppler is the preliminary examination for studying the extension of the VM, its patency and the competence of the superficial and deep venous systems, the morphology and functional status of the venous valves and to exclude the presence of arterio-venous fistulas (415,416).

CT and MRI scans permit an accurate definition of the extension of the VM and its anatomical relationships with internal organs and the musculo-skeletal structures, particularly when the malformations are deep (417).The diagnosis will be completed with phlebography which is indispensable to obtain a full morphological and hemodynamic picture of the malformations and the entire superficial and deep venous system. The examination should be done in the ascending and descending phases and with direct puncture of the malformation, as these all give complementary information (407,413,414).

The ascending phase explores the patency and conformation of the main venous axes, showing up hypo/aplasia with great diagnostic accuracy. The descending phase gives a picture of valve competence, showing any primary venous insufficiency whose severity can be assessed on the basis of the retrograde opacity in the deep venous system.

These investigations are completed with a selective hemodynamic study by direct injection, which is vital for the examination of lacunar VM with low flow, or for embryonal veins which can be visualised all the way to the confluence. By using tourniquets and hemostatic cuffs or other systems of selective compression, isolated parts of the venous circulation can be examined in all phlebography phases. This procedure can even be done intraoperatively, so that the VM can be checked in real time during scleroembolising treatment. It can also serve for an immediate postoperative check on the results.

Treatment

Treating VM poses serious problems for the vascular surgeon as these are often extremely complex malformations, appearing in babies or young children, with very serious hemodynamic, functional and esthetic implications. Treatment aims at partial or complete regression of the malformation, reduction or disappearance of the signs of venous insufficiency, functional rehabilitation of the limb, elimination or reduction of blemishes.

A complete preoperative diagnostic evaluation is absolutely vital before any treatment is decided; the instrumental findings must guide each individual therapeutic program so that surgical procedures and/or percutaneous treatments can be combined as most appropriate for each patient.

The indications and weight of the recommendations for the various treatment options in the different forms of VM are summarized in Table XVII.

Table XVII

Therapeutic options for venous malformations (VM)

Cranio-facial VM	Percutaneous sclerotherapy (++)
Guided sclerotherapy (++++)	
Surgery (+)	
Simple Subcutaneous peripheral VM	Percutaneous sclerotherapy (+++)
Guided sclerotherapy (+++)	

Surgery (++)

Simple intramuscular peripheral VM Percutaneous sclerotherapy (+)
Guided sclerotherapy (++++)

Simple intra-bone peripheral VM Guided sclerotherapy (++++)

Complex peripheral VM with hypo/aplasia Wait and see (+++)
Surgery (+)

Complex peripheral VM Surgery (++)
with valvular incontinence

Complex peripheral VM with embryonal vein Surgery (+++)
Guided sclerotherapy (++)
Percutaneous sclerotherapy (+)

Direct percutaneous sclerotherapy can be done on isolated, superficial, small VM. If they are more extensive and deeper it is better to do the sclerotherapy under radiosopic guidance, using the direct injection phlebography technique. This allows close control of the injection site and the diffusion of the sclerosing mixture, giving immediate confirmation of the results.

Various sclerosing mixtures are used. The choice will depend on the morphological characteristics, anatomical site and extent of the malformation (418,419,420). For spider veins and small-caliber VM, particularly on the lips and tongue, a 2-3% polydocanol solution is recommended. For large-caliber, extensive VM (lacunar veins), frequently found in the temporo-mandibular area, a more powerful sclerosing agent is called for, such as 95% ethanol - Ethibloc® (421,422,423,424). The dosage of the sclerosing agent should be proportional to the size of the malformed veins, up to a maximum of 2 mL/kg body weight.

The sclerotherapy technique must obviously be extremely rigorous because accidental injection of the sclerosing mixture outside the vein can provoke serious complications such as thrombophlebitis, cutaneous necrosis, granuloma, neurological damage. A normal, reversible side effect is loco-regional inflammation/edema, varying in severity and extension, which normally disappears in a few weeks; it can be treated, if necessary, with a steroidal anti-inflammatory drug.

Surgery plays a fundamental role in the complex overall treatment strategy for VM (397,403,406,421). The most common surgical procedure is to strip lacunar or reticular malformed veins in the lower limbs, preferably by a micro-invasive technique, through micro-incisions in the skin and using special phlebectomy hooks.

For a persisting embryonal venous trunk the only therapeutic procedure is surgical removal (407,426,427). This must also be done with the least invasive technique possible. In the past large incisions were made along the outer surface of the limb, but nowadays only minimal skin incisions are needed, so the outcome is esthetically more acceptable. Detailed preoperative mapping must be done on the embryonal vein, and when feasible, mini-strippers can be used.

When dealing with congenital valvular incompetence, and preoperative ultrasound examination indicates the presence of dysplastic valvular flaps, the venous valves can be surgically reconstructed

(428) by external venoplasty with reinforced Dacron or PTFE prostheses. The correct positioning of the prosthetic band – of the right caliber – will restore valve competence by drawing the dysplastic flaps closer together, while maintaining the patency of the veins.

For segmentary hypoplasia of the deep venous circulation secondary to extrinsic compression from an abnormal fibrous muscle band, as is often seen in the popliteal cavity, a decompression procedure can be employed to facilitate the development of the hypoplastic venous structures (405).

In cases of deep vein agenesis with compensatory hypertrophy of superficial veins such as the greater saphenous vein and its collaterals, surgical removal of the malformed veins is obviously contra-indicated, as they serve as hemodynamic substitutes.

Therefore the therapeutic strategy must be carefully thought out and planned for each patient on the basis of the clinical and instrumental findings (429), with particular reference to the site, the morphology and the extension of the VM, and taking account of the architecture and the hemodynamics of the loco-regional venous circulation.

The site of the malformation can be a major factor in choosing treatment. In the facial and genital areas sclerotherapy is preferred as it has fewer esthetic and functional implications, whereas surgery, being more radical, is used more for the peripheral forms. The complexity and size of the VM are in direct proportion to the surgical approach selected. Simple or isolated VM are treated by elective intravascular percutaneous sclerotherapy under venographic guidance. Complex VM call for corrective and/or reconstructive surgery, depending on the anatomical and hemodynamic abnormalities present.

In the majority of cases, combined therapy is the preferred option. Percutaneous treatment combined with surgery offers the best clinical, morphological and functional results. Ligature and stripping the malformed veins can be combined with preliminary or intraoperative sclerosing treatment, so that minimally invasive techniques can be employed to remove moderately sized dysplastic lacunar or spider veins.

Similarly, after stripping the main trunk of an embryonal vein the intervention can be completed by percutaneous sclerotherapy on the numerous collateral veins, particularly the terminal end near the confluence with the deep venous system.

In conclusion, surgery and percutaneous sclerotherapy are not alternatives but can be usefully combined in the complex and delicate strategies for treating VM. An important point, particularly in cases of extensive VM, is that numerous sequential surgical operations or sclerotherapies may be necessary to obtain complete regression of the malformations.

Recommendations:

Thorough preoperative diagnostic assessment is essential, including direct X-rays, color-echoDoppler, CT or MRI, and phlebography. Grade C

Phlebography should be done in the ascending and descending phases and with direct injection of the VM, to obtain a complete morphological and hemodynamic picture.

Grade C.

Arteriography gives no useful information for pure venous malformations and should therefore be avoided. Grade C

Sclerotherapy is a minimally invasive, low-risk technique for VM and can be considered a valid alternative or useful complement to surgery, for facial, genital and peripheral VM.

Grade C

For extensive or deep-lying VM sclerotherapy should preferably be done under radiosopic

guidance, using direct-injection intraoperative phlebography. Grade C

Surgery is useful especially for persisting embryonic veins, which should be removed using a mini-invasive technique after thorough preoperative echographic mapping. Grade C Valvuloplasty may be needed for congenital deep venous insufficiency with dysplastic valves. Grade C

The therapeutic strategy for VM must be carefully thought out and planned for each patient on the basis of the clinical and instrumental findings, with particular reference to the site, morphology and extension of the malformation, and the hemodynamics of the loco-regional venous circulation. Grade C

For most cases a combined approach is called for, as surgery and sclerotherapy can be scheduled to give better clinical results. Grade C

It is extremely important to choose the right time for surgery, to take account of the patient's growth, the development of the malformation and its hemodynamic repercussions. Grade C

QUALITY OF LIFE

There are many reasons for considering the Quality of Life (QoL) as part of the therapeutic outcome, in CVI like in other diseases (1,430,431). The current method of generic measuring, considered the standard in the USA and in Europe, is the Medical Outcomes Study Short Form Health Survey – 36 (MOS SF36) or the Nottingham Health Profile (NHP) (432,433).

Specific questionnaires for CVI (Aberdeen Q; CVIQ1 and CVIQ2; Tübingen Q.) have been used since 1992, with surprising results for a disease that has hitherto been so seriously underestimated. CVI has a profoundly negative effect on the patient's everyday life and the results illustrate its impact on morbidity and confirm the efficacy of drug therapy (434,435). These specific questionnaires can currently only be used with permission, and against payment. There are also specific questionnaires for patients with VU (436).

Evaluation of randomised controlled trials on surgery and its effect on QoL is more complicated (437). Trials are still in progress to assess recent surgical techniques for CVI such as subfascial endoscopic ligation of the perforating veins (SEPS) and valvuloplasty. QoL questionnaires should ideally be routinely used in clinical follow-up (67,438,439,440).

The use of compression for the prevention and treatment of VU and prophylaxis of recurrences has proved effective in clinical practice and economical as regards savings in dealing with the acute disease and its frequent recurrences. Recent surveys of the effects on QoL in patients with severe CVI (CEAP 3-5) found major changes in the scores for physical and emotional wellbeing, with an important socio-economic impact. It is therefore to be hoped that the national health service will take on the costs of compression therapy, and reimburse the expenditure at least for patients in advanced CEAP classes (438,441).

Recommendations:

The analysis of clinical parameters for evaluating the QoL should use standard psychometric criteria which are reproducible, valid and acceptable. The SF-36 and NHP surveys have proven scientific worth for CVI. Grade B

Specific questionnaires for QoL in various languages, for use in international trials and routine clinical practice, need to be available freely.

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GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF LYMPHATIC DISEASES

General Considerations

Lymphedema is a chronic disease, frustrating both for the patient and the doctor. It is caused by a defect in the lymphatic system leading to a build-up of lymph in the interstitial space, mainly at a suprafascial level in the first instance but then throughout the subcutaneous tissues. The lymphatic system's prime function is to remove large molecules and water from the interstitial space and to allow a turnover of the cells of the system (1).

From a physio-pathological point of view lymphatic insufficiency can be classified as dynamic or

mechanical. Dynamic (or high-capacity) insufficiency occurs in an intact lymphatic system which must deal with a protein load higher than its capacity. Mechanical (or low-capacity) insufficiency is caused by either primary or secondary damage to the lymphatic system, which subsequently cannot deal with a normal protein load (2). The proteins stimulate the influx of mast cells and neutrophils, triggering a process of non-specific granulation, which in time leads to interstitial fibrosis with irreversible structural damage (3).

Epidemiology

It is difficult to obtain a clear idea of the prevalence of lymphedema worldwide, partly because it is always hard to make an immediate and specific diagnosis. Epidemiological data however shows that this is a widespread complaint throughout the world, with no major differences in its clinical manifestations. A third of the world's population has some sort of edema, the most serious being lymphedema – there are 150 million recorded cases. The majority of these cases (45m) are due to parasites; postoperative lymphedema or trauma is responsible for another 25m, and between 5 and 20m are primary lymphedema (4,5). The risk of filaria infection and its consequences probably involves two million people throughout the world (5).

In Europe, Spain has a high incidence of lymphedema in women (84%) between the ages of 45 and 59.

Primary lymphedema makes up 79% of cases, secondary lymphedema 21%; 76.5% of primary lymphedema is in patients under the age of 45, and 80% of secondary lymphedema cases are over the age of 45. The incidence of secondary lymphedema is highest in orthopedics (33%), followed by trauma (25.5%) and malignant tumors (18.9%). with 90% of these post-mastectomy, which accounts for 6-30% of lymphedema (6). The upper limbs are affected in 21.7% and the legs in 79% (7).

In Italy, there is little data on primary lymphedema, which probably accounts for 30-40% of the total. Forty percent of secondary lymphedema is post-mastectomy (8,9,10). Reliable epidemiological figures on lymphedema are still scant, both in Italy and elsewhere.

Prevention

Primary lymphedema is a clinical condition that occurs suddenly and cannot, therefore, be predicted. However, secondary lymphedema can be clinically predicted, although not when it is likely to occur.

Authoritative proposals on the prevention of lymphedema only concern secondary lymphedema and are mainly aimed at surgeons (for example, type of incision and surgical technique, preserving the lymphatic drainage areas of most use to the limb), or oncologists (moderately aggressive radiotherapy, if possible).

The proposals involve analysing the lymphatic system before post-operative lymphedema arises, by isotopic lymphangiography within 2-3 months of the operation to study the anatomy and the residual function of the limb at risk (11), and the prevention of infection (dermato-lymphangio-adenitis) by administering lifelong benzatin-penicillin. (12).

In most cases current strategies aim at preventing the complications of lymphedema, infections in particular. However, we believe it should be aimed primarily at preventing gross progression, that is, the increase in size of the affected limb. This is only possible if, as the ISL Consensus Document officially recognised in 1995 (13), a complete long-term physical treatment protocol is promptly devised and administered, modifying it to suit the individual clinical picture. It should include all the advice the patient needs (such as lifestyle advice, exercise at home, psychotherapy, self-help) This applies to any type of lymphedema but is particularly fruitful early in the clinical course when the edema is soft and either intermittent or remitting. It is abundantly clear that prevention of lymphedema means stopping it happening, if possible, or at least preventing progression. Where complications have not yet set in, these aims can be achieved if the patient undergoes early

treatment, which includes kinesitherapy, meaning lymph drainage, and pressure therapy, and compression (with multiple bandages, elastic bandages or stockings), as well as “lymphotropic” drugs. The prevention of secondary lymphedema also depends on the availability of skilled kinesitherapists, on the patient’s expectations and ability to cooperate, and on cost (14,15,16,17).

Recommendations:

Give patients information about their disease and on the probability of lymphedema, so they are ready to deal with the problem. Early diagnosis and physiotherapy are basic steps in the treatment of lymphedema. In oncological surgery and radiotherapy the possibility of secondary lymphedema must be borne in mind. Grade C.

Clinical and Instrumental Diagnosis

Clinical diagnosis

Often, a detailed clinical history and objective examination can reveal the cause of edema and suggest the diagnosis of lymphedema. Further thorough instrumental examinations should then be scheduled. Although the etiology of primary and secondary lymphedema differs, the clinical picture and the objective signs of the disease are often similar (13,18). A clinical history can exclude the existence of underlying pathologies - cardiac, renal, and so on - and establish the date of onset, how it appeared and its course up to the present time.

The patient with lymphedema must be examined in the standing and lying positions. The examination should assess the condition of the skin, the distribution of the edema, the existence of spontaneous or evoked pain, the depth of skin folds, any lymphatic exudation, whether there is a network of varicose veins or lymphatic varices, lymphadenopathy, signs of lymphangitis or other skin lesions, past or present. Palpation helps to assess spontaneous or evoked pain and the consistency of the edema – the examining doctor might look for pitting, and the Stemmer sign, and measure the limb (19). It is also important to examine all lymph nodes that can be reached, and note the patient’s weight and height.

Certain “key points” are often employed in the clinical classification of lymphedema of the limbs. These are: the temporo-spatial distribution and severity of the edema, the condition of the skin and adnexa, limb function, present and past lymphangitis and lymphatic exudate (18). The following classifications have been proposed: etiopathogenic, anatomical, functional and clinical.

Lymphedema is normally divided into two broad groups:

primary, due to dilatation, stenosis or aplasia of the lymphatic collector vessels;

secondary, caused by extrinsic lesions arising from surgical removal of the lymph nodes or damage to lymphatic vessels.

Both primary and secondary lymphedema may become malignant.

A few examples are given here of the different classifications used today: criteria committee of the N.Y. Heart Association (1964), Zierman (1996), Battezzati-Domini (1967), Howard (1968), Földi (1971,1982), Cordeiro (1983), Martorell (1972), Hunt (1972), Kinmonth (1982), Pietravallo (1988), operative classification (Donini 1992, modified in 1998), Campisi (1997).

In these guidelines we have mainly used the Domini clinical, anatomical and functional operative classification (1992, modified in 1998) which organises lymphedema into five clinical stages. This classification is the result of a critical analysis of the various existing classifications of lymphedema of the upper limb and relating the clinical and histopathological pictures.

Alongside this classification is the modified Battezzati-Donini etiopathogenic classification (Tosatti

1967) which classifies lymphedema on the basis of the anatomical or functional damage to the lymphatic system as diseases involving the collecting system, diseases due to altered lymphogenesis and absorption, and diseases of mixed etiopathogenesis.

Instrumental methods

Currently, lymphoscintigraphy and echography are the techniques most used in the diagnosis of lymphedema in the lower limbs. Other methods include venous echo-Doppler, microlymphangiography, CT and MRI scans, venography, lymph node biopsy and lymphography (in selected cases and in specialized centers) (13). The diagnosis of lymphedema was enormously facilitated by the introduction of Kinmonth's technique for direct incannulation of lymphatic vessels, and the development of lymphoscintigraphic radiodiagnosis (20,21).

Lymphoscintigraphy with ^{99m}Tc in the form of radiolabeled colloid is used for morphological and functional examination of the lymphatic system of the lower limbs (22). Ultrasound examination (echography) of soft tissues shows up free lymph in the suprafascial and interstitial areas (13,20,23,24,25,26,27).

Other examinations serve to complete the diagnosis when further investigations are made in specialized centers. CT scan with contrast medium, venography, lymphography and lymph node biopsy help exclude complex congenital malformations or neoplastic diseases (28). Fluorescent microlymphangiography is a non-invasive method for assessing the spontaneous lymphatic drainage of specific substances injected intradermally (25).

Recommendations:

First level diagnostic examinations: US of the soft tissues and echoDoppler;

Second level examinations: radioisotopic lymphoscintigraphy;

Third level examinations: fluorescent microlymphangiography, venography, CT, MRI scans and other instrumental examinations. Grade A.

Treatment

Lymphedema of the limbs is mainly conservative, surgery being reserved for selected cases of advanced disease.

Conservative treatment

This heading comprises pharmacological measures and physical compression. Compression includes various procedures, such as manual lymphatic drainage (MLD), compression, and pressure therapy (PT), elevation and heat treatment (29). Drugs include the benzopyrones such as coumarin which has a direct effect on inflammation, and especially on the macrophages; if used on a continuing basis, it accelerates protein degradation thus activating extra-lymphatic absorption (30). Benzopyrones are used at every stage of lymphedema, whether primary or secondary. There are reports of severe hepatotoxicity of high-dose synthetic coumarin given to treat secondary lymphedema (31). Antibiotics and antimycotics are used if infective complications arise (lymphangitis); the use of diuretics is not recommended as they eliminate more water than proteins (32).

Physical treatment should not be limited to one type, but should involve a combination of different treatments, selected depending on the stage of the lymphedema and the strategy applicable at the time (33,34). Combined physical therapy is divided into two stages. The first is aimed at reducing the interstitial lymphatic load and, consequently, reducing the size of the limb; while the second stabilises and if possible improves on the results (35)

The first stage combines lymphatic drainage, pressure bandages, physical exercise and meticulous skin care. In the second stage patients are required to wear elastic stockings on a daily basis, to do specific exercises and to ensure meticulous skin care. Pressure therapy is sometimes recommended in this second stage (35,36,37,38). Elevation is certainly effective in reducing edema (39). Heat treatment is widely used, but its effectiveness is still under study (40).

Recommendations:

It is important to use more than one type of physical treatment, and to combine the different methods strategically, depending on the stage of the lymphedema. Grade B.

Surgery

Many techniques are currently used in the surgical treatment of lymphedema of the limbs. The physiological approach aims to restore the normal lymphatic flow by creating venous-lymphatic and lymphatic-venous-lymphatic anastomoses, and uses autologous lymphatic tissue transplants with lympho-lymphatic anastomosis (41).

The radical approach does not follow a strict physiopathological principle, but involves destroying large areas of skin, subcutaneous and fascial tissue. Combinations of these two approaches use both concepts. Thompson's operation is the precursor of these methods.

Among the excision types of operation, the Charles operation has proved effective in some patients whose extensive edema did not respond to conservative treatment and who had severe trophic skin alterations (42,43). The Thompson operation has been tested clinically on a wider scale, with encouraging long-term results, though lymphangiography did not document the presence of new anastomoses between the superficial and deep systems. In selected cases, it may be effective in reducing late edema, though t serious post-operative infective complications are a risk (44,45).

The Homans operation has given better results in serious cases, with functional recovery of the limb in primary lymphedema; in secondary forms the results tend to differ depending on the various case series (46,47).

Lymph liposuction removes the layers of fluid, and can halve the edema within a year. It is much less invasive than other methods (48).

The principal of all the strategies derived from these main techniques is the creation of lymphatic-venous anastomoses. This approach was initially very successful in lymphology but there are doubts about the long-term effectiveness, because it is not easy to prove long-term patency. However, in some series 74% of patients still enjoyed an improvement one year after treatment (49,50). Other related methods have been largely abandoned because of the poor one-year results and the attendant complications. These include lymphatic graft (51); the Kinmonth technique or mesenteric bridge (23); and the Goldsmith omental transposition method (52,53).

Recommendations:

The best indication for surgical excision is the loss of limb function due to excessive lymphedema resistant to conservative treatment. A combination of lymph liposuction and a modified Homans operation gives best results, though international studies limited. No multicenter studies have been done to document the real effectiveness of the "derivative" methods.

Surgery should in any event be carried out in highly specialised hospitals by surgeons with specific experience. Grade C.

Quality of life

In Italy, most lymphedema is managed by specialists such as angiologists, cosmetic and plastic surgeons, physiatrists, general and vascular surgeons, and microsurgeons, who each tend to view the problem from their own point of view. This leads to a confused approach to treatment and, therefore, a poor quality of life for the patient.

Primary lymphedema and secondary forms consequent to cancer surgery - especially breast cancer - are reference conditions for illustrating the repercussions on the patient's quality of life (54). Recent surveys agree that the patient tends to worry more about the difference in size of the two limbs than the actual symptoms of the edematous limb (55). Edema of the hand causes greater mental distress than edema of the whole arm because that can be "hidden".

In the case of post-mastectomy lymphedema, the swollen limb can be a real handicap, especially if the main side is affected. It affects gross movements such as washing, doing one's hair, putting on a blouse, washing up; it also impedes finer movements such as fastening a necklace or writing, and chores or hobbies, such as ironing, carrying heavy objects, gardening, and so on.

The quality of life of a patient suffering from lymphedema depends on early diagnosis, ample information and treatment that best meets the patient's needs. Good results are hard to achieve because of the lack of centers specialised in treating lymphedema, the lack of schools or courses for specialist training in lymphatic diseases, the high cost of treatment and its lifelong duration. Other specific constraints, mainly compliance, further reduce the chances of success.

Patients' approval and understanding of the treatment strategy makes for 40% of its success. Esthetic considerations (asymmetry of the limbs), functional damage (inadequacy or loss of some functions) and relational problems (embarrassment with the partner or at work) are at the heart of the emotional reactions to the disease.

The patient's acceptance of the various treatment options can at times be an obstacle for the lymph specialist. MLD and PT are the preferred methods even though they must be repeated regularly. In contrast, patients find it harder to tolerate wearing bandages or support hose. Although there is no substitute for them, provided they are appropriately prescribed and worn properly, patients dislike their appearance, and consider them a sign of the disease; also, they must be worn every day, at rest and while doing exercises, such as decongestant movements.

The patient's own social and family environment plays an important role in compliance. The psychological support and encouragement to self-help which a patient may receive in the family must be followed up by the family's active participation in caring for the affected limb (MLD, bandages, helping with decongestant exercises), under the guidance and instructions of the lymph specialist (34,54,55,56,57).

Recommendations:

Early diagnosis, taking into account the pathogenic factors;

Check whether adequate treatment had been attempted before this diagnosis;

An individual treatment strategy should be proposed taking account of the clinical stage and the patient's requirements. Grade B

Lymphatic malformations

Although congenital malformations of the lymphatic system are rare, they are highly disabling as they can cause severe functional and esthetic disorders. Congenital malformations of the lymphatic system arise from anomalies of the embryonic lymphatic capillaries or of the main lymphatic vessels of the limbs, head and chest (58). They occur mainly in peripheral areas, especially the legs,

but forms involving the neck and face, chest and pelvis are also reported (59,60).

A useful anatomic-pathological classification distinguishes capillary types from trunk types according to which part of the lymphatic tree is mainly affected (Table XVIII).

Table XVIII

Anatomical-clinical classification of lymphatic malformations

Lymphatic capillary malformations	Diffuse tissue lymphangioma
Microcystic lymphangioma	
Lymphatic vessel malformations	Cystic hygroma
Congenital lymphedema	

Lymphatic capillary malformations are commonly known as lymphangioma. There is usually a dense network of microscopic lymphatic vessels in the skin, mucous membranes or soft tissues. They vary widely in size, from a small nodule to a large tumor-like mass. They are most frequent on the skull and face, especially on or around the tongue and eyebrows, in the axillary cavity and groin (58). Some have a diffuse, infiltrating appearance (diffuse tissue lymphangioma) whereas others present a microcystic structure with typical lymphatic vesicles (microcystic lymphangioma).

Lymphatic vessel malformations are caused by congenital abnormalities in the medium and large lymphatic trunks. Cystic hygromas are abnormal dilatations with sac-like ectasia of large collecting vessels at the main drainage points of the lymphatic system. They usually occur in the masseter, submandibular, lateral-cervical, axillary and inguinal regions (61). Mediastinal cystic hygromas are rare but can cause complications by compressing vital structures such as the trachea and central veins.

Congenital lymphedema involves massive, progressive edema in a limb, caused by hypoplasia or agenesis of the main peripheral lymphatic trunks, leading to blockage of lymphatic outflow and interstitial stasis.

Schematically, it is also useful to distinguish pure lymphatic malformations, involving isolated alterations in the lymphatic vessels, and mixed lymphatic-venous forms in which there are congenital abnormalities of both the lymphatic circulation and the superficial and/or deep venous system.

The natural history of lymphatic malformations may vary widely. Lymphangiomas and cystic hygromas are usually present at birth and may grow gradually over the years, especially in concomitance with various factors and events, which may be hormonal, traumatic or infective. In some cases, there is a gradual involution of the lymphatic mass or sac after puberty.

Congenital lymphedema tends to manifest itself at birth, during childhood or adolescence, but sometimes becomes obvious only in adulthood. It progresses slowly. The most frequent complications are generally local (Table XVIV).

Table XVIV

Complications of lymphatic malformations

Lymphangioma	Lymphorrhagia
Skin necrosis	
Cystic hygromas	Intracystic hemorrhage
Infection	
Compression of vital organ(s)	
Congenital lymphedema	Lymphangitis
Pachyderma	
Skin ulcers	

Clinical Picture

The clinical picture of lymphatic malformations depends on the type and severity of the anatomical abnormalities, and the part of the body affected. Surface lymphangiomas appear as subcutaneous swelling or raised whitish skin patches with an irregular, warty surface. In their microcystic form, there are frequently translucent microvesicles containing serous fluid. They are often accompanied by dystrophic skin lesions.

Cystic hygromas appear as large subcutaneous swellings which tend to be soft and spongy. They float, and are fairly responsive to antigravity manipulations; they do not pulsate. If a complication such as intracystic hemorrhage sets in, they may become hard and bluish, creating problems of differential diagnosis

The first symptom of congenital lymphedema is a gradual increase in the size of a limb. There are sporadic and familial forms. They usually involve the lower limbs but, less frequently, the arms too. They may be unilateral or bilateral. Lymphatic edema is usually doughy in its initial stages, becoming progressively harder and fibrous. There is massive enlargement of the limb, especially in the acral regions, with little improvement when the limb is raised. In the advanced stages, complications may set in, such as hypertrophic skin lesions with verrucosis and pachyderma, eczema and exudative lymphangitis.

Diagnosis

The diagnostic tools for lymphatic malformations include ECD, MRI, lymphography and lymphoscintigraphy (62). The indications and the relative strengths of these tools for diagnosing lymphatic malformations are summarized in Table XX below.

Table XX

Diagnostic approaches to the patient with lymphatic malformations.

Lymphangioma	Echo-color-Doppler (++)
	MRI or CT (+++)

Cystic hygroma	Echo-color-Doppler (++++) MRI or CT (+++) Direct lymphography (++++)
Congenital lymphedema	Ascending lymphography (++) Lymphoscintigraphy (++++) Echo-color-Doppler (+)

The ECD examination is used first to exclude any alterations of the arterial and venous circulation, in order to confirm the clinical suspicion of lymphatic vessel malformation. Usually, lymphangiomas cause significant thickening of the skin, in which small cavities can be observed, giving a signal typical of fluid; these can be only slightly compressed with the probe, and the Doppler examination shows no flow. US scan shows cystic hygromas as large expansive formations containing fluid; they vary in size, and sometimes have only one chamber, but are more often multilobulate, with thick, hyperechogenic walls. Color-Doppler examination shows no arterial or venous blood flow.

In lymphedema, ECD examination does not provide significant direct information on changes in the lymphatic system but gives a good picture of the superficial and deep venous circulation, showing up any association with congenital or secondary venous insufficiency.

MRI serves to assess the extent, the size and the anatomical relations of localised lymphatic malformations (63).

Direct injection lymphography of the lymphatic cistern is essential in the case of cystic hygromas for a morphological study of the sac and especially for percutaneous scleroembolisation.

Ascending lymphangiography, carried out by cannulating a lymphatic vessel in the foot, is useful for investigating the anatomy of the lymphatic circulation in congenital lymphedema.

Lymphoscintigraphy involves injecting radiolabeled albumin subcutaneously in the foot. It is used widely to study lymphatic drainage in peripheral lymphedema as it shows up obstructions, hypoplasia, and atresias in lymphatic vessels in a minimally invasive manner.

Treatment

Treatment strategy is based on a thorough pre-operative diagnostic assessment and mainly depends on the type of lymphatic malformation, its extent and site (64). Treatment should be as conservative as possible, as the surgical removal of lymphatic malformations is accompanied by a high incidence of recurrences and often unacceptable esthetic effects. Table XXI summarizes the treatment options for the various lymphatic malformations and indicates the strength of the recommendations.

Table XXI

Treatment of lymphatic malformations

Microcystic tissue lymphangioma	Percutaneous sclerosis (+++) Surgery (+)
Diffuse tissue lymphangioma	Surgery (++)

Cystic hygroma

Scleroembolisation (+++++)

Congenital lymphedema

Surgery (++)

Percutaneous sclerotherapy is the first-choice treatment for microcystic tissue lymphangioma, and especially for cystic hygromas, because it is non-invasive, and gives excellent clinical results, with complete regression of lymphatic vesicles and cisterns. The size of the lesion dictates the choice of the sclerosing medium; for small lymphangiomas and cystic hygromas polydocanol is preferred, whereas large lymph sacs need ethanol, Ethibloc or picibanyl (65,66,67). A sclerosing injection must always be followed by selective locoregional compression, especially in the case of large lacunae.

Surgery is recommended in diffuse tissue forms with a tendency to progress, and in localised peripheral forms, where radical surgical removal can be carried out without causing disfigurement or functional disability. In advanced lymphedema with a hugely swollen limb, cuto-lipo-fassectomy may be necessary to enable the patient to regain motor function of the limb.

The results with various operations to reconstruct the lymphatic system proposed in recent years, such as lymphatic-venous anastomosis, are not yet good enough to allow their routine use. In selected cases, even with lymphatic malformations, it may be useful to combine surgery and sclerotherapy to achieve the best functional and esthetic results.

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