

Editor's Choice — Management of Chronic Venous Disease

Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS)

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ABBREVIATIONS

AASV	Anterior Accessory Saphenous Vein
AC	AntiCoagulation
AP	Ambulatory Phlebectomy
APG	Air-PlethysmoGraphy
ASVAL	Ambulatory Selective Varices Ablation under Local anaesthesia
AVMs	ArterioVenous Malformations
AVP	Ambulatory Venous Pressure
AVVQ	Aberdeen Varicose Veins Questionnaire
BMI	Body Mass Index
CEAP	Clinical Etiologic Anatomic Pathophysiological
CHIVA	Conservatrice et Hémodynamique de l'Insuffisance Veineuse en Ambulatoire
CIVIQ	Chronic Venous Insufficiency Questionnaire
CT	Computed Tomography
CTV	Computed Tomography Venography
CVD	Chronic Venous Disease
CVI	Chronic Venous Insufficiency
CVMs	Congenital Vascular Malformations
CW	Continuous Wave
DUS	Duplex UltraSound
DVT	Deep Venous Thrombosis
EBM	Evidence Based Medicine
ESVS	European Society for Vascular Surgery
EVLA	EndoVenous Laser Ablation
EVTA	EndoVenous Thermal Ablation
GSV	Great Saphenous Vein
GWC	Guideline Writing Committee
HCSE	Horse CheStnut Extract

HL	High Ligation
HL/S	High Ligation/Stripping
IPC	Intermittent Pneumatic Compression
ISSVA	International Society for the Study of Vascular Anomalies
IVC	Inferior Vena Cava
IVUS	IntraVascular UltraSound
KTS	Klippel-Trenaunay Syndrome
LMWH	Low Molecular Weight Heparin
MOCA	Mechanochemical ablation
MPFF	Micronized Purified Flavonoid Fraction
MR	Magnetic Resonance
MRV	Magnetic Resonance Venography
NIVL	Non-thrombotic Iliac Vein Lesions
OR	Odds Ratio
PASV	Posterior Accessory Saphenous Vein
PTA	Percutaneous Transluminal Angioplasty
PTS	Post Thrombotic Syndrome
PWS	Parkes-Weber Syndrome
QALYs	Quality-Adjusted Life Years
QoL	Quality of Life
RCT(s)	Randomized Controlled Trial(s)
REVAS	REcurrent Varices After Surgery
RFA	RadioFrequency Ablation
SEPS	Subfascial Endoscopic Perforator Surgery
SFJ	SaphenoFemoral Junction
SPJ	SaphenoPopliteal Junction
SSV	Small Saphenous Vein
STS	Sodium Tetradecyl Sulphate
TCL	TransCutaneous Laser

TIPP	Transilluminated Powered Phlebectomy
UGFS	Ultrasound Guided Foam Sclerotherapy
VCSS	Venous Clinical Severity Score
VDS	Venous Disability Score

VEINES	Venous Insufficiency Epidemiological and Economic Study
VMs	Venous Malformations
VSDS	Venous Segmental Disease Score

INTRODUCTION

Members of this Guideline Writing Committee (GWC) were selected by the European Society for Vascular Surgery (ESVS) to represent physicians involved in management of patients with chronic venous disease (CVD). The members of the GWC have provided disclosure statements of all relationships that might be perceived as real or potential sources of conflicts of interest. These disclosure forms are kept on file at the headquarters of the ESVS. The GWC report received neither financial support nor support from the ESVS or any pharmaceutical, device, or surgical industry.

The ESVS guideline committee was responsible for the endorsement process of this guideline. All experts involved in the GWC have approved the final document. The guideline document was reviewed and approved by the EJVES editorial board and ESVS guideline committee.

THE PURPOSE OF THESE GUIDELINES

The ESVS has developed clinical practice guidelines for the care of patients with CVD in the lower extremities.

The aim of this document is to assist physicians in selecting the best management strategy for patients with CVD. This guideline, established by members of the GWC, who are members of the ESVS or non-members with specific expertise in the field, is based on scientific evidence completed with expert opinion on the matter. By summarizing and evaluating all available evidence in the field, recommendations for the evaluation and treatment of patients with CVD have been formulated.

Guidelines have the purpose of promoting a standard of care according to specialists in the field, in this case represented by members of the ESVS. However, under no circumstance should this guideline be seen as the legal standard of care in all patients. As the word guideline states in itself, the document is a guiding principle, but the care given to a single patient is always dependent on the individual patient (symptom variability, comorbidities, age, level of activity, etc.), treatment setting (techniques available), and other factors.

The recommendations are valid only at the time of publication, as technology and disease knowledge in this field changes rapidly and expanding recommendations can become outdated. It is an aim of the ESVS to revise the guidelines when important new insights in the evaluation and management of CVD become available.

METHODOLOGY

Strategy

The GWC was convened in 2011 at the annual ESVS meeting in Athens. At that meeting the tasks in creating the guideline were evaluated and distributed among the committee members. The final version of the guideline was submitted on December 22, 2014.

Literature search and selection

A clinical librarian performed the literature search for this guideline systematically in PubMed, Embase, Cinahl, and the Cochrane Library up to January 1, 2013. Reference checking and handsearch by the guideline committee members added other relevant literature.

The members of the GWC performed the literature selection based on information provided in the title and abstract of the retrieved studies.

Criteria for search and selection were:

<u>Language:</u>	English, German, and French
<u>Level of evidence:</u>	Selection of the literature was performed following the pyramid of evidence, with aggregated evidence in the top of the pyramid (systematic reviews, meta-analysis), then randomized controlled trials, then observational studies. Single case reports, animal studies, and in vitro studies in the bottom of the pyramid were excluded, leaving expert opinions at the bottom of the pyramid. The level of evidence per section in the guideline is dependent on the level of evidence available on the specific subject.
<u>Sample size:</u>	If there were large studies available, with a minimum of 15 subjects per research group, only these were included. If not available, smaller studies were also included.

Several relevant articles published after the search date or in another foreign language were included, but only if they were of paramount importance to this guideline.

Weighing the evidence

To define the current guidelines, members of the GWC reviewed and summarized the selected literature. Conclusions were drawn based on the scientific evidence.

The guidelines in this document are based on the European Society of Cardiology grading system. For each recommendation, the letter A, B, or C marks the level of

Table 1. Levels of evidence.

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Table 2. Classes of recommendations.

Classes of recommendations	Definition
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.
Class IIa	<i>Weight of evidence/opinion is in favour of usefulness/efficacy.</i>
Class IIb	<i>Usefulness/efficacy is less well established by evidence/opinion.</i>
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.

current evidence (Table 1). Weighing the level of evidence and expert opinion, every recommendation is subsequently marked as either class I, IIa, IIb, or III (Table 2). The lower the class number, the more proven is the efficacy and safety of a certain procedure.

CHAPTER 1: GENERAL CONSIDERATIONS

The term CVD has been used to describe both visual and functional manifestations of abnormalities in the peripheral venous system. It can be defined as “(any) morphological and functional abnormalities of the venous system of long duration manifest either by symptoms and/or signs indicating the need for investigation and/or care.”¹

The prevalence of CVD in the adult population has been reported to be as high as 60%, particularly affecting populations in the developed world.^{2,3} It has become clear that CVD is an important cause of patient distress and significantly impacts on healthcare resources.^{4,5}

Although a complete understanding of the pathophysiology of CVD remains elusive, chronic venous hypertension is widely accepted as the predominant cause of advanced venous skin changes and ulceration. A sound understanding of the disease process and its clinical presentations is paramount in assessment and management of the patient with CVD.

1.1. History

1.1.1. Pathophysiology

In ancient times, venous problems were described occasionally. Hippocrates (460–377 before Christ) stated that an upright position was inappropriate for a leg with ulceration, assumingly not knowing the real background at that time. In 1544, a Spanish anatomist, Vassaseus, gave a description of venous valves and their function.⁶ At the beginning of the seventeenth century, Harvey published his contribution to the understanding of the physiology of the venous circulation, and Malpighi demonstrated the existence of capillaries and thereby clarified the final connection in the circulatory system.⁷ At the same time, Brodie described symptoms and signs of chronic venous insufficiency (CVI).⁸ In 1670, Lower described venous return as a result of the arterial propagating pulsation (“vis a tergo”), and also described the muscle pump.⁷ The pressure changes caused by thoracoabdominal respiration, enhancing the venous return — “vis a fronte” — to the heart, were described in 1710 by Valsalva.⁷

In 1891, the classical test was invented to differentiate between superficial and deep reflux/retrograde flow by Trendelenburg, and 5 years later a test to verify patency of the deep veins was proposed by Perthes, both tests using compression of the limb.⁷ Homans pointed out that ulceration was different in behaviour dependent on whether it was a result of superficial or deep disease.⁹ Linton introduced the concept of ambulatory venous hypertension as the fundamental pathophysiological theory for terminal and distinct CVD.¹⁰

1.1.2. Treatment

Hippocrates recommended puncture of varicose veins followed by compression.⁸ Four-hundred years later, Celsus performed an avulsion technique with hooks of varicose veins. The French surgeon Pravaz has been given credit for the design of the syringe and needle technique for vascular injection in 1831, and later Pétrequin introduced the method of sclerotherapy for varicose veins. After unsatisfactory results by Smith in 1939, the technique was discredited for many years.¹¹ In 1944, Orbach introduced the so called “air-block” technique to avoid dilution of the injected sclerosant and, at the same time, create close contact with the endothelium, which indeed was a step forward and also a precursor towards foam sclerotherapy.¹² Trendelenburg proposed great saphenous vein (GSV) ligation at mid-thigh in 1891 as being a step to control distal varicosities.¹³ The most used methods have been the external stripping by Mayo and the Babcock method with the intraluminal technique, both at the beginning of the twentieth century, and later pin-stripping by Oesch in 1963.¹⁴ Muller revisited the accompanying hook phlebectomy in 1956 through minimal incisions.¹⁵

Elastic stockings were invented in 1930 as a result of the personal experience of Jobst, an engineer, who himself suffered from a venous ulceration. While bathing in his pool, he noticed that his symptoms were less pronounced, coming to the conclusion that the increasing depth of the water was the secret of the “healing” component. Thus, graduated compression stockings were invented.¹⁶

1.1.3. Development in the last 50 years

Bypass procedures were popularized as the May-Husni operation at the femoral level,¹⁷ and the Palma operation for iliac occlusion.¹⁸ Gloviczki presented experimental work on abdominal bypass surgery with prosthetic grafts and arteriovenous fistulae some years later.¹⁹ Eklöf suggested the benefit of using an arteriovenous fistula after iliac thrombectomy.²⁰ At the same time, the pioneers Kistner and Raju performed valve reconstructions and valve transfer.^{21,22} Hauer introduced subfascial endoscopic perforator surgery (SEPS) in 1985.²³ Balloon dilatation and implantation of stents in the venous system was published for the first time in 1991 by Okrent using ballooning and in 1994 by Semba, who used the more durable stenting technique. Both procedures were used as additional treatments to catheter directed thrombolysis at the ilio-femoral level.^{24,25} Stenting of iliac obstruction in patients with CVI was popularized by Néglen in 2000 in a large scale study.²⁶

The endovenous procedures for varicose veins were developed in the 1990s as thermal, chemical, and mechanochemical vein ablation for truncal varicose disease but were based on the initial work of electro puncture and cauterizations of varicose veins dating back to the 1960s.

1.2. Epidemiology

Clinical reporting, usually indicated as the C of the CEAP classification (from C0 to C6, see further 2.2.1) makes it possible to report prevalence numbers for each clinical class as well as progression rates through the clinical classes over time and relationship to gender, age, obesity, and other risk factors. The prevalences of CVD differ according to these risk factors. The newest and most comprehensive epidemiologic studies from this century will be presented here. Telangiectasiae (also known as spider veins) (C1) have been reported to affect up to 80% of the population.² Varicose veins (C2) are also extremely common, with a variable reported incidence ranging from 20% to 64%.^{2,27–29} The more advanced stages of venous disease, CVI (C3–C6), appear to affect about 5% of the population, with the prevalence of the end stages of CVI (active and healed venous ulcers, C5+C6) estimated at 1–2%.³⁰

1.2.1. Risk factors

1.2.1.1. Age. Several studies have revealed older age as the most important risk factor for varicose veins and CVI. In the San Diego study, older age showed a significant odds ratio (OR) up to 2.42 for varicose veins and up to 4.85 for CVI.³¹ In the Bonn Vein study, the most important risk factor for varicose veins and CVI was older age (OR in the age 70–79 years were 15.9 for varicose veins and 23.3 for CVI).³²

1.2.1.2. Gender. C2 disease is more common in female adults than male adults: 13.9–46.3% females and 11.4–29.3% males based on 50,974 persons with most between 16 and 90 years in the five classical studies from Europe and the USA.^{31–35} In the same studies, C3 varied from 4.5% to 13.6% and the prevalence of C4–C6 varied from 3.6% to 12%.^{31–33,35} A similar prevalence of C2 was found in women who had never been pregnant, and in men.³⁶ In the same studies, the influence of gender on C0–C1 is inconclusive.

However, it has to be mentioned that in the Edinburgh Vein study, varicose veins (C2) were more common among male subjects in the general population.²⁹

The incidence of varicose veins per year is 2.6% in women and 1.9% in men.³⁷ The gender influence diminishes with age.³⁸ No obvious gender difference is shown concerning CVI.^{32,34,35}

Oral hormone replacement and contraceptives do not increase the risk of varicose veins.^{32,39} The number of pregnancies increased the OR from 1.3 to 2.2 for development of varicose veins.³² Another recent large scale study could not demonstrate change in GSV reflux following pregnancies.⁴⁰

Half of the general population in the Bonn Vein study reported venous symptoms, 49.1% of the males and 62.1% of the females, and the prevalence increased with age.⁴¹ Symptoms were more frequently reported in limbs with deep venous involvement compared with superficial, and were also more frequent in women.³¹

In a recent global collection of prospective epidemiologic data on chronic venous disorder in 91,545 subjects including areas outside Europe and the USA, almost the same observations were made, but on a larger scale. Symptomatic C0 was more frequent in men and C2–C3 more frequent in women, but C4–C6 did not differ between men and women.²⁷

1.2.1.3. Obesity. A body mass index (BMI) greater than 30 increases the risk for CVI significantly, with ORs for men and women of 6.5 and 3.1, respectively.⁴¹ Another study found a positive correlation between a BMI of more than 30 and varicose veins (OR 5.8) in postmenopausal women.⁴² Other authors found an association between severe obesity (BMI 40 or more) and increasing limb symptoms without anatomic evidence of venous disease, suggesting that the obesity itself contributed to the venous insufficiency.⁴³ Similar findings were published in a larger scale investigation with a threshold of BMI of 25.⁴⁴

1.2.1.4. Family history. Many studies have shown a correlation between a positive family history for varicose veins or venous disease and the risk of varicose veins.³² A cohort study revealed that a family history of hospital treatment for varicose veins was associated with an increased risk of similar treatment among relatives.⁴⁵ Responsible genetic disturbances have not been found to explain the obvious heredity. Genome-wide association studies should be considered to further unravel the genetic basis of venous disease.⁴⁶

1.2.1.5. Ethnicity. For many years, prevalence studies have been based on figures and numbers from the western world. Data from Europe, Latin America, the Middle East, and the Far East are now available in the large scale Vein Consult Program with 91,545 subjects over 18 years of age. C1–C6 involved 63.9% of the subjects. The incidence of C2 was significantly lower in the Middle East, whereas C1 was significantly higher. C5 and C6 were unequally distributed in the regions.²⁷

1.2.2. Prevalence of reflux

In the Edinburgh Vein study with 1,566 subjects, the aim was to correlate venous reflux with clinical features. Reflux was defined as reversed flow longer than 0.5 seconds. No reflux was found in 36.5% of the patients. One third of the

subjects had incompetence limited to the superficial system. The frequency of reflux in both superficial and deep segments increased with the clinical severity of disease. CVI increased with age. Symptoms were strongly related to the severity of CVI.⁴⁷ Pattern of reflux has also been examined in the Bonn Vein study with 3,072 subjects.⁴⁸ Pathological reflux was defined as longer than 0.5 seconds. The prevalence of superficial reflux was significantly higher in women, whereas deep venous reflux was significantly higher in men. Both types correlated with progression in C stages, but only superficial reflux showed a marked increase with age.⁴⁸

1.2.3. Progression of varicose veins

The prevalence of C6 disease varies from 0.1 to 0.5%.^{32,33} However, this does not reveal the rate of progression from lower to higher C classes. A study including 116 limbs with varicose veins used a second duplex scan a median 19 months after the initial examination in the period waiting for surgery. Approximately one-third of the patients had progression, and in 95% of the patients the changes were noted after 6 months or more.⁴⁹ In the large scale Bonn Vein study, the progression rate from varicose veins to CVI was 4% per year.⁵⁰

1.3. Anatomy

1.3.1. The superficial veins of the lower extremity

The full length of the GSV is covered by a connective tissue lamina called the “saphenous fascia,” and typically lies in the saphenous compartment.⁵¹ On B-mode ultrasound it resembles an “Egyptian eye” in transverse scan with the saphenous fascia easily being identified.⁵² In the GSV compartment there is usually only one truncal vein. Very rarely (in 1% of patients) the GSV is duplicated, which means two veins are situated in the same saphenous compartment.⁵³

A few millimetres distal to the saphenofemoral junction (SFJ), the GSV has a terminal valve, and a few centimetres distal to that valve there is often another valve, called the pre-terminal valve.^{54,55} Important tributaries (i.e. superficial circumflex iliac, superficial epigastric, and superficial external pudendal veins) join the GSV between these valves. The anterior accessory saphenous vein (AASV) and the posterior accessory saphenous vein (PASV) are frequently present and run parallel to the GSV in the thigh in their own saphenous compartment.

The SSV ascends upwards on the posterior aspect of the calf between the two heads of the gastrocnemius muscle. In the popliteal fossa, the main trunk of the SSV frequently drains into the popliteal vein. Often, a cranial extension of the SSV, called the “thigh extension,” continues upwards and uncommonly the SSV does not drain into the popliteal fossa but instead continues cranially and eventually empties into the femoral vein or the GSV. Veins connecting the GSV and SSV are called “intersaphenous veins.” A particular intersaphenous vein is the Giacomini vein running from the SSV in the popliteal fossa to the GSV.⁵⁵ The SSV lies in its own saphenous compartment, delineated by the superficial fascia and the muscular fascia.^{56,57}

Perforating veins are variable in arrangement and distribution, and are numerous (more than 100 in each limb). The medial perforating veins are most significant but their role in CVI and venous ulcers is not well defined.^{58–61}

1.3.2. The deep veins of the lower extremity

Venous blood from the foot drains through the deep plantar venous arch, which at the medial malleolus becomes the posterior tibial veins.⁶² On the dorsum of the foot the deep dorsal digital veins drain into the dorsal metatarsal veins. The dorsalis pedis vein located on the dorsum of the foot becomes the anterior tibial veins at the ankle. The tibioperoneal trunk and the anterior tibial veins join and form the popliteal vein in the popliteal fossa.

The main tributaries of the popliteal vein are the gastrocnemius veins, the tibial veins, and the SSV, although the gastrocnemius veins may join the SSV before joining the popliteal vein. The saphenopopliteal junction (SPJ) is often located within 5 cm of the popliteal skin crease, but this level varies.

The popliteal vein continues in a cephalad direction, and ascends in the adductor canal becoming the femoral vein (the previously used term “superficial femoral vein” has been abandoned).⁶³ Approximately 10 cm below the inguinal ligament, the femoral vein joins with the deep femoral vein to form the common femoral vein. The common femoral vein is situated medially to the corresponding artery and it ends at the inguinal ligament. The vein receives the GSV at the SFJ. Both the popliteal and the femoral vein may be duplicated in segments of various lengths.^{64,65} Above the inguinal ligament the common femoral vein continues as the external iliac vein, and at the junction of the internal and external iliac veins anterior to the sacroiliac joint they form the common iliac vein.

As well as the superficial veins, the deep veins contain valves. The frequency of valves increases from the more proximal veins to the more distal. The calf veins contain numerous valves, whereas the femoral and popliteal veins have only one or two valves.^{66,67} Additional valves are seen, however, in the femoral vein near the junction with the deep femoral vein. The common femoral vein usually contains only one valve. Cranial to the SFJ, there is only one or no valve. In the common iliac vein, valves are practically absent or rudimentary, and valves are absent in the inferior vena cava (IVC).⁶⁶

1.4. Physiology

The venous circulation is a low pressure, low velocity, large volume, low resistance vascular system. The primary function of the venous system is to return blood to the heart. Venous return is influenced by the interaction between a central pump (the heart), pressure gradients, the peripheral venous pump, and competent valves in patent veins. In an upright position these factors work together to overcome the hydrostatic pressure induced by gravity, which is quite different in the supine position. Furthermore, the system is characterized by its capacitance, which allows pronounced fluid variations. Finally, the system has an impact on the regulation of body temperature.

In steady state, the venous return equals the cardiac output. The venous system contains at least 60% of total resting blood volume, with half of this being in the post-capillary venules in the lower extremity. About 25% resides in the splanchnic circulation.^{68,69}

1.4.1. The relationship of capacitance/volume to pressure
Variations in venous blood volume of up to 10–20% are tolerated.^{68,70} A simple shift from a supine to an upright position can be responsible for a 10% volume change in the lower extremity.⁶⁹ An increase in capacitance is normal late in the day after standing or sitting, and almost 20% of normal volunteers will demonstrate valvular dysfunction.⁷¹

The system has a unique function based on the vein compliance. To maintain an acceptable low positive pressure of 5 mmHg, the veins become flaccid, and the pressure can even be negative with minimal volume. In contrast, a considerable increase in volume will result in only a relatively modest change in pressure. A change in vein shape from elliptic to circular indicates high volume and high pressure. In other words: over a normal pressure range of 5–25 mmHg, volume can change remarkably without affecting either flow or pressure.⁷⁰

1.4.2. The hydrostatic and dynamic pressure

In the non-supine situation, gravity exercises a hydrostatic influence on the venous system. The hydrostatic pressure at a given anatomical point is determined by measuring the vertical distance between the heart and the point of interest.⁷² In the upright position, the hydrostatic pressure, measured in a dorsal foot vein, is determined by the blood column between the right atrium and the foot. For example in a person 175 cm tall, the venous pressure at the foot may reach approximately 95 mmHg, with the pressure at the groin being 30–35 mmHg, dependent on the anthropometric shape of the body.

The dynamic pressure is basically caused by propagation of arterial pulsation from the pumping heart. Through pre-capillary arterial vasoconstriction - among other factors - most of the dynamic pressure is decreased, resulting in a pressure of 12–18 mmHg in the venous side of the capillary. The atrial pressure of 4–7 mmHg causes the resulting dynamic pressure gradient to facilitate return of blood to the heart in the supine position. The respiratory influence is positive for venous return. Inspiration creates a negative pressure in the thoracic cavity, creating a kind of “suction” of blood, while increased abdominal pressure during inspiration reduces flow in the abdomen. During expiration the opposite flow pattern is seen. This mechanism is mostly seen in the supine position.⁷³

1.4.3. The vein valves

The valves divide the column of blood into segments and prevent retrograde flow.⁷⁴ The greater number of valves in the infrapopliteal segment suggests their greater functional importance at this level.⁷⁵ A normal valve can resist a pressure above 300 mmHg, but reflux will occur at a higher pressure. In patients with superficial or deep vein valvular incompetence reflux develops at a much lower pressure because of valve disease and/or vein dilatation.⁷³ In the presence of normal valve function the blood is conducted from the superficial

veins to the deep veins through the perforating system. An exception is the perforating veins in the foot, where bidirectional flow is normal.⁷⁵ One study has described the valves creating jet streams in the venous system.⁷⁶ This flow pattern is later described as helical, especially at venous junctions.⁷⁷

1.4.4. The calf muscle and the foot pump

These pumps act together during walking. Intramuscular pressure can increase up to 200–300 mmHg, creating a pressure three times higher in the muscle veins than in the superficial veins, thus creating a pressure gradient cranially and from the calf.⁷⁸ During relaxation the blood is directed from the superficial veins to the deep veins, with the lowest pressure at this stage. The foot pump is quite different in function with elongation of the plantar veins during walking, thus squeezing the blood antegradely.⁷⁹ The compression of the plantar venous plexus during walking is a primer of the calf pump.⁶² Half of the blood can be ejected upwards in one single contraction.^{80,81} The contribution of thigh muscle contraction is minimal compared with the above mentioned pumps.⁸¹

1.4.5. Venous tone

Venous tone is managed by the muscle layer in the vein wall. Several mechanisms, such as sympathetic-adrenergic nerve activity, circulating vasoactive substances, and local metabolites will stimulate it.⁷³

1.4.6. The venous pump: main transport system in the non-supine position

In an upright position venous return is still influenced by the dynamic effect from the heart. The increase in hydrostatic pressure is the same in both the arteries and veins. Fortunately the potent veno-arterial reflex, activated by the venous dilatation, involves an arteriolar constriction restricting the arterial blood flow by 50%.^{73,82} Even in a so called relaxed standing position there will be muscle contractions, which will diminish the capillary pressure distally in the extremity. With use of the muscle pumps and the valves, together called the venous pump, the pressure distally will be decreased to approximately 30 mmHg during walking or tiptoe/heel raising manoeuvres. This pressure is called the ambulatory venous pressure (AVP), which can be monitored through a needle in a foot vein. Measuring AVP is potentially meaningful. It has been shown that no ulceration was observed in limbs with AVP less than 30 mmHg, but there was 100% incidence with AVP above 90 mmHg.⁸³

1.5. Pathophysiology

The pathophysiology of CVD is characterized by reflux, obstruction, or a combination of both. This results in reduced ability to empty the leg veins efficiently during exercise, which means the AVP remains high and this eventually leads to all the clinical features of venous hypertension. Apart from reflux and obstruction, other underlying factors may compromise adequate venous emptying, such as failure of the calf and foot muscle pump (decreased mobility of the ankle joint and other neuromuscular problems).^{80,83,84} Whereas most patients with uncomplicated varicose veins (C2) still have normal venous

pressures during ambulation, all those with more advanced stages of CVD progressively develop venous hypertension, characterized by symptoms and signs of CVI (C3–C6). The clinical manifestations of CVI are oedema and skin changes, from hyperpigmentation, eczema, atrophie blanche and lip-odermatosclerosis to venous ulcers.

Deep vein valve incompetence will result in minor or no reduction in AVP, and venous obstruction will even elevate the pressure during calf contractions, both representing ambulatory venous hypertension.^{85,86} Outflow obstruction at ilio-femoral level with or without valvular incompetence in the femoral and/or popliteal vein can lead to venous claudication described as a “bursting” pain while walking, only relieved by rest or even better by elevation. In multi-level post-thrombotic obstruction, the iliac vein lesions are the key pathology as infrainguinal obstructions are better tolerated because of adequate collateralization.⁸⁷ The pathophysiological combination of reflux and obstruction is significantly more common in patients with venous ulceration than in those with less advanced stages of CVD.⁸⁸

1.5.1. Venous reflux and obstruction

In incompetent superficial veins, reflux is primarily caused by vein wall abnormalities.^{89,90} Varicose veins contain an increased amount of collagen and decreased number of smooth muscle cells and elastin leading to disorganization of muscle components, disruption of elastic fibres, and fibrosis.^{91–93} The weakness of the vein wall results in dilatation and enlargement of the valve ring, making the valve unable to work sufficiently, with reflux as the consequence.⁹⁴ The reflux can be axial or segmental. For many years, it has been accepted that this process starts cranially, mainly at the level of the SFJ or SPJ, and from there extends to the main trunks and further to the superficial tributaries. This is the so called “descending” pathophysiological theory. More recent research has proposed a rather multifocal origin of varicose veins, which states that, first, tributaries become dilated and incompetent, and only thereafter the main trunks, and eventually the junctions. This corresponds with the “ascending” theory of varicose vein development.⁹⁵

The pathology in the deep veins is more complex. Acute obstruction occurs in the case of deep vein thrombosis. This is not discussed further in the present guideline. Chronic obstruction, resulting in increase of resistance to blood flow, is mainly caused by post-thrombotic changes consisting of stenosis, occlusion, intraluminal synechia, and increased rigidity of the vein wall, or any combination of these abnormalities.⁹⁶ Valves may be damaged and collaterals will develop at any place parallel to a deep obstruction, and even these can be incompetent. Chronic deep venous incompetence occurs in 80% of cases because of post-thrombotic valvular changes, and in 20% because of primary valvular incompetence.⁷⁵

Ilio-femoral venous occlusion is less likely to recanalize compared with other venous segments. Almost two thirds will remain more or less obstructed with variable collateralization.⁹⁷ Obstruction in combination with reflux occurs in 55% of symptomatic patients.^{97,98} In patients with ulceration, the cause is distributed almost equally between superficial and

deep venous incompetence.⁹⁹ Perforator incompetence has proven to be a significant factor in the determination of CVD severity.¹⁰⁰

CHAPTER 2: CLINICAL PRESENTATION OF CVD

2.1. Clinical presentation

The symptoms of CVD are extremely variable and cause significant morbidity to patients, negatively impacting on quality of life (QoL).^{101,102} Self reported symptoms are worse in women.^{5,35} Patients present with heaviness, tiredness, itching of the skin, nocturnal cramps, and throbbing and aching of the legs, which is exacerbated by prolonged standing.¹⁶ These symptoms can interfere with day to day activities and work, particularly in patients who need to stand for prolonged periods of time. Symptoms are worse at the end of the day, and symptomatic relief may be achieved by leg elevation, mobilization, and exercise.

In patients with chronic outflow obstruction, venous claudication may typically occur during walking or climbing stairs.

Superficial veins can thrombose, resulting in painful thrombophlebitis and localized cellulitis. Deep venous thrombosis, particularly if found in the ilio-femoral segment, may lead to the development of venous claudication, a bursting pain affecting the buttocks, thighs, or legs when walking, requiring rest and leg elevation to achieve symptomatic relief.

Uncommonly, bleeding can be a presentation of CVD. This is commonly associated with a traumatized superficial varicosity, but significant bleeding can also arise from an area of ulceration. The resulting blood loss may be profound and even life threatening.¹⁰³

Studies have demonstrated that clinical signs correlate with patterns of venous reflux as identified by duplex ultrasound (DUS) examination. This is true for the superficial venous system (including both great and small saphenous)¹⁰⁴ and the deep venous system.⁴⁷ There is evidence suggesting that clinical signs of disease also correlate with GSV vein diameter, with increasing diameter being associated with greater disease severity.¹⁰⁵

QoL scores also correlate with disease severity. Patients with more severe signs and symptoms report worse QoL scores.¹⁰⁶

Clinical recurrence of varicose veins may present in a similar fashion to primary superficial venous disease. A multicentre study was performed to assess the presence of recurrence in patients who had undergone previous varicose vein surgery.¹⁰⁷ Following the CEAP classification,¹²³ the vast majority had recurrence associated with oedema (C3) (70.9%), while 29.1% had skin changes (C4). Varicose veins were present in 24.6% (C2), in 43% two clinical classes were present, and in 24% four classes were present. There was a mixture of C0–C6 classes, from reticular veins and telangiectasiae, to varicose veins, oedema, hyperpigmentation, and ulceration.

2.2. Classification of chronic venous disease

The diverse nature of presenting signs and symptoms of patients with CVD means that objective classification of disease severity presents a significant challenge.

Classification of CVD may be performed using clinical, anatomical, haemodynamic, or patient reported criteria. A comprehensive classification system would ideally take into consideration all of these factors.

Dramatic variations and inconsistencies in the assessment of disease severity have made it difficult to interpret and compare published reports in the literature. The challenge of inconsistent reporting and the recognition that there was a need for a uniform, applicable and standardized classification system for venous disease, was the main motivation for the development of classifications, particularly the CEAP classification.

2.2.1. Clinical Etiological Anatomical Pathophysiological (CEAP) classification

The CEAP classification was published in 1994 by an international ad hoc committee of the American Venous Forum and endorsed by the Society for Vascular Surgery.¹⁰⁸ Following the meeting, it was published in 26 journals and books and in nine languages, making it a truly universal document in the field of CVD. It was revised in 2004 and is a widely endorsed classification system for clinical papers reporting on CVD (Table 3).¹⁰⁹

The CEAP classification system was developed to take into account not only clinical (C) aspects of venous disease, but also etiological (E), anatomical (A), and pathophysiological (P) components, enabling a more comprehensive assessment of the severity of venous disease. The CEAP classification system has largely replaced the previous severity tools, allowing a standardized approach to the signs and symptoms of CVD and enabling correlation between different studies and reports. Nonetheless, CEAP has been

Table 3. CEAP Classification.

C: Clinical Classification

- C0: no visible or palpable signs of venous disease
- C1: telangectasia or reticular veins
- C2: varicose veins
- C3: oedema
- C4a: hyperpigmentation or eczema
- C4b: lipodermatosclerosis or atrophie blanche
- C5: healed venous ulcer
- C6: active venous ulcer

s: symptomatic, including ache, pain, tightness, skin irritation, heaviness, muscle cramps

a: asymptomatic

E: Etiological Classification

- Ec: congenital
- Ep: primary (undeterminate cause)
- Es: secondary (e.g. post thrombotic)
- En: no venous cause identified

A: Anatomical Classification

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

P: Pathophysiological Classification

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

reported as having moderate inter-observer reproducibility when deciding medical indication for treatment.¹¹⁰

2.2.1.1. Clinical classification: C0–C6. Clinical signs form the basis of the clinical component of CEAP, which is scored from 0 (no evidence of venous disease) to 6 (active ulceration). Although increasing C classification is generally considered to represent increasing disease severity, this should not be considered a linear progression or severity score. Unlike the Widmer and Porter classifications, the CEAP classification allows more detail to be recorded. Symptoms of CVD, including aching, pain, tightness, skin irritation, heaviness, and muscle cramps are denoted by the letter S in subscript, for example C2_S (symptomatic) or C2_A (asymptomatic). Even if skin changes have occurred, a patient may be asymptomatic, for example C5_A.

2.2.1.2. Etiological classification: Ec, Ep, Es, En. Assessment and management of CVD varies depending on the underlying etiological process. The CEAP classification recognizes and records three different causative factors: congenital (Ec), primary (Ep), and secondary or post-thrombotic (Es). In cases where no etiology is found, (En) is used.

Congenital factors are present from birth, and are related to disorders in the development of the venous system. Klippel-Trenaunay syndrome (KTS), Parkes-Weber syndrome (PWS), and vascular malformations are examples of congenital anomalies.

Primary venous disease commonly results in superficial venous incompetence, particularly located at the connecting points between deep and superficial veins, SFJ, SPJ, or perforating veins. Incompetence (or reflux) of the superficial venous system may result in venous hypertension and the development of signs and symptoms of CVD.

Secondary venous disease usually occurs as a result of previous deep venous thrombosis, although trauma and intra-abdominal masses may also result in impaired venous drainage and the development of CVD.

2.2.1.3. Anatomical classification: As, Ap, Ad, An. The anatomical classification allows accurate description of the location of venous disease. The classification recognizes superficial (As), perforating (Ap), and deep (Ad) venous systems as the site of venous incompetence.

This can be inferred with the aid of clinical tests and the handheld Doppler probe, but determined much more reliably with DUS examination. Where examination cannot identify the location of venous incompetence, the patient is classified as (An). Superficial disease may affect either the great or small saphenous systems. Clinical examination and DUS imaging can provide detailed information to enable targeted assessment and management planning.

2.2.1.4. Pathophysiological classification: Pr, Po, Pr/o, Pn. The pathophysiological mechanism for CVD has been defined as reflux (Pr), obstruction (Po), both (Pr/o), or not identified (Pn). In the advanced CEAP classification, the venous system has been described as 18 named (and numbered) venous segments, which could be included in the classification to provide a detailed description of CVD in each leg, in an individual patient. Although the detailed elaboration in the advanced CEAP may seem unnecessarily complex or

intimidating, it is the only classification to provide a widely accepted and understandable description of all aspects of CVD.

2.2.1.5. Level of investigation. The diagnostic evaluation of venous disease can be classified as¹¹¹:

- Level 1: history and examination, with or without handheld Doppler assessment
- Level 2: non-invasive imaging with colour venous duplex and plethysmography, if available
- Level 3: invasive or complex imaging, including venography, computerized tomography, or MR imaging.

2.2.1.6. Applying the CEAP. The CEAP classification is widely accepted as the best available (and most widely used) classification system, and should be used by investigators reporting on CVD.¹¹² It is important to realize that this is a measure that can be repeated to classify changes in patient's clinical presentation. It should be initialized at the first patient encounter and revised on follow up. Many of the limitations of CEAP have been addressed during revisions, resulting in updated terminology and amended definitions.¹⁰⁹ However, there are aspects that are not taken into account by this classification system, including mixed arterial/venous disease, venous neuropathy, venous claudication, corona phlebectatica, and obesity.¹⁶ Furthermore, it has been acknowledged that CEAP cannot be used as a reliable technique to rationalize patient treatment.^{113,114} Nevertheless, the CEAP classification is currently the most commonly used assessment tool for venous disease.^{105,106}

2.2.2. Venous Clinical Severity Score, Venous Segmental Disease Score, and Venous Disability Score

Although the CEAP classification provides a descriptive classification tool for patients with CVD, there have been criticisms that it lacks responsiveness in the long term and with repeated evaluation of patients. Three other clinical

tools have been described to address some of these criticisms.

2.2.2.1. Venous Clinical Severity Score: measure of severity.

The Venous Clinical Severity Score (VCSS) was developed to supplement (rather than replace) the CEAP classification. VCSS offers a broad quantification of the severity of venous disease and is not a detailed descriptive tool for CVD in an individual patient. It takes into account the disease severity, and the degree to which patients are affected by it (Table 4). A total of 10 clinical characteristics are evaluated by a healthcare worker and graded from absent (score 0) to severe (score 3), with a total of 30 points attributable. It was developed to assess the progression of CVD and also to give additional weight to more severe clinical disease (C4–C6).^{115,116}

The VCSS provides a more accurate measure of the severity of disease and the effect on the patients' day to day activities. Although it is used as a severity score, it has also been found to be a useful screening tool because of its correlation with severity on imaging.^{117,118} It has been used and evaluated in different studies, and appears to be appropriate for measuring changes after surgery, although it may not be appropriate in studies investigating the use of stockings, as the scoring system takes this into account.¹¹⁹

The VCSS has been employed minus the stocking component (VCSS-S) for example, in the assessment of mechanical suppression of angiogenesis in varicose vein surgery.¹²⁰

2.2.2.2. Venous Segmental Disease Score: pathophysiology and anatomy.

The Venous Segmental Disease Score (VSDS) takes into account the anatomical and pathophysiological mechanisms involved in the presentation of CVD (Table 5).^{115,121} VSDS accounts for anatomical location and nature (reflux or obstruction) of venous disease, providing a global assessment of pathophysiological disease severity. It relies on duplex scan assessment of the superficial and deep venous systems and provides a score out of 10 for reflux or obstruction. Although the pathophysiology and abnormal

Table 4. Venous Clinical Severity Score (VCSS).

Attribute	Absent (0)	Mild (1)	Moderate (2)	Severe (3)
Pain or other discomfort (ie aching, heaviness, fatigue, soreness, burning Presumes venous origin)	None	Occasional	Daily, interfering with, but not preventing regular daily activities	Daily limiting most regular daily activities
Varicose Veins	None	Few, scattered Also includes corona phlebectatica	Confined to calf <u>or</u> thigh	Involve calf <u>and</u> thigh
Venous oedema (presumes venous origin)	None	Limited to foot or ankle	Extends above ankle but below knee	Extends to knee or above
Skin Pigmentation	None or focal	Limited to perimalleolar area	Diffuse over lower third of calf	Wider distribution (above lower third of calf)
Inflammation	None	Limited to perimalleolar area	Diffuse over lower third of calf	Wider distribution (above lower third of calf)
Induration	None	Limited to perimalleolar area	Involving lower third of calf	Involving more than lower third of calf
Number of active ulcers	None	1	2	>2
Active ulcer duration	None	<3 months	>3 months but <1 year	>1year
Active ulcer size	None	Diameter <2 cm	Diameter 2–6 cm	Diameter >6 cm
Compression Therapy	Not used	Intermittent use of stockings	Uses stockings most days	Full compliance with stockings

Table 5. Venous Segmental Disease Score (VSDS).

Reflux		Obstruction	
½	Small saphenous		
1	Great saphenous	1	Great saphenous (if thrombosed from groin to below knee)
½	Thigh perforators		
1	Calf perforators		
2	Calf veins, multiple (Posterior Tibial only = 1)	1	Calf veins, multiple
2	Popliteal vein	2	Popliteal vein
1	Femoral vein	1	Femoral vein
1	Profunda femoris vein	1	Profunda femoris vein
1	Common femoral vein and above	2	Common femoral vein
		1	Iliac vein
		1	Inferior Vena Cava
10	Maximum reflux score	10	Maximum obstruction score

venous segments can be described accurately using the advanced CEAP classification, VSDS attributes different scores to different venous segments to indicate the level of overall impact on venous function.

Reflux describes all valves in a specific segment as incompetent. Obstruction describes a total occlusion at a point in the investigated segment or a >50% stenosis in at least half the segment. Importantly, traumatic obstruction, ligation, or excision of deep venous segments count as thrombosis. However, the same is not true for superficial veins. Perforator interruption and saphenous ligation/ablation count as a reduction of the reflux score, not as an obstruction score.

VSDS was found to correlate with clinical scores, with the magnitude of reflux correlating with symptom severity.¹¹⁹

2.2.2.3. Venous Disability Score: functional impact. The Venous Disability Score (VDS) provides a simple measure of the functional impact of CVD, using a 4 point scale (0–3; Table 6).¹¹⁵ This evaluates the effect of CVD on daily activities. VDS has been validated against the CEAP as a measure of disease severity, and has been used as a

measure of change following venous surgery.¹¹⁹ As with VCSS, VDS is designed to complement the CEAP classification by providing greater detail on the level of disability experienced by the patient.

2.2.3. Villalta-Prandoni Scale

The Villalta-Prandoni Scale was described in the 1990s to classify the severity of post-thrombotic syndrome (PTS), a complication of deep venous thrombosis.¹²² Essentially, the scale consists of five symptoms (patient rated) and six physical signs (clinician rated), with each of the 11 factors scored out of 3 (total score out of 33; Table 7). A score of >14, or the presence of venous ulceration, indicates severe PTS.

The Villalta-Prandoni Scale is specific to the post-thrombotic limb and is a reliable, valid measure of PTS in patients with confirmed deep venous thrombosis (DVT).¹²³ It also correlates well with patient perceived health burden and QoL scores. A drawback of this scale is that it does not take into account venous claudication or venous ulcer severity, as the presence of a venous ulcer is given a fixed score irrespective of severity.

Recommendation 1	Class	Level	References
Use of the Clinical Etiological Anatomical Pathophysiological (CEAP) classification is recommended as a standardized, descriptive classification tool to assess disease severity in patients with chronic venous disease for research and audit.	I	B	108, 109, 112
Recommendation 2			
Use of one or more of the following scoring systems should be considered for chronic venous disease: Venous Clinical Severity Score to assess clinical severity, Venous Segmental Disease Score for pathophysiological and anatomical evaluation, Venous Disability Score for functional evaluation, and the Villalta-Prandoni Scale to assess severity of post-thrombotic syndrome.	Ila	B	115, 119, 122, 123

Table 6. Venous Disability Score (VDS).

- 0 – Asymptomatic
 - 1 – Symptomatic but able to carry out usual activities without compressive therapy
 - 2 – Able to carry out usual activities only with compression and/or limb elevation
 - 3 – Unable to carry out usual activities even with compression and/or limb elevation
- Usual activities: defined as patient activities before the onset of disability from venous disease

2.3. Quality of life measures in venous disease

The burden of CVD lies with the patients, with up to 30% displaying symptoms suggestive of a depressive illness.¹²⁴ Assessment of QoL in patients with CVD is integral to a complete and thorough evaluation of their disease status. Evidence shows that increasing clinical severity correlates strongly with deterioration in QoL measures, both general and disease specific.¹¹³ Similarly, clinical improvement correlates with progression in QoL measures.¹²⁵ Clinical classification systems

Table 7. Villalta-Prandoni Scale.

[severity scoring: *none (0), mild (1), moderate (2), severe (3)*]. Each sign/symptom is scored 0–3; scores are added to obtain the final result (maximum of 33).

5 Venous symptoms	- Pain - Cramping - Heaviness - Pruritus - Paraesthesia
6 Clinical signs	- Oedema - Induration - Hyperpigmentation - Venous ectasia - Redness - Calf tenderness
Severity of post thrombotic syndrome (PTS)	- No PTS <5 - Mild PTS 5-9 - Moderate PTS 10-14 - Severe PTS >14 or venous ulceration - Total points range 0–33

are in place to assess the severity of CVD. QoL tools are available to assess patient reported outcomes. The ideal QoL tool should be generally applicable to any disease process, irrespective of severity, outcome measures, or geographic location.¹⁶ The tool should be valid (i.e. measure what is intended), reliable (i.e. provide the same measurements for a single individual despite different conditions), and responsive (i.e. sensitive to assess change e.g. after treatment). Ideally, it should also assess all aspects of QoL, including physical, mental and social wellbeing. A number of global QoL instruments exist; however, they lack sensitivity to changing clinical conditions. Health related measures are used instead. A large number of tools have been developed and are in widespread use. There have been greater efforts to standardize the use of QoL assessments in recent years.

Generic and disease specific instruments measuring health related QoL in patients with CVD are discussed below.

2.3.1. Health related generic tools

2.3.1.1. SF-36, Medical Outcomes Study 36 Item Short Form. The SF-36 form is a widely used, generic QoL assessment tool with both physical and mental domains, providing a global assessment of patient wellbeing (Table 8).¹²⁶ The physical component of this patient completed questionnaire has been shown to correlate with venous disease severity. Studies have shown that all sub-domains of the physical component (*physical role, pain, physical functioning, and general health perception*) correlate significantly with disease severity as measured by the CEAP classification. This is not true for the mental component, as correlations with vitality¹²⁷ and mental health¹²⁸ are weak and inconsistent.

Table 8. SF-36.

- Physical function	Physical component
- Role physical	
- Bodily pain	
- General health	
- Mental health	Mental component
- Role emotional	
- Social function	
- Vitality	

2.3.1.2. EuroQoL, 5D. The EuroQoL group is a multinational, multicentre, and multidisciplinary network of researchers dedicated to the measurement of health status. The EuroQoL questionnaire was devised in the 1990s with the aim of developing a standardized, simple, and generic measure of health for clinical and economic appraisal.¹²⁹ It consists of a descriptive part, evaluating five dimensions (EuroQoL – 5D), and a vertical, visual analogue scale (VAS), recording the respondent's self-rated health (EuroQoL – VAS).

Together, the EuroQoL, 5D and EuroQoL-VAS, provide a comprehensive measure of health state. This tool is particularly useful for measuring utility or quality-adjusted life years (QALYs; a measure of disease burden), and has been used as a QoL measure in the assessment of patients with symptomatic varicose veins (Table 9).¹²⁴

2.3.2. Disease specific tools

2.3.2.1. Aberdeen Varicose Veins Questionnaire. The Aberdeen Varicose Veins Questionnaire (AVVQ), is a patient completed QoL assessment tool comprising 13 questions with domains including physical symptoms, social effect, and cosmesis (Table 10).¹³⁰ Each question is graded in

Table 9. EuroQoL – 5D.

1. Mobility	- No problems - Some problems - Bed bound
2. Self care	- No problems - Some problems washing or dressing - Unable to wash or dress
3. Usual activities	- No problems - Some problems - Unable to perform
4. Pain/discomfort	- None - Moderate - Extreme
5. Anxiety/depression	- None - Moderately - Extremely

Euro – QoL VAS
Perceived health

Visual analogue scale
0 (worst state)–100 (best state)

terms of severity/presence or absence, and the results are collated into the Aberdeen Varicose Veins Symptom Severity Score from 0 to 100, where the higher the score, the worse the QoL.

The AVVQ has been validated as a measure of health outcome in patients with varicose veins against the SF-36 questionnaire.¹³¹ It was found to be reliable, with significant association with patient symptoms. Many consider the responsiveness and sensitivity of the AVVQ to be greater than generic QoL questionnaires. However, generic QoL tools allow simpler calculation of health utility (QALYs), which is a necessity for meaningful health economy comparisons.

2.3.2.2. Chronic Venous Insufficiency Questionnaire. Developed in 1996 in France, the Chronic Venous Insufficiency Questionnaire (CIVIQ) is a 20-item self reporting QoL tool covering four dimensions: physical, psychological, social functioning, and pain (Table 11).¹³² The items are graded on a 5 point Likert scale.¹³³ The questionnaire has been vali-

consistency, reliability, and value in assessing changes in QoL after treatment.¹³⁶

2.3.2.3. Venous Insufficiency Epidemiological and Economic study. The Venous Insufficiency Epidemiological and Economic study (VEINES) was an international, prospective cohort study evaluating the epidemiology and outcomes of CVD.¹³⁷ As part of this project, a validated venous disease specific QoL and symptom measure was developed (VEINES QoL/Sym; Table 12).¹³⁸ The aim of this tool was to provide an assessment of QoL and symptoms across the range of conditions in CVD (including telangiectasia, varicose veins, oedema, skin changes, and leg ulcers). Psychometric testing revealed the questionnaire to be acceptable, reliable, and valid in four different language versions, as well as demonstrating correlation with both SF-36 and C class. The VEINES QoL/Sym was also found to be reliable and valid as a measure of QoL and symptoms in patients with acute DVT.¹³⁹

Recommendation 3	Class	Level	References
Use of both generic and disease specific assessment tools should be considered to provide a complete evaluation of a patient with chronic venous disease.	IIa	B	124, 127, 128, 130, 131, 136, 139
Recommendation 4			
Disease severity and burden of disease should be reliably assessed by generic tools in the form of the physical component of the SF-36 and the EuroQoL-5D, respectively.	IIa	B	127-130
Recommendation 5			
The use of disease specific tools in the form of the Aberdeen Varicose Veins Questionnaire, Chronic Venous Insufficiency Questionnaire, or Venous Insufficiency Epidemiological and Economic study questionnaire should be considered to assess responsiveness to treatment.	IIa	B	131, 135-137, 139

dated in its French version, as well as in a number of other languages.^{134,135}

In 2010 psychometric validation was carried out, revalidating the questionnaire and providing evidence for its

Table 10. AVVQ.

1. Distribution of veins
2. Duration of pain
3. Duration of analgesia
4. Degree of ankle swelling
5. Use of support stockings
6. Extent of itching
7. Presence of discolouration
8. Presence of rash or eczema
9. Presence of skin ulcer
10. Degree of concern at appearance
11. Influence on choice of clothes
12. Interference with work/household jobs
13. Interference with leisure

(score 0–100; 0 best, 100 worst)

CHAPTER 3: DIAGNOSTICS

Introduction

This chapter describes the value of available diagnostic tools used in patients with CVD. It describes the physical examination and additional tests including continuous wave [CW] Doppler, duplex ultrasound [DUS], phlebography, plethysmography, venous pressure measurement, and modern imaging techniques such as magnetic resonance venography [MRV] and computed tomography venography [CTV], as well as describing clinical and radiological diagnostic criteria of recurrent disease.

In the diagnostic work up the nature of the problem and the severity of the disease should be determined.

3.1. Clinical examination

3.1.1. History

Scientific evidence. Patients with varicose veins and/or signs of CVD should be asked, prior to any clinical or

diagnostic investigation, about symptoms suggestive of venous pathology.¹⁴⁰ This applies also to patients with recurrent varicose veins following intervention, who may present with characteristic symptoms of CVD. Possible thromboembolic antecedents should be investigated, together with any allergy, medication (oral contraceptives primarily), and concomitant relevant diseases including heart and renal failure, which may influence CVD.¹⁴⁰ Finally, the number and timing of pregnancies should be noted.¹⁴¹

A differential diagnosis is very important. Even in the presence of trunk varices, many lower limb symptoms could have a non-venous cause.^{5,142}

examined.¹⁴⁶ Distinctions were made between the iliac veins, the femoro-popliteal axis, deep veins in the calf, and superficial and perforating veins. Both normal subjects and patients with known CVD were studied and compared, including the differences between supine and upright examination by DUS.

When the duration of retrograde flow in patients with CVD was compared with healthy subjects, there was a significant ($p < .0001$) difference for all segments in the affected leg. The cut off values defining venous incompetence (reflux) during ultrasound examination are set at retrograde flow longer than 0.5 s in the superficial venous

Recommendation 6	Class	Level	References
History taking from the patient with chronic venous disease is recommended before further investigation, targeting especially specific symptoms, any thromboembolic antecedent and relevant drug intake.	I	C	5, 140, 142

3.1.2. Physical examination

Scientific evidence. Patients with CVD are examined in a physiological upright standing position. Both legs should be examined completely. When signs of severe CVD or secondary (e.g. post-thrombotic) varices are present, the abdominal region should be inspected for the possible presence of venous collaterals. Venous collaterals on the lower abdomen, flanks, and pubic region are pathognomonic of iliac or ilio-caval outflow obstruction.

Corona phlebectatica paraplantaris should be noted as this may indicate advanced venous stasis.¹⁴³

In recurrent disease, it is important to bear in mind the patient's pre-operative state and assess any amelioration or worsening in signs such as skin changes or ulceration.

During physical examination, it is important to consider alternative pathology such as signs of arterial insufficiency, orthopaedic, rheumatological, or neurological pathology (muscle pump function). The main circumferences of both legs should be measured when indicated (e.g. phlebolymphedema, suspicion of vascular malformations).

Traditional clinical tests such as Trendelenburg, Perthes, and others have proven unreliable and have no place in the mapping of venous incompetence in general, and of varicose veins in particular.^{144,145}

3.2. Diagnostic tools

3.2.1. Definition of reflux

Scientific evidence. In a study using DUS, reflux times in the various venous segments of the lower extremity were

system, the deep femoral vein, and the calf veins, longer than 1 s in the common femoral, femoral vein, and popliteal vein, and longer than 0.35 s in perforating veins.¹⁴⁶

An additional finding of this study is that an erect position is the only reliable way to detect reflux.¹⁴⁶

Previous international consensus held 0.5 s as a cut off value in all leg vein segments, but this appears to vary with the type of venous segment. The present consensus recommends 1 s as the cut off duration for reflux in femoral and popliteal vein, whereas above 0.5 s is considered reflux in saphenous veins, lower leg veins, and perforators.¹⁴⁶

The GSV, AASV, PASV, thigh extension, and SSV all situated in their saphenous compartment, are the main superficial conduits to be imaged for morphology and tested for possible reflux, and its segmental distribution.¹⁴⁷ Main thigh or lower leg perforators, mostly on the medial aspect of the limb, should be examined with diameters measured at fascia level. Perforators should also be tested for their inward and/or outward flow during distal calf compression (systole) and release (diastole).¹⁴⁷ Saphenous diameter should be measured at specific locations: the GSV 3 cm below the saphenofemoral junction, at mid-thigh, at the knee, and lower leg; the AASV 3 cm below the SFJ and at mid-thigh when still lying in its saphenous compartment; and the SSV 3 cm below the SPJ.¹⁴⁸ The terminal and pre-terminal valves of GSV must be tested for their function, as Cappelli demonstrated that GSV

Recommendation 7	Class	Level	References
Physical examination of patients should always be performed, looking for varicose veins, oedema, and skin changes.	I	C	140,142
Recommendation 8			
The traditional diagnostic tests Trendelenburg, Perthes, and other such tests are not recommended in the work up of patients with chronic venous disease.	III	B	144,145

Table 11. CIVIQ – 20.

In the past four weeks, to what extent did your leg problems interfere with.../cause you...

Physical Items	<ol style="list-style-type: none"> 1. Climbing stairs 2. Crouching/Kneeling 3. Walking briskly 4. Doing the housework
Psychological Items	<ol style="list-style-type: none"> 1. Feeling on edge 2. Becoming tired easily 3. Feeling like a burden to people 4. Needing to take precautions 5. Embarrassment to show one’s legs 6. Being easily irritable 7. Feeling handicapped 8. Having difficulty getting going in the morning 9. Not feeling like going out
Social items	<ol style="list-style-type: none"> 1. Going out in the evening 2. Practicing a sport 3. Travelling by car/bus/plane
Pain items	<ol style="list-style-type: none"> 1. Pain in the ankles or legs 2. Interference with work or daily activities 3. Interference with sleeping 4. Interference with standing for a long time

diameter at proximal thigh is strictly related to the presence or absence of reflux at the terminal valve and at the iliac-femoral valve.^{149,150}

Assessment of venous reflux and of perforators is largely based on DUS. Limitations diminish for the abdominal and or pelvic veins. Antegrade flow and reflux are elicited through the creation of a pressure gradient, with specific manoeuvres (e.g. Valsalva manoeuvre and compression/release manoeuvre). Patency of the main deep veins of the

lower limbs (common femoral vein, femoral vein, popliteal vein, gastrocnemius veins, peroneal and tibial veins) should be highlighted, especially when detection of deep vein thrombosis or its sequelae (post-thrombotic syndrome) is required.

3.2.2. Handheld continuous wave Doppler

Scientific evidence. Doppler examination is a non-invasive procedure using ultrasound information to determine venous flow. CW Doppler provides no information on venous morphology, therefore it is unsuitable for the determination of any anatomical component of any venous disease. Reliability of CW Doppler examination in detecting obstruction/reflux in deep veins is extremely low in abdominal and lower leg veins. Research has shown that pre-operative planning on the basis of CW Doppler alone, instead of DUS, results in inadequate treatment in a significant proportion of patients.¹⁵¹ In a study of 40 patients it was found that DUS is much more reliable than both physical examination and CW Doppler, with little difference in reliability between the last two.¹⁵²

3.2.3. Duplex ultrasound examination

3.2.3.1. Efficacy. Scientific evidence. DUS examination is based on a combination of ultrasound imaging and pulsed wave Doppler with which information can be obtained on both the anatomy and the hemodynamic features of the venous system. Additional colour flow imaging is routinely employed to quicken and improve DUS accuracy.

Anatomy, valvular incompetence, and venous obstruction can be easily detected using DUS.^{153–157} With DUS it is also possible to investigate the deep venous system in most segments with adequate accuracy.¹⁵⁸ In addition to good reproducibility, the non-invasive nature of duplex scanning is a great asset. With the development of this technique, invasive tests such as phlebography have been reserved for a few selective indications (see 3.2.5), as well as making former non-invasive devices such as handheld Doppler obsolete. DUS examination should be considered as the gold standard in the diagnosis of CVD.

However, DUS investigation has a lower reliability to elicit patency, obstruction, or occlusion of deep veins in the lower leg, whereas a higher accuracy has been reported in the

Recommendation 9	Class	Level	References
To define venous incompetence the following cut off values are recommended: retrograde flow lasting more than 0.5 s in the superficial venous system, the deep femoral vein, and the calf veins, more than 1 s in the common femoral vein, the femoral vein, and the popliteal vein, and more than 0.35 s in perforating veins.	I	B	¹⁴⁶

Recommendation 10	Class	Level	References
Continuous wave Doppler is not recommended for the diagnostic work up of chronic venous disease.	III	B	^{151, 152}

Table 12. VEINES QoL/Sym.

During the last 4 weeks how often did you have:

- | | |
|------------------------------|------------------------|
| 1. Heavy legs | - Every day |
| 2. Aching legs | - Several times a week |
| 3. Swelling | - Once a week |
| 4. Night cramps | - <Once a week |
| 5. Heat or burning sensation | - Never |
| 6. Restless legs | |
| 7. Throbbing | |
| 8. Itching | |
| 9. Tingling sensation | |

At what time of day is the problem most intense?

- On walking
- At midday
- At the end of the day
- During the night
- At any time of day
- Never

Compared to one year ago, how would you rate your leg problem now?

- Much better
- Somewhat better
- About the same
- Somewhat worse
- Much worse
- I did not have a problem last year

Does your leg problem limit you in the following activities?

- | | |
|---|----------------------|
| 1. Daily activities at work | - I do not work |
| 2. Daily activities at home (housework) | - Yes, a lot |
| 3. Standing for long periods | - Yes, a little |
| 4. Sitting for long periods | - Not limited at all |

During the past 4 weeks, have you had any of the following at work/during your day as a result of your leg problem?

- Yes
- No

1. Cut down the amount of time you spent at work/doing activities
2. Accomplished less than you would like
3. Limited in the kind of work or other activities
4. Difficulty performing the work or other activities

During the past 4 weeks, to what extent has your leg problem interfered with your normal social activities with family, friends, neighbours or groups?

- Not at all
- Slightly
- Moderately
- Quite a bit
- Extremely

How much leg pain have you had during the past 4 weeks?

- None
- Very mild
- Mild
- Moderate
- Severe
- Very severe

How have you felt over the past 4 weeks as a result of your leg problem?

Table 12-continued

- | | |
|--|--------------------------|
| 1. Concern about the appearance of your leg(s)? | - All of the time |
| 2. Irritable? | - Most of the time |
| 3. Burden to your family or friends? | - A good bit of the time |
| 4. Worried about bumping into things? | - Some of the time |
| 5. Has the appearance of your leg(s) influenced your choice of clothing? | - A little of the time |
| | - None of the time |

femoro-popliteal segment.^{159,160} Transvaginal DUS evaluation of pelvic veins is not yet fully defined.^{161,162}

Additional colour flow imaging resulted in facilitation of the overall approach to the insonated segment to assess patency and competence. In the post-thrombotic syndrome, DUS identifies residual obstruction, persistent occlusion, and valvular incompetence in the affected segments, with greater accuracy in the infrainguinal areas. Phlebography or MRV/CTV have a definite role in the diagnostic work up of the veins in the abdominal/pelvic area.

With the introduction of duplex ultrasound, other non-invasive techniques such as Doppler and plethysmography (except certain parameters of air-plethysmography) have lost most of their value, and are no longer used in the routine evaluation of CVD.

DUS is an ideal tool for follow up. DUS performed 1 year after surgery focusing on detection of neovascularization, has a high accuracy in predicting recurrence at the SFJ after 5 years.¹⁶³ DUS is also used in the pre-operative assessment of patients undergoing surgery, as recommended by the clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum.¹⁴⁰

3.2.3.2. Technique. The extent of DUS depends on the symptoms. In severe CVD, after a deep vein thrombosis or persistent or rapidly recurrent varicosities, it is important to fully scan the deep system including the iliac tract. With primary varicose veins it is sufficient to scan below the groin in most cases. When pelvic vein incompetence and/or obstruction is suspected, complementary scanning in the pelvic area is recommended. Alternative methods (e.g. CTV, MRV, and especially phlebography) are to be used for a more complete diagnosis and for planning possible treatment.

The five major components that define a complete DUS examination are: anatomical information, flow visualization (presence or absence of reflux), provocation manoeuvres for flow augmentation, morphology (patency or obliteration), and compressibility (thrombosis diagnosis).

Standardized DUS examination to determine reflux in superficial and perforating veins must be performed with the patient in a physiological standing position with external rotation of the examined limb in a relaxed position, while supporting the weight on the contralateral limb. Investigation of patency of iliac and patency and incompetence of common femoral veins should be performed with the patient in supine position, whereas femoral and popliteal vein segments should be investigated with the patient standing

as for competence, although patency also can be elicited in supine and prone position, respectively.¹⁴⁷ Lower leg deep veins should be examined with relaxed calf muscles.

High frequency broadband linear transducers are generally used to investigate the lower limbs, whereas low frequency broadband curved array transducers are used when investigating deeper veins (e.g. obese patients, abdominal veins). An appropriate transducer for transvaginal ultrasound may be used in case of suspected pelvic vein incompetence. An adequate pulse repetition frequency setting is required to detect low velocities (5–10 cm/s) and/or reflux.¹⁴⁷

3.2.3.3. Imaging recurrent disease. Recurrent disease can be reliably assessed by DUS. DUS can provide the necessary anatomical and functional information about the nature of recurrence and is a fundamental component of the assessment of the lower limb after venous intervention.¹⁴⁸ Studies reporting on recurrent varicose veins largely use DUS examination in their assessment of the venous system.^{164–167} As recurrent disease will be most likely secondary to intervention in the GSV or SSV systems, DUS is an appropriate, low risk imaging modality to assess these patients.

It is important to understand that DUS examination diagnosed recurrence may be present in the absence of clinical recurrence. Patients may have recurrent reflux identified during DUS examination that does not cause any clinical symptoms. The 5 year recurrence rate on DUS has been reported at 64%, with a clinical recurrence rate of 4%.^{168,170}

3.2.4. Plethysmography and venous pressure measurements

3.2.4.1. Strain-gauge plethysmography. Scientific evidence. This was first described in 1953 by Whitney, and then developed as a method for indirect venous function measurement.¹⁷¹ It was then developed for DVT detection or for quantification of post-thrombotic syndrome (PTS). By determining a pressure volume relationship, this technique can translate the volume reduction into a pressure decrease.¹⁷²

3.2.4.2. Photoplethysmography. Scientific evidence. The principle of photoplethysmography (also known as light reflection rheography), in which the transmission of light reflection in the subdermal venous plexus is detected as a measure of the change of blood volume in the skin, was described in 1937 by Hertzman.¹⁷³ This technique was initially used for arterial research, but adapted by Abramowitz in 1979 for venous applications.¹⁷⁴ In the 1980s, Wienert and Blazek developed the technique towards a standardized digital form.^{175,176}

Recommendation 11	Class	Level	References
Duplex ultrasound is recommended as the primary diagnostic test of choice in suspected chronic venous disease, to reliably evaluate the specific venous anatomy and to identify the source and pattern of reflux.	I	A	147, 151, 152
Recommendation 12			
In the presence of suspected abdominal and or pelvic venous pathology, duplex ultrasound is recommended before phlebography, computed tomography venography, and magnetic resonance venography examinations.	I	C	169
Recommendation 13	Class	Level	References
Duplex ultrasound is recommended for the assessment of recurrent varicose veins to identify the source of recurrence.	I	C	148, 165, 170

The main parameter of venous plethysmography is the refill time. There is a good correlation between the refill time and direct venous pressure measurement and photo-plethysmography.^{173,177} However, there is no good relationship between the refill time and the degree of venous disease.^{178,179}

3.2.4.3. Air-plethysmography. Scientific evidence. Using air-plethysmography (APG), volume changes can be measured, with venous filling index (VFI) being the most important parameter.^{180,181} Also reflux quantification and ejection fraction have been assessed and APG parameters give an overall evaluation of the functional impairment of the limbs as to venous obstruction/valvular incompetence, quantifying calf pump dysfunction as well.⁸⁵

Since the advance of DUS and other alternative methods, plethysmographical examination techniques have been considered of less importance in routine investigation, and they are no longer considered as stand alone diagnostic tools in patients with CVD. Plethysmography may be considered for assessment of quantitative parameters related to venous function for research purposes and post-treatment follow up.

3.2.4.4. Foot volumetry. Foot volumetry is performed in the standing position by immersing the leg in a container with water.¹⁸² The expelled volume (EV) in mL and the refilling rate (Q; mL/100 mL × minute), as well as the total foot volume (mL), are measured. It has been used to assess compression treatment in venous insufficiency and to predict results of interventions on the superficial venous system in case of venous ulceration.

3.2.5. Phlebography

Scientific evidence. The indication for using phlebography in CVD patients with varicose veins has decreased significantly with the advent of DUS. In the evaluation of superficial, perforating, and deep vein incompetence, DUS is at least as reliable as phlebography.^{155,156} However, in the diagnosis of pelvic vein obstruction or incompetence (gonadal veins, iliac veins) and of vascular malformations, when alternative imaging techniques are inconclusive, phlebography can represent a necessary investigation.

In the presence of vascular malformation, complex post-thrombotic cases, or cases of complex recurrent varicose veins, phlebography may help to elicit possible abdominal and/or pelvic vein involvement.

3.2.6. Other imaging methods

3.2.6.1. Scientific evidence. Both CTV and MRV have evolved significantly in recent years and it is now possible to obtain detailed three dimensional reconstructions of the venous system.^{183–188} Ilio-caval and pelvic venous pathology (post-thrombotic obstruction, venous compression/stenosis like Nutcracker syndrome or May-Thurner syndrome and pelvic varicocele) can be reliably identified.^{189–193} However, there is insufficient scientific evidence to adequately judge the true effectiveness of both techniques for visualization of the venous vasculature given the heterogeneity of the published studies. Furthermore, in varicose vein disease the use of CTV and MRV should be limited to the specific indications mentioned above.

Recommendation 14	Class	Level	References
Plethysmography may be considered for the assessment of quantitative parameters related to venous function.	IIb	C	85, 180, 181
Recommendation 15			
Foot volumetry is not recommended in the routine diagnosis of patients with chronic venous disease.	III	C	182

Recommendation 16	Class	Level	References
Phlebography may be considered in cases where other diagnostic tools are inconclusive (mainly in the diagnosis of abdominal/pelvic vein diseases).	IIb	B	155, 156

In patients with (severe) renal impairment, administration of intravenous contrast in both MRV and CTV examinations may be contraindicated. A disadvantage of the MRV examination is that the acquisition time is significantly longer compared with CTV. Unlike MRV, however, CTV involves exposing the patient to radiation. Both techniques can be used to diagnose deep venous obstruction, but MRV has the advantage of displaying more heterogenic information of intravascular abnormalities, which may be useful in determining the therapeutic (endovascular) options.¹⁸³ The decision of whether to perform MRV or CTV is still mainly dependent on the local expertise in performing and evaluating these studies.

Complementary to the aforementioned techniques, intravascular ultrasound (IVUS) is suitable for determining ilio-caval venous compression.^{169,194–198} To assess chronic venous obstruction or incompetence and for planning a deep venous reconstruction, DUS examination, CTV or MRV, ascending and descending phlebography and in selected cases IVUS have to be performed. In addition, venous pressure measurement can be performed to clarify whether the venous collaterals are capable of adequately reducing ambulatory venous hypertension.^{154,169,194,199–203}

CHAPTER 4: TREATMENT OPTIONS IN CHRONIC VENOUS DISEASE

Introduction

A variety of treatment methods are currently available for patients with CVD, and these are presented in detail below.

4.1. Dressings for venous ulcers

Scientific evidence. A large number of types of wound dressing are in current use for venous ulcers. Two separate Cochrane reviews concluded that alginate and foam dressings do not increase venous ulcer healing rates and that more research is needed before recommending them.^{204,205} Similar results have been shown for hydrocolloid dressings.²⁰⁶ There is also no evidence to support the routine use of silver donating dressings beneath compression for venous ulceration.²⁰⁷

Another Cochrane review showed that the use of topical cadexomer iodine was more effective than standard care in achieving complete healing when added to compression therapy (risk ratio 6.7, $p = .011$). However, use of compression with povidone iodine versus hydrocolloid dressings was equivalent in achieving complete wound healing.²⁰⁸

Recommendation 17	Class	Level	References
To evaluate patients with post-thrombotic syndrome or clinical suspicion of other forms of iliac or inferior vena cava obstruction, duplex ultrasound examination of the veins of the lower limbs and abdominopelvic veins is recommended (whenever feasible).	I	C	154, 169, 194, 200, 201
Recommendation 18			
In patients with clinical signs of persistent venous hypertension (clinical class C3-C6, symptoms of venous claudication, venous collaterals on pubis or abdomen, or rapid recurrence of varicose veins) with or without a history of deep venous thrombosis, additional investigation of the venous system should be considered. This should include imaging of the iliac veins and inferior vena cava.	IIa	C	154, 169, 194, 199-203

Recommendation 19	Class	Level	References
If there is an indication to treat supra-inguinal venous pathology, additional imaging (magnetic resonance venography and computed tomography venography) is recommended.	I	C	169, 194-198
Recommendation 20			
If both magnetic resonance venography and computed tomography venography are inadequate, intravascular ultrasound may be considered as an additional technique for identifying and treating ilio-caval obstruction.	IIb	C	189-193

Zinc oxide impregnated paste bandages have been shown to achieve better ulcer healing compared with alginate dressings and the zinc oxide stockingette.²⁰⁹ Further research is needed to investigate the role of zinc dressings on wound healing.

Local allergic side effects might limit the use of topical antimicrobial dressings.

graduated elastic compression.²¹¹ Higher pressure at calf level during walking also seems to be the reason why inelastic bandages are haemodynamically more effective than stockings, which give way during muscle contraction.²¹² Despite the popularity of elastic stockings, evidence of their efficacy is unclear, based on the lack of randomized controlled trials for both superficial venous incompetence and the post-thrombotic leg.^{213,214}

Recommendation 21	Class	Level	References
Wound dressings may be considered to promote healing of venous ulceration.	IIb	A	204, 205, 208
Recommendation 22			
Zinc dressings and cadexomer iodine may be considered to promote venous ulcer healing as first and second choice, respectively.	IIb	C	209

4.2. Compression therapy

Introduction. Compression therapy, despite significant improvements in dressing materials and other methods, remains the cornerstone of conservative treatment. This is because of its ease of use, non-invasive nature, and also efficacy in managing venous hypertension, the main pathophysiological mechanism of CVD.

The most common forms of therapeutic leg compression are elastic stockings, including tights, non-elastic and elastic bandages (short and long stretch), and intermittent pneumatic compression. The mechanisms of action include compression of superficial and deep veins and improvement of the muscle pump function, both leading to reduction of ambulatory venous pressure and reduction of oedema.

However, there is ample lower quality evidence based on non-RCTs and clinical experience, to suggest their use because they improve patient symptoms²¹³ and they improve patients' QoL.²¹⁵ In general, there are issues putting on and removing elastic stockings, especially in the elderly, which along with the sensation of warmth and deterioration of pre-existing pruritis associated with venous eczema, could account for the suboptimal patient compliance.²¹⁶ Additional issues include potential skin damage, and contraindications to use including peripheral arterial disease. Also, elastic stockings require proper fitting and, to remain effective, should be replaced at intervals of 3–4 months, according to the manufacturers' instructions.

Recommendation 23	Class	Level	References
Elastic stockings are recommended as an effective treatment modality for symptoms and signs of chronic venous disease.	I	B	213, 215
Recommendation 24			
Temporary use of elastic stockings may be considered in patients with chronic venous disease awaiting further investigation, and as a definite treatment in patients who are not managed by invasive methods.	IIb	C	

4.2.1. Chronic venous disease without ulceration (C0–C4)

Scientific evidence. Elastic stockings in the form of graduated compression have been the cornerstone of conservative management of CVD C0–C4 for decades. They compress varicose veins, reduce venous reflux, and improve calf muscle pump function. More recently it has been shown that progressive graduated compressive stockings (higher pressure at the calf compared with the ankle) are more effective than the usual degressive graduated compressive stockings (higher pressure at the ankle) in improving pain and lower leg symptoms. Furthermore, they were easier to apply.²¹⁰ These beneficial effects might be related to the observation that progressive graduated compressive stockings have a more pronounced effect on venous pumping function than

4.2.2. Venous ulceration (C5–C6)

4.2.2.1. Venous ulcer healing. Scientific evidence. Compression bandages have been shown to improve healing rate of ulcers compared with standard care without compression.^{217–219} An alternative to traditional bandaging is non-elastic compression, including the Unna boot (a compression dressing impregnated with zinc oxide paste) and a non-elastic compression system based on adjustable Velcro bands that can be changed and adjusted daily eliminating odorous secretions.²²⁰ However, involving an elastic component in a bandage system seems more effective in terms of wound healing than when it is not involved.²¹⁹

In a RCT, sustained compression of at least 40 mmHg with a four layer compression bandage over a week has been

shown to be more effective than lower grades of compression.²²¹ However, other bandage types applying sustained high pressure compression (including two or three layer compression bandages, the Unna boot, paste bandages, or high compression stockings) have been shown by the vast majority of studies to be equally effective as four layer compression bandages.^{222–230} This is likely to be the result of improved properties of the former materials (including adhesiveness of bandaging material allowing it to be kept in place) and familiarity of use.²³¹ However, use of a four layer bandage does result in faster healing of ulcers compared with a short stretch bandage.²¹⁹

Until several trials with conclusive results favouring one particular compression system are published, the initial treatment modality should be the one with which the person applying the compression is most familiar. However, the differential properties of the various bandage types deserve further investigation.²³²

4.2.3. Intermittent pneumatic compression for venous ulceration

Scientific evidence. Intermittent pneumatic compression (IPC) improves venous flow significantly in patients using elastic bandages,²³⁷ while, in combination with elastic stockings, it has been shown to increase healing rates and overall healing of venous ulcers compared with elastic stockings alone.²³⁸ Three subsequent trials either failed to demonstrate any benefit when IPC was used in conjunction with compression,²³⁹ or this was marginally significant.^{240,241} This raises concerns regarding its efficacy.²⁴² However, in a trial that included patients with venous ulcers not using background compression, rapid IPC (one short compression period of 6.5 s three times a minute) healed 86% of venous ulcers compared with 61% with slow IPC (one long compression period of 90 s every 3 minutes) at 6 month follow up, $p = .003$.²⁴³

It has been proposed that IPC should be provided only for patients with refractory oedema and significant leg ulceration

Recommendation 25	Class	Level	References
Compression bandages and walking exercises are recommended as the initial treatment modality to promote healing in patients with venous leg ulcers.	I	A	217, 218
Recommendation 26			
The use of high compression pressures of at least 40 mmHg at the ankle level should be considered, to promote ulcer healing.	IIa	B	221

4.2.2.2. Venous ulcer recurrence. Scientific evidence.

Compression is important to prevent ulcer recurrence and most benefit is seen from high compression; however, this is more likely to be associated with patient intolerance.²³³ Following healing of the ulcer, compression bandages should be replaced by elastic stockings. The latter could be the definitive treatment, particularly in patients with deep vein occlusion or gross incompetence not amenable to widely accepted surgical or interventional solutions. Patients should wear the highest level of compression that is comfortable, preferably 25–35 mmHg at ankle level.²³⁴ In the ESCHAR trial, compression in the form of four layer bandaging was shown to be equally effective with surgery and compression in achieving healing of venous ulcers, although long-term effects were less durable in terms of recurrence compared with surgery.²³⁵

Another trial reached similar conclusions but surgery combined with ambulatory compression therapy was more durable than compression alone in patients with medial and/or recurrent ulceration, who should receive superficial and perforating vein surgery.²³⁶

tion after a 6 month treatment course, with standard methods such as compression stockings, has failed.²⁴⁴

IPC is also effective in CVI and higher compression pressures have been reported to be associated with greater leg volume reduction in patients with chronic venous oedema.²⁴⁵ IPC is able to provide symptom relief in patients with PTS.^{246,247}

More research is needed to establish which kind of compression may, in combination with IPC, be most beneficial in ulcer healing. Also the IPC impact should be studied in relation to ulcer characteristics (duration since onset, surface area and depth).

4.2.4. Compression after venous intervention

Scientific evidence. A meta-analysis has shown that short duration (about a week) compression after varicose vein surgery is as good regarding post-operative pain, leg volume, incidence of complications and absence from work as longer use (3–6 weeks) of compression.²⁴⁸ Additionally, after EVLA, use of high compression profile (35 mmHg) elastic stockings for 7 days significantly reduced pain and

Recommendation 27	Class	Level	References
Compression with elastic or non-elastic bandages or other compression devices is recommended as the initial treatment modality for venous leg ulcers; however, the possibility of an active venous intervention should be explored and offered to maintain healing.	I	B	235, 236

Recommendation 28	Class	Level	References
Intermittent pneumatic compression is recommended to provide symptomatic relief in patients with chronic venous disease (C3-C6) if standard methods are not indicated or if they have failed.	I	A	245-247
Recommendation 29			
Intermittent pneumatic compression should be considered in patients with venous ulcers after a 6 month treatment course when standard methods have failed.	IIa	B	238

improved both physical function and vitality when compared with use for 2 days.²⁴⁹

Similarly, after foam sclerotherapy, compression bandaging for 24 hours and thromboembolus deterrent stockings for a fortnight were equivalent to 5 days of bandaging, confirming results shown by a previous study with a similar design.^{250,251} However, use of low compression profile elastic stockings after foam sclerotherapy of larger veins had no effect on efficacy, side effects, and satisfaction scores compared with a control group without compression.²⁵² Following superficial vein surgery for venous ulceration, especially after GSV stripping to the knee or residual deep or superficial venous reflux, continuation of compression could be considered.

Use of elastic stockings (23–32 mmHg) for 3 weeks after sclerotherapy for leg telangiectasias, compared with no such intervention, was associated with an improved efficacy as determined by clinical vessel disappearance.²⁵³

Further studies are needed to establish the duration of compression as well as the type of compression (full length or knee length) following superficial vein surgery for ulceration.

function and dynamic calf muscle strength can be improved with exercise,^{256,257} as can the range of ankle movement.²⁵⁸

One small underpowered RCT showed a non-significant trend for reduced ulcer size with physiotherapy compared with no intervention.²⁵⁹ Another RCT showed that the group of patients who received lifestyle counselling had increased physical activity and reduced wound days compared with the control group, but a larger RCT of 40 patients failed to demonstrate any effect of home based progressive resistance exercise on ulcer healing parameters.^{260,261}

Properly powered studies are needed on the effect of supervised exercise on healing rates of venous ulcers.

4.3.2. Leg elevation

Scientific evidence. Leg elevation has been used for a long time and is still recommended to patients to ameliorate venous stasis, provide symptomatic relief, reduce leg oedema, and promote healing of ulcers in patients with CVD.^{262,263}

Leg elevation in patients with CVD classified as C3–C6 has been shown to reduce leg volume and venous pressure, and to enhance the microcirculatory flow velocity in lipodermatosclerotic skin.^{264–266}

Recommendation 30	Class	Level	References
Post-procedural compression is recommended after superficial venous surgery, endovenous truncal ablation, and sclerotherapy.	I	A	248-251, 253

4.3. Physiotherapy, leg elevation, and leg massage

4.3.1. Physiotherapy for leg ulceration

Scientific evidence. A reduced range of joint mobility has been described in CVD, correlating with the disease severity (CEAP clinical class) and haemodynamic changes on air plethysmography.²⁵⁴ A fixed ankle joint and reduced range of movement have been shown to be independent parameters associated with non-healing of venous ulcers, indicating that these findings are related to the impairment of the calf muscle pump.²⁵⁵ Furthermore, calf muscle pump

In the past, elevation has been used as the main measure to heal venous leg ulcers or as an adjunctive measure in patients wearing elastic bandages.^{267,268} It is still practiced in combination with antibiotics and debridement in cases of infected ulcers where compression cannot be tolerated because of pain associated with cellulitis in the surrounding areas. In a retrospective study, elevation was a statistically significant predictor of ulcer free survival among other variables, while in a structured education programme, patients who were allocated to the study group spent more

Recommendation 31	Class	Level	References
Physiotherapy is not recommended as a measure to enhance healing of venous leg ulceration. However, patients with venous ulcers should be kept as mobile as possible.	III	A	259, 261

time with their legs elevated each day and had a reduced ulcer recurrence rate.^{269,270} Others reported that in the presence of compression, there was no correlation between median leg elevation per 24 hours and percentage decrease in ulcer size.²⁶⁵ Although still recommended, treatment cannot rely on this otherwise simple advice, because patient compliance is poor and ulcer recurrence is extremely common even after a period of prolonged hospitalization.^{271,272} Finally, leg elevation has been used before bandages are applied and could also be used to reduce leg swelling before elastic stockings are fitted.²⁷³

Prospective, randomized studies should be performed investigating the role of leg elevation in healing venous leg ulcers. But even with the lack of strong evidence, practice and physiology suggest that leg elevation is helpful.

that there was insufficient evidence to support the use of all venoactive drugs in the treatment of CVD. However, it also showed that micronized purified flavonoid fraction (MPFF) was the most effective at reducing symptoms of oedema and restless legs. Calcium dobesilate reduced cramps and restless legs. MPFF helped in healing venous ulcerations and was also useful in treatment of cramps and swelling. Rutosides decreased venous oedema.^{275,276}

A Cochrane review of 17 randomized controlled trials (RCTs) showed that horse chestnut extract (HCSE) was effective at decreasing oedema, pain, and itching.²⁷⁷

Numerous studies have been conducted especially with MPFF, showing that these products lead to improvement of symptoms by increasing the venous tone.^{278–282} The

Recommendation 32	Class	Level	References
Leg elevation may be considered for patients with leg ulcers when compression cannot be tolerated because of acute inflammation or as an adjunct to compression during resting periods.	IIb	C	268-270

4.3.3. Leg massage

Scientific evidence. This method can be part of a multi-component regimen aimed at reducing tissue oedema by applying deep massage around the ulcer area, before formal compression is applied, or as an adjunct. Leg massage entails a form of light massage over elastic compression with a stocking.^{267,274} Further studies are necessary to assess the role of leg massage in patients with venous oedema, but IPC has largely replaced leg massage.

RELIEF study included 5,052 CVD patients with clinical class C0 to C4. They were divided into two groups: with and without reflux. All patients received MPFF over 6 months. Assessment was made of presence and/or severity of pain, heaviness, sensation of swelling, and cramps in lower limbs. Oedema was measured using the Leg-O-Meter. In both treatment groups, MPFF significantly reduced symptoms and signs, and reduced ankle oedema.¹²⁵

Recommendation 33	Class	Level	References
Leg massage may be considered as an adjunctive treatment to reduce oedema in patients with chronic venous disease.	IIb	C	267, 274

4.4. Medical treatment

Introduction. Medical treatment has been used for decades, but its place as a treatment modality for CVD is a topic of continuing debate. Venoactive drugs are widely prescribed in some countries but are not available in others. They can be classified into two groups: natural and synthetic drugs, such as naftazone and calcium dobesilate, respectively. The main modes of action of venoactive drugs are to decrease capillary permeability, diminish release of inflammatory mediators, or improve venous tone. Non-venoactive drugs like pentoxifylline, reduce white cell activation, and acetylsalicylic acid inhibits platelet function and also has an anti-inflammatory effect.

4.4.1. Chronic venous disease without ulceration (C0–C4)

Scientific evidence. In 2005, a Cochrane review of 110 publications was published with 44 studies (CEAP classification C0–C4) considered valid. This review concluded

Another RCT compared MPFF with placebo and could only show a difference in night cramps without changing other symptoms of CVD.²⁸³

Calcium dobesilate is a synthetic venoactive drug which has been evaluated in a few RCTs and one meta-analysis published in 2004. A recent large RCT with 509 patients could not show a difference between its study groups.²⁸⁴ However, a double blind, placebo controlled trial showed that calcium dobesilate reduces leg oedema and improves the symptoms of objectively diagnosed CVD independent of the concomitant usage of compression stockings.²⁸⁵

The effect of Red vine leaf extract was evaluated in a prospective randomized trial including 248 patients. Efficacy endpoints were changes in limb volume determined by water displacement volumetry, clinical CVD symptoms assessed on a visual analogue scale and global efficacy evaluations. Red vine leaf extract reduced lower limb

Recommendation 34	Class	Level	References
Venotonic drugs should be considered as a treatment option for swelling and pain caused by chronic venous disease.	Ila	A	125, 275-282, 285, 286

volume and CVD related symptoms significantly more than placebo.²⁸⁶

4.4.2. Venous ulceration (C5–C6)

Scientific evidence. A Cochrane database review showed that pentoxifylline is effective as an adjuvant therapy to compression, but it also appeared to be effective in the absence of compression.²⁸⁷ Other studies showed an accelerating healing time when patients were treated with pentoxifylline,^{288,289} in addition to wound care.²⁹⁰

Other products, like acetylsalicylic acid and oral zinc, are not routinely recommended for the promotion of healing venous leg ulcers.^{291–294} Some studies showed an acceleration of healing in a patient group treated with acetylsalicylic acid, but these were small studies and there was large

findings.^{298,299} However, according to a Cochrane review, the studies mentioned above showed shortcomings in terms of blinding and allocation.³⁰⁰

In 2005, a meta-analysis of five RCTs was performed (723 patients with venous ulcers). This showed that at 6 months, the chance of healing certain subtypes of ulcers was 32% higher in patients treated with MPFF as an adjunctive treatment in comparison with conventional therapy alone.³⁰¹

A more recent review concluded that in prospective randomized studies, MPFF and other flavonoid derivatives, and pentoxifylline have demonstrated clinical benefits in patients with CVD (clinical class C4–C6).²⁸⁴ Therefore pharmacotherapy should be part of a range of treatment options in the modern management of patients with CVD.

Recommendation 35	Class	Level	References
Sulodexide and micronized purified flavonoid fraction should be considered as an adjuvant to compression therapy in patients with venous ulcers.	Ila	A	295, 297-299, 301
Recommendation 36			
The routine use of zinc, oral antibiotics, horse chestnut seed extract, and pentoxifylline is not recommended in patients with venous leg ulceration.	III	B	208, 287-290, 294, 296
Recommendation 37			
Acetylsalicylic acid is not recommended to promote healing of venous leg ulcers as routine treatment, but it may be considered in therapy of resistant ulcers.	III	C	291-293

variation in the number and size of ulcers. Further research is necessary on this subject.^{291–293}

The effectiveness of routine use of systemic antibiotics for venous ulcers could not be demonstrated in a Cochrane review based on 25 RCTs.²⁰⁸ However, in light of the increasing problem of bacterial resistance to antibiotics, current guidelines recommend that antibacterial preparations should only be used in cases of clinical infection and not for bacterial colonization.

There is some evidence that sulodexide can support ulcer healing in combination with compression therapy.²⁹⁵

Although it was thought likely that HCSE would attenuate the pathogenesis of venous insufficiency and, in turn, facilitate venous ulcer healing, a study by Leach did not support this.²⁹⁶ A possible reason is that reducing oedema alone is insufficient to treat venous ulcers.

The time to complete ulcer healing was compared in a study of patients taking MPFF versus placebo.²⁹⁷ There was a significant reduction in healing time in the treated group compared with the placebo group. Other symptoms, like heavy sensation of the legs, were evaluated and were also shown to be reduced. Other studies have confirmed these

4.5. Sclerotherapy

Introduction. Sclerotherapy involves injection of dilated veins, including major refluxing trunks or tributary varicosities, venules, or telangiectasias, with liquid or foam chemical agents to damage the endothelium and eventually ablate the veins.

Scientific evidence. A number of chemical agents — sclerosants - with a variety of mechanisms of action have been used to damage and denude the vessel endothelium, including polidocanol, sodium tetradecyl sulphate (STS), morrhuate sodium, glycerin, and hypertonic saline, either as pure agents or in the form of foam, in increasing concentrations according to the size of vein being treated. Some of these have been mixed with lidocaine to reduce pain during injection.^{302,303} Post-procedural compression is an integral part of this type of treatment, which can be used to treat the entire spectrum of refluxing superficial veins, including the saphenous veins, and telangiectasias with a great degree of efficacy and safety.³⁰⁴ The reader is referred to section 4.2.4. for further information. However, patients should be informed of possible side effects (such

as skin necrosis, telangiectatic matting, hyperpigmentation, and also allergic reactions) and complications (such as deep vein thrombosis, pulmonary embolism, or cerebral embolic event for foam sclerotherapy in the presence of a right to left cardiac shunt).^{305,306}

Liquid sclerotherapy is more effective than placebo injection for telangiectasias and reticular and/or varicose veins.^{307,308} However, in two Cochrane reviews, there is no evidence suggesting superior efficacy of any one sclerosant over another.^{309,310} Lower concentrations of the sclerosant agent are used for smaller veins. In addition to effectiveness,^{307,311} sclerotherapy is less time consuming and is an easily repeatable treatment. It provides faster recovery with less pain and is relatively inexpensive compared with surgery or endovenous thermal ablation (EVTA). However, varicose vein recurrence, as high as 90% after 6 years,³¹² and the need for additional treatment (more often compared with surgery) are inherent major problems,^{312,313} as summarized also by a Cochrane review.³¹⁴ This is true not only for the major saphenous trunks, but also for varicose tributaries if the source of incompetence has not been eliminated.³¹⁵ On the other hand, good long-term results in the primary treatment of isolated varicose veins, not associated with saphenous vein incompetence have been demonstrated.³¹² Treatment of recurrent varicose veins following surgery is another indication, by avoiding the morbidity (40% in one study) associated with redo surgery.³¹⁶

an adjuvant treatment of varicose tributaries following endovenous ablation of the main refluxing trunk,³²¹ or high ligation (HL),³²² or to treat recurrent varicose veins.^{323,324} It is also widely used to treat telangiectasias and reticular veins, although there is no evidence that foam sclerotherapy is better than liquid sclerotherapy in this setting.

UGFS is characterized by a higher recanalization rate when treating veins larger than 5–7 mm in diameter.^{325–327} Foam sclerotherapy is associated with a higher recanalization rate and similar results in terms of symptoms and QoL assessment when compared with surgery, laser or radio-frequency endovenous ablation for treating GSV reflux.^{328–331} Foam sclerotherapy proved significantly cheaper³²⁹ and it may be considered an attractive minimally invasive alternative to surgery to treat superficial incompetence,^{332,333} particularly in elderly and frail patients and especially in those with venous leg ulcers.^{334,335} Repeat treatment may be considered an integral part of UGFS in some of the treated patients and the additional cost incurred must be integrated into the global cost when it is compared with the other techniques (surgery or thermal ablation). Foam sclerotherapy is becoming an increasingly popular choice in the management of patients with recurrent varicose veins.^{315,324,332} Long catheter foam sclerotherapy has been introduced recently and its short-term efficacy is equal or superior to the usual UGFS for GSV reflux.^{336–339} Long-term results are awaited.

Recommendation 38	Class	Level	References
Liquid or foam sclerotherapy is not recommended as the first choice treatment for chronic venous disease C2-C6 due to saphenous vein incompetence. It should be used only as primary treatment in selected cases.	III	A	317-320, 328-331
Recommendation 39			
Foam sclerotherapy is recommended as a second choice treatment of varicose veins (C2) and for more advanced stages of chronic venous disease (C3-C6) in patients with saphenous vein incompetence, not eligible for surgery or endovenous ablation.	I	A	314, 328, 329
Recommendation 40			
Foam sclerotherapy should be considered as primary treatment in patients with recurrent varicose veins, and in elderly and frail patients with venous ulcers.	IIa	B	334, 335
Recommendation 41			
Liquid sclerotherapy should be considered for treating telangiectasias and reticular veins (C1).	IIa	B	308

Foam sclerotherapy, usually guided by DUS (ultrasound guided foam sclerotherapy, UGFS), has been shown to be more effective than liquid sclerotherapy because of the enhanced sclerosing properties of the foam form of the sclerosant.^{317–320} Foam sclerotherapy has been used as

4.6. Transcutaneous laser

Introduction. Surface transcutaneous laser (TCL) has been used for the treatment of telangiectasias and reticular veins since the 1970s. The mechanism behind this treatment is to

cause endothelial injury of the vein by heating the haemoglobin and eventually to obliterate the lumen. The advent of laser technology with delivery of sufficiently controlled energy has enabled achievement of pan-endothelial necrosis without affecting more superficial structures such as the epidermal layer. High intensity pulsed light therapy, which was introduced in 1990, represents a further development in the field as it allows treatment of reticular veins by emitting a spectrum of light rather than a wavelength to obliterate the vein.

Scientific evidence. TCL is an effective treatment for telangiectasias and reticular veins, although not capable of making them to disappear completely.³⁴⁰ Laser light is emitted from the laser equipment and transmitted through the skin to the targeted vessel, where it is selectively absorbed by the oxyhaemoglobin and converted to thermal energy leading to heating of the telangiectatic vein, coagulation, and vessel destruction. Different settings of laser are used for blood vessels of different diameter and skin type and/or colour.^{341,342}

TCL is less effective than sclerotherapy at managing leg telangiectasias, requires more treatment sessions,^{343,344} and is more expensive. However, particular indications include: 1. known allergy to sclerosant solutions, 2. needle phobia, 3. telangiectatic matting after sclerotherapy, 4. failure of sclerotherapy,³⁴⁵ and 5. vessel size less than 0.5 mm.

Recent technical modifications have been reported to significantly improve the efficacy of TCL.^{346,347} Indocyanine green (ICG)-augmented diode laser therapy has been shown to be superior to pulsed dye laser and the diode laser without ICG.³⁴⁶ Similarly, improved results have been demonstrated in combination with sclerotherapy.³⁴⁸

More studies are needed to establish which telangiectatic veins, and at what site in the lower limb, are better managed with TCL. Also, the role of elastic compression after TCL should be further investigated.

(RFA). Another endovenous thermal ablation (EVTA) technique is steam ablation.³⁵⁰ Other more recently introduced techniques are mechanochemical ablation (MOCA)³⁵¹ and injection of cyanoacrylate glue.³⁵²

The use of EVTA (EVLA, RFA, Steam) techniques requires injection of tumescent liquid around the target vein. The purpose of this is to protect the perivenous tissue from the heat created during treatment. The tumescent liquid acts as a heat sink.³⁵³ Other purposes of the tumescent liquid injection are to create spasm of the vein and to obtain local compression and anaesthesia. The new non-thermal ablation techniques (MOCA and glue injection) can be performed without injection of tumescence during the ablation.

The scientific evidence for cyanoacrylate glue injection is too little to warrant further attention in this chapter because of the lack of publications. Steam ablation seems to give results comparable with other thermal ablation techniques at 1 year follow up,³⁵⁴ but more studies are necessary to confirm those results in the medium and long term.

4.7.1. Endovenous thermal ablation

Introduction. To evaluate the two most commonly used EVTA techniques, EVLA and RFA, six meta-analyses,^{355–360} 31 RCTs,^{328,361–390} six non-randomized comparative clinical trials,^{391–396} seven prospective clinical trials,^{397–403} and one technical review article were selected.⁴⁰⁴

4.7.1.1. Great saphenous vein. Technique. The technique is similar for all EVTA methods. The procedure is performed percutaneously with ultrasound guidance. A laserfibre or RFA catheter is inserted and positioned 1–2 cm distal to the SFJ, and tumescent liquid is injected around the saphenous vein. A very dilute solution of local anaesthetic combined with bicarbonate and epinephrine is used for this purpose. It is important to empty the vein of blood as much as possible. While withdrawing the catheter or fibre, energy is emitted intraluminally to cause irreversible ther-

Recommendation 42	Class	Level	References
Transcutaneous laser may be indicated for treatment of teleangiectasias, only when sclerotherapy is not applicable.	IIB	C	345

4.7. Endovenous treatments

Introduction. Endovenous techniques in the treatment of saphenous vein incompetence have become very popular as a minimally invasive alternative to classical surgery (HL and stripping). In countries where reimbursement is available, the vast majority of patients are treated endovenously. It was Carlos Boné in 1999, who first treated patients with endovenous laser.³⁴⁹ In the past 10 years, endovenous techniques have evolved quickly and performance has improved.

The two most frequently used techniques are endovenous laser ablation (EVLA) and radiofrequency ablation

mal destruction of the endothelium of the vein wall. Compression post intervention is recommended (see section 4.2.4.), but the duration of compression is not clearly defined.^{405,406}

Effectiveness. Occlusion rates of EVLA vary between 77%³⁶⁵ and 99%³⁶² at 1 year. Compared with surgery (HL and stripping), most studies report no significant difference in varicose vein recurrence (clinical) or recurrent reflux (according to DUS) after treatment.^{328,356,364–366,368–370,391} Other studies report a higher recurrence rate after surgery (20% vs. 4% at 1 year)³⁶² or after EVLA (7.4% vs. 0% at 2 years).³⁶³ Neovascularization at the SFJ is an important

cause of varicose vein recurrence after treatment. This was seen more commonly after surgery, although this was not significantly different,³⁵⁹ compared with EVTA.^{366,372} Compared with RFA, surgery seems to be more efficient^{373,376} or equally effective.^{371,372} In cases in which surgery was more efficient, RFA was performed using the older “Closure Plus” catheter (VNUS Med Tech, San Jose, CA, USA). Meta-analyses show that RFA and EVLA are as effective as surgery in the treatment of GSV incompetence.^{355,357,359} The first published meta-analysis on EVTA reports superior results of EVLA compared with surgery and RFA.³⁵⁵ This study, however, only includes trials using either EVLA with lower wavelength or RFA with the “Closure Plus” catheter, and uses heterogeneous definitions of treatment failure.

Safety. No difference in safety including the risk of venous thromboembolism could be determined, comparing EVTA and surgical treatment for saphenous vein incompetence.^{367,391}

The reported incidence of DVT varies between 0.2% and 1.3% in EVTA, and seems to be higher in patients treated with RFA compared with EVLA.³⁵⁷ The latter meta-analysis mainly included the old RFA techniques and EVLA with bare tip fibres and lower wavelength. Development of thrombus extension at the SFJ (often called endovenous heat induced thrombosis) can be found in a limited number of cases. Case series report a frequency varying between 0.3% and 7.8% of patients after EVTA.^{395,397–399} When thrombus extends into the common femoral vein treatment by anticoagulation (AC) is advised. Pulmonary embolism was reported in 0.0% to 3% after EVLA.^{395,398} Nevertheless, the role of routine use of pharmacologic prophylaxis remains uncertain and more studies are necessary.

Thrombo-prophylaxis can be prescribed for high risk patients (previous venous thromboembolism, documented thrombophilia, obesity, immobilized patients, patients with neoplasm, and older patients).^{407,408} However, risk factors should be weighted for each individual patient using a specific risk assessment score such as the Caprini score.⁴⁰⁹ Patients can be treated in an outpatient setting under local tumescent anaesthesia, which permits early ambulation reducing the risk of possible thromboembolic complications.

Side effects. Post-operative complications in EVTA are limited. Reported complications are thrombophlebitis (7%),³⁵⁹ thermal skin injury (<1%),³⁵⁹ bruising, hyperpigmentation (5%),³⁵⁹ paresthesia (1–2%),^{364,369} and haematomas (0–7%).^{364,369,374,378} Compared with EVTA, surgically treated patients more frequently develop complications, such as wound infection (2–6% for surgery vs. 0% for EVTA)³⁵⁶ and haematomas (5% for surgery vs. 2% for EVTA).³⁵⁹ Patients treated with EVTA have, on average, less pain compared with patients treated surgically.^{356,365,369,374,377,378} Post EVTA as opposed to surgery, swelling and bruising is reduced.³⁹¹ This results in quicker recovery^{357,362,375,376} and faster return to normal activities.^{364,365,374,378,392} Endovenously treated patients also

seem to have an equal^{364,366,367} or better³⁶¹ QoL after treatment. The risk of superficial thrombophlebitis appears to be significantly higher (2.3 times) in RFA than in surgery.³⁵⁶

EVLA: different wavelengths and fibres. To reduce possible side effects of EVLA (pain, bruising, and haematoma), higher laser wavelengths have been introduced and different fibre tips have been developed. Theoretically, light of lower wavelength lasers (810, 940, 980, 1320 nm) is less specifically absorbed by their chromophores (haemoglobin, water, proteins) compared with the light of higher wavelength lasers (1320, 1470, 1500 nm).⁴⁰⁴

The clinical use of higher wavelength lasers should result in equal occlusion rates (97–100%) and less post-operative pain.^{396,402,403} There is only one randomized clinical trial comparing the use of lower and higher wavelength lasers.³⁷⁹ Also, most studies reporting results of higher wavelengths use a lower energy level which makes it difficult to draw any conclusions regarding outcome and potential side effects. As the use of a bare fibre creates unequal energy delivery at the vein wall resulting in local vein wall perforations and perivenous tissue destruction, new fibres have been designed.^{380,400,404} The purpose of these new fibre designs is to increase the heated surface area, resulting in lower energy density. The use of these new fibres, Never-touch (AngioDynamics, Latham, NY, USA),³⁹³ Radial fibre (Biolitec, Wien, Austria),^{394,400} and Tulip fibre (Tobrix, Waalre, the Netherlands),³⁸⁰ may be safe and effective in the treatment of saphenous vein reflux.

There is a lack of RCTs comparing these fibres with a standard bare fibre. Only one RCT reports fewer side effects and an equal occlusion rate using a Tulip fibre compared with a bare fibre.³⁸⁰

RFA versus EVLA. EVLA and RFA have the same occlusion rates, but patients treated with RFA have less post-operative pain and bruising.^{328,381–384} This can result in an equal³⁸³ or faster³²⁸ return to normal activities. In trials comparing EVLA and RFA, however, the ClosureFast catheter was compared with lower wavelength lasers using a bare fibre. No trials have been published comparing the use of ClosureFast with higher wavelength lasers and new fibre tip design.

Consideration must be given to the fact that in the last decade the technique and the fibres or catheters used have improved. The more recently introduced ClosureFast catheter (VNUS Med Tech, San Jose, CA, USA), although no RCTs are available, seems to be more effective, faster (shorter operative time), and induces fewer side effects compared with the older “Closure Plus” catheter.⁴⁰¹

UGFS versus EVTA/surgery. The advantage of foam sclerotherapy is its simplicity. There is no need to inject tumescent liquid, the treatment is cheap, and easy to repeat if necessary.

Complications of UGFS include hyperpigmentation, thrombophlebitis, matting, and pain at the injection site. Also, some neurologic events, such as visual disturbances, migraine, and stroke, have been reported.^{410–413}

Myers et al. reported primary and secondary success rates of 52.4% and 76.8% respectively.³²⁷ Compared with surgery, UGFS is less efficient^{328,329,355,356,414,415} but has significantly fewer side effects (less pain, better post-operative QoL, faster return to normal activities).^{322,328,329,356,414–416}

Occlusion rates of saphenous veins treated with UGFS seem to be inferior to those of veins treated with EVTA.^{355,356,361} Compared with EVLA, patients treated with UGFS have somewhat less post-operative pain, but no difference could be found compared with RFA.³²⁸

The results (occlusion rates and side effects) of EVTA in the treatment of saphenous vein reflux also depend on a good technique (e.g. detailed pre-operative ultrasound, correct positioning of the catheter or the fibre tip, targeting injection of tumescent fluid, regular pull back speed). The vein to be treated should be emptied of blood far as possible.

Recommendation 43	Class	Level	References
For the treatment of great saphenous vein reflux in patients with symptoms and signs of chronic venous disease, endovenous thermal ablation techniques are recommended in preference to surgery.	I	A	328, 354, 356, 357, 359, 361-378, 391, 392
Recommendation 44			
For the treatment of great saphenous vein reflux in patients with symptoms and signs of chronic venous disease, endovenous thermal ablation techniques are recommended in preference to foam sclerotherapy.	I	A	322, 328, 329, 355, 356, 414-416

4.7.1.2. Small saphenous vein. Scientific evidence. EVTA of the SSV has excellent early and mid-term results.^{386,388,389} Access at the lateral malleolus results in a higher paresthesia rate compared with mid-calf access, because of the proximity of the sural nerve to the SSV in the distal part of the calf.³⁸⁶ EVLA of the SSV is associated with a significantly higher incidence of sensory disturbance compared with EVLA of the GSV.³⁸⁷ SPJ ligation and stripping of the SSV often fails because of the complex anatomy.³⁶⁰

Compared with surgery, EVTA seems to be more efficient and results in fewer post-operative side effects (less paresthesia, pain, and a faster return to normal activities).³⁸⁸

UGFS for the treatment of SSV incompetence can be an alternative to EVTA and surgery. Two articles on UGFS showed success rates varying from 82% to 100% (follow up 1.5–60 months). Thrombophlebitis (5%) and hyperpigmentation (24%) were common complications.^{326,360,417} There are no RCTs comparing foam sclerotherapy with surgery or EVTA in treatment of SSV incompetence.

Recommendation 45	Class	Level	References
For the treatment of small saphenous vein reflux in patients with symptoms and signs of chronic venous disease, endovenous thermal ablation techniques should be considered. Access to the small saphenous vein should be gained no lower than mid-calf.	Ila	B	386, 387, 389

4.7.2. Mechanochemical endovenous ablation

Introduction. Recently, a new hybrid (dual injury) technique has been developed (ClariVein Vascular Insights, Quincy, MA, USA). Endomechanical abrasion is produced by the tip of the

catheter’s rotating wire (mechanical component) and endovenous chemical ablation via the simultaneous injection of sclerosant over the rotating wire (chemical component). This technique is under development as the optimal dosage of sclerosans still needs to be determined.

Scientific evidence. To date, there have been only two cohort studies including a small number of patients treated with MOCA.^{351,418} The occlusion rate at 6 months is 96.7% and side effects seem to be minimal.

4.8. Surgery of the superficial veins

Introduction. For many years the gold standard for treatment for CVD patients with superficial venous incompetence was surgery.

4.8.1. High ligation with/without stripping

Scientific evidence. It has been reported that surgical treatment of varicose veins is superior to conservative management. In the REACTIV trial,⁴¹⁹ the results of surgery were compared with results of compression alone in 246 patients with uncomplicated varicose veins, the surgical treatment comprising high ligation/stripping (HL/S) of the GSV and multiple phlebectomies.⁴²⁰ At 2-year follow up the results showed more symptomatic relief, better cosmetic results, and much improved QoL for surgery compared with conservative management by compression.

In a prospective cohort study, 203 consecutive patients who underwent varicose vein surgery were monitored, and reported an improvement in QoL 2 years after surgery, with a significant improvement in the health related AVVQ score and the SF-36 score.⁴²¹ In addition, improvement in QoL from varicose vein surgery has been shown to be statistically significant and clinically relevant.⁴²²

Comparative studies relating to traditional surgical treatment compare isolated HL and HL/S.^{423–426} In a randomized trial in 100 patients and 133 legs, HL was compared with HL/S.⁴²⁴ The need for reoperation was 6% in

patients who underwent HL/S versus 20% in those patients who underwent HL alone ($p < .02$). In another study it was shown that the HL group and the sclerotherapy group with intention to close the GSV, had significantly higher recurrence rates than HL/S at 4 years.⁴²⁵ Cosmetic results, both judged by the patient and the surgeon, were significantly better ($p < .05$) in the stripped limbs than in the limbs with HL and sclerotherapy.⁴²⁶ They also found that CW Doppler evidence of reflux of the saphenous vein was less frequent ($p < 0.001$) after the stripping operation. Better results after aggressive and extensive surgical treatment of the refluxing veins and the sources of the reflux were reported. A randomized trial showed a significant reduction of risk of re-operation in a HL/S group compared with a HL alone group at 11 years of follow up, even if there was no difference for the rate of visible recurrent veins.⁴²³

In a RCT it was shown that patients in whom the stump of the GSV had been invaginated with a non-absorbable suture, had less neovascularization in comparison with those who had the endothelium of the stump exposed.⁴²⁷ According to a single centre prospective cohort study, interposition of an anatomical barrier, by closing the cribriform fascia after SFJ ligation, also reduced ultrasound detected neovascularization at the SFJ after 1 year.⁴²⁸ In a RCT of 389 limbs by van Rij, polytetrafluoroethylene (PTFE) patch coverage of the SFJ created a significant reduction of recurrence at 3 year follow up by reducing neovascularization at the groin.¹²⁰ The potential benefit of inserting a PTFE patch in recurrent varicose vein operations could not be proven in another small RCT.⁴²⁹

Traditional HL/S has evolved towards a less invasive technique by invagination under tumescent local anaesthesia, giving post-operative results as good as endovenous ablation techniques or foam sclerotherapy in terms of

haematoma, pain, and QoL as shown by Rasmussen in a randomized control study.³²⁸ A non-comparative prospective study showed that the use of isotonic sodium bicarbonate as excipient for tumescent anaesthesia reduced intra-operative pain and improved cost-effectiveness of surgery.⁴³⁰

As endovenous procedures have shown good results without HL, stripping of the saphenous vein has also been described without HL. A retrospective study showed that stripping of the GSV without HL led to low neovascularization and SFJ reflux rates at 3 year follow up (0.9% and 1.8%, respectively).⁴³¹ In a RCT at 8 year follow up, a group treated by stripping without HL had significantly less recurrence than a group treated by HL/S (9.8% vs. 29%, $p = .014$).⁴³²

Several RCTs have been performed comparing HL/s with endovenous techniques (EVLA, RFA, foam sclerotherapy). Among them, Rasmussen published a four arm RCT comparing HL/S under tumescent local anaesthesia by invagination stripping with EVLA, RFA, and foam sclerotherapy. The results showed that the post-operative average pain scores at 10 days were significantly lower in the groups treated with RFA and foam sclerotherapy compared with HL/S and EVLA, with a shorter time to resumption of normal activities and work. But the VCSS, the AVVQ scores, and the clinical recurrence were not different between HL/S and the other treatments at 3 years. The conclusion was that beyond a higher pain score in the post-operative period and a higher total cost for HL/S and EVLA, the efficiency of the four modalities was not significantly different.⁴³³

There is no evidence in the literature for continuing indications for HL/S, unless there is lack of availability of the endovenous techniques for financial or other reasons. On the other hand, HL/S is not inferior compared with the new modalities of treatment in the mid term.

Recommendation 46	Class	Level	References
For non-complicated varicose veins (C2, C3), surgical treatment is recommended instead of conservative management, to improve symptoms, cosmetics, and quality of life.	I	B	420, 421, 434
Recommendation 47			
In cases in which surgical treatment of the refluxing saphenous vein is performed, high ligation and stripping is recommended instead of high ligation only.	I	A	423-426
Recommendation 48			
Surgical stripping of the saphenous vein without high ligation leaving a 2 cm stump may be considered.	IIb	B	431, 432
Recommendation 49			
If high ligation is performed, oversewing the great saphenous vein stump, interposition of a polytetrafluoroethylene patch, or closure of the cribriform fascia may be considered, in order to reduce the effect of neovascularization at the saphenofemoral junction.	IIb	B	120, 427, 428
Recommendation 50			
The use of tumescent anaesthesia should be considered for surgical treatment of great saphenous vein reflux to reduce post-operative side effects.	IIa	C	328, 430

4.8.2. Phlebectomy

Scientific evidence. The technique of ambulatory phlebectomy (AP; stab or hook or mini-phlebectomy) was described by Muller in 1966 with removal or avulsion of varicose veins through small incisions performed with hooks and forceps.¹⁵ Numerous authors have reported that ambulatory phlebectomy is a safe and immediately effective procedure for the treatment of varicose veins,^{315,434–438} which can be done under local anaesthesia in an office based setting.

Phlebectomy can be considered as an adjunctive treatment in association with stripping or endovenous ablation of the main refluxing truncal vein,^{439–442} or as the exclusive procedure for the treatment of varicose veins.^{15,315,435,443,444}

A randomized study showed that ambulatory phlebectomy compared with liquid sclerotherapy plus compression for accessory vein incompetence caused significantly fewer recurrences at 1 and 2 years of follow up (respectively, 1/48 vs. 12/48 and 1/48 vs. 18/48 $p < .001$).³¹⁵

Some publications advocate limiting the treatment to thermal ablation of the SV without treating the tributary varicose veins.^{445,446} According to these papers, secondary treatment (foam sclerotherapy, phlebectomy, stripping) for residual varicose veins was only necessary in 17–62.5% after a short follow up period (3–9 months). On the contrary, another prospective study in 67 patients showed that the performance of concomitantly performed phlebectomy with an EVLA of the saphenous vein obviates the need for subsequent procedures.⁴⁴⁷ The authors found that an additional treatment by sclerotherapy or by phlebectomy was performed in only 4% and 1% at 1 and 12 weeks. In a randomized study of 50 patients between EVLA alone and EVLA with concomitant ambulatory phlebectomy (EVLA/AP), it was shown that at 3 months in the EVLA/AP group the requirement for a secondary procedure was less common (1/25 vs. 16/24, $p < .001$), the VCSS was lower (0(0 + 1) vs. 2 (0–2), $p < .001$), and the AVVQ score was better (7.9 vs. 13.5 $p < .001$).⁴⁴⁸

intrafascial saphenous vein, leading to decompensation of the saphenous vein wall, moving on to eventually reach the saphenofemoral or saphenopopliteal junction.

Scientific evidence. The theory for the development of varicose veins is historically based on the descending theory. Anatomical, DUS examination, and morphological information confirmed the theory that the reflux begins at the saphenous junctions and progresses downwards through the saphenous axis leading to venous hypertension, wall dilatation, and dilatation of tributaries which become varicose veins. Cotton reported in an anatomical study that normal veins have a significantly higher number of valves than varicose veins.⁹⁰ Cooper assessed in a retrospective analysis of venous DUS examinations that the incompetence of the SFJ has a major influence on the extension of the reflux and that the venous incompetence was most commonly proximal in presence of varicose veins.⁴⁴⁹ Takase described numerous alterations in structure of valves induced by venous hypertension in association with varicose veins.⁴⁵⁰

However, numerous publications challenge the theory of descending disease progression, citing the possibility of local or multifocal early distal evolution, sometimes ascending or antegrade, based on precise and detailed DUS investigations.^{49,431,451–456} The fact that the terminal valve at the SFJ is frequently competent (in >50% of cases) in the presence of truncal reflux has been clearly proven.^{449,457–459}

The disappearance of reflux in the GSV following phlebectomy^{460–463} or after thermal ablation of an incompetent tributary⁴⁶⁴ has been reported in the literature. Quill and Fegan also found such reversibility of the saphenous reflux following sclerotherapy.⁴⁶⁵ The diameter of the GSV was observed to be reduced after ablating a refluxing tributary.⁴⁶⁶

In addition, the evolution of CVD, whether ascending or descending, remains largely unknown, as prospective longitudinal studies with a lengthy period of observation and a large sample size, are missing and RCTs are needed.

Recommendation 51	Class	Level	References
When performing endovenous thermal ablation of a refluxing saphenous trunk, adding concomitant phlebectomies should be considered.	IIa	B	447, 448
Recommendation 52			
To treat tributary varicose veins, ambulatory phlebectomy should be considered.	IIa	C	15, 434–437, 443, 444

4.8.3. Ambulatory Selective Varices Ablation under Local anaesthesia

Introduction. The Ambulatory Selective Varices Ablation under Local anaesthesia (ASVAL) method, consisting of single phlebectomies with preservation of the saphenous trunk, is based on the concept of ascending or multifocal evolution of varicose veins. According to this pathophysiological concept, progression of the disease could begin in subcuticular veins, outside the saphenous compartment, creating a dilated and refluxing venous network. When this refluxing network becomes large enough, it could create a “filling” effect in the

A retrospective cohort of 303 limbs treated by ASVAL reported complete abolition of the saphenous reflux after 1, 2, 3, and 4 years in 69.2%, 68.7%, 68.0%, and 66.3% of cases, respectively, and reduction in SFJ vein diameter, marked symptom relief, and low recurrence rates.⁴³¹ In this study, the cohort of patients operated on with ASVAL was younger, more frequently asymptomatic, with a less extensive reflux, and lower average diameter of the SFJ compared with the patients who underwent stripping during the same period of time.

In a prospective study including 94 patients with large varicose tributaries and GSV reflux assessed by DUS

examination, single phlebectomies led to abolition of the GSV reflux in 50% of the cases, with a significant reduction of the GSV diameter and a significant improvement of the AVVQ score.⁴⁶⁷

4.8.5. Powered phlebectomy

Introduction. Transilluminated powered phlebectomy (TIPP) consists of removal of large varicose vein clusters, with a decrease in the number of incisions needed and a faster

Recommendation 53	Class	Level	References
In selected patients, with less evolved varicose veins (C2-C3), single phlebectomies with preservation of the saphenous trunk should be considered.	Ila	B	431, 463, 467

4.8.4. Cure conservatrice et Hémodynamique de l'Insuffisance Veineuse en Ambulatoire (CHIVA)

Introduction. CHIVA was described by Franceschi in 1988. It aims to improve the haemodynamics of the superficial venous network by splitting the column of hydrostatic pressure and disconnecting venovenous shunts by interrupting the incompetent trunks at strategic levels (SFJ, perforating veins) depending on a precise pre-operative DUS examination, to obtain a well-drained superficial venous system with low pressure and high flow.

Scientific evidence. One RCT, concerned with treatment of venous ulcers, showed that the group treated by CHIVA had a similar healing rate (100% vs. 96%) and a lower recurrence rate (9% vs. 38%) at 3 years follow up than the group treated by compression.⁴⁶⁸

The clinical and DUS recurrence of varicose veins was studied in two RCTs: the results were in favour of CHIVA versus HL/S in both studies, 8% vs. 35% ($p < .004$) at 10 year follow up in one study⁴⁶⁹ and 31.1% vs. 52.7% ($p < .001$) at 5 year follow up in the other.⁴⁷⁰

Some observations must be noted: in the paper by Carandina, there is an important bias concerning the randomization and follow up.⁴⁶⁹ In another study all stripping procedures were done under general or epidural anaesthesia whereas the CHIVA treatments were performed under local anaesthesia, which acted as a confounder for the evaluation of the post-operative side effects.⁴⁷⁰ The most serious limiting concerns in both studies were how "failure" by recurrence was defined: it is unclear if the presence of visible recurrent varicose veins or the presence of refluxing veins during the DUS evaluation or both were considered to define the failure of the treatment.

performance of the procedure, often combined with saphenous vein ablation procedures or HL/S.

Scientific evidence. A published series of 114 patients, in a prospective, non-comparative, multicentre, pilot study reported the safety and efficacy of TIPP.⁴⁷¹ The patients, an independent nurse, and the surgeon subjectively scored the evaluation of outcomes in this study.

Other authors have stated in observational studies that a learning curve exists to minimize bruising and that other local complications may vary.^{472–474} Complications observed include haematoma (4.9–95%), paresthesias and nerve injury (9.5–39%), skin perforation (1.2–5%), superficial phlebitis (2.4–13%), swelling (5–17.5%), and hyperpigmentation (1.2–3.3%).^{475,476}

More recently, a new system with important technical modifications (lower oscillation frequency, larger volume of tumescence, dermal drainage, flushing of hematoma, and residual tissue fragments), has improved the results of TIPP with a lower rate of complications.⁴⁷⁷

A limited number of studies with many limitations (pilot study, non-randomized, observational) have been published and clearly lack data to show a significant advantage of TIPP over phlebectomy. It seems that the newer generation system and modified technique enable TIPP to be less invasive. Further studies are required to confirm the potential benefits of TIPP.

4.9. Treatment of deep vein pathology

Introduction. Annually one to two adults per 1,000 in the Western population develop a DVT of the lower extremity. Treatments using low molecular weight heparin (LMWH) or unfractionated heparin and vitamin K antagonists in the acute phase will not be discussed here. Despite adequate

Recommendation 54	Class	Level	References
Ambulatory conservative hemodynamic treatment of venous incompetence (Cure Conservatrice et Hémodynamique de l'Insuffisance Veineuse en Ambulatoire, CHIVA) may be considered in patients with chronic venous disease, if performed by physicians exclusively performing CHIVA.	Iib	B	468-470

Recommendation 55	Class	Level	References
Transilluminated powered phlebectomy (using a low oscillation speed and a large volume of tumescence) may be considered as an alternative to phlebectomy, to reduce the number of incisions.	Iib	C	477

treatment according to this regimen, residual venous lesions occur in a substantial number of these patients (20–50%). The incidence of residual lesions is greater after a recurrent DVT in the ipsilateral leg aggravating venous hypertension because of deep venous obstruction and valvular incompetence. The effect of this is the development of oedema and dysfunction of the (micro)circulation, which can lead to the clinical characteristics of post-thrombotic syndrome (PTS). Also in well or partially recanalized veins, residual venous obstruction may be important, because the scarred venous outflow causes increased outflow resistance, especially during and after activity. As a result of chronic venous obstruction, collaterals develop, which partly take over the outflow capacity of the thrombosed venous segments. However, these collaterals often feature a relatively low outflow capacity, and are mainly used when venous pressure rises significantly. These collaterals are clinically visible at the level of the thigh, lower abdomen, and pubis. Less commonly, the cause of obstruction is extrinsic compression on the vein, for example by a malignant tumour. There are also specific iliac vein compression syndromes caused by non-thrombotic iliac vein lesions (NIVL) such as May-Thurner syndrome, in which the left common iliac vein is compressed between the right iliac artery and the spine. There are several forms of congenital deep venous anomalies causing obstruction of the outflow tract. One severe anomaly is atresia (congenital absence) of the IVC in which the sub-hepatic segment of the IVC has not developed. This may cause CVD because of outflow obstruction, often complicated by recurrent ilio-femoral DVT and subsequent post-thrombotic problems.⁴⁷⁸

In patients who have suffered from extensive DVT, apart from residual venous obstruction, deep venous reflux may occur, secondary to valvular damage. However, deep venous reflux can also be induced by a very important proximal outflow obstruction, causing dilatation of the deep veins in the leg, and eventually failure of the valves to close completely. The increased hydrostatic pressure leads to venous hypertension, damage of the microcirculation, and symptoms and signs of CVD. In some patients there may be a congenital hypo- or aplasia of valves in the deep venous system. This form of deep venous reflux is very rare.

The current standard treatment for symptoms and signs of chronic venous obstruction or deep venous reflux is compression therapy. However, its effectiveness may be suboptimal in selected cases, especially when compression therapy has limited effect on venous symptoms or the compliance is poor.

4.9.1. Treatment of chronic deep venous obstruction

This can be performed either by percutaneous transluminal angioplasty (PTA) and stenting, or by surgical correction, usually bypass.

4.9.1.1. Percutaneous transluminal angioplasty and stenting. Introduction. The endovenous treatment of ilio-caval obstruction includes traversing the obstruction with a guide wire (occlusions need to be recanalized, i.e., a new lumen

created), followed by placement of a stent to cover the obstructed vein segment. Self-expandable stents should be used in the veins, ideally with a high radial force and sufficient flexibility. The aim is for the stent to support the vein wall and prevent recoil/collapse, and thereby to maintain patency in the long-term. The largest longer term experience reported from multiple centres utilizes a braided stent made of elgiloy (main content cobalt, chromium and nickel). Although clinical results are favourable, these stents have potential design inherited disadvantages, mainly foreshortening and rigidity, and could possibly be improved. Recently, dedicated venous stents of nitinol (nickel and titanium) have therefore been designed to specifically treat venous obstructions with these disadvantages in mind. Nitinol is commonly used in the arterial system and is known for its superelasticity and shape memory (recovers its designed form at body temperature). Clinical results using dedicated venous stents and comparison between different types of stent are lacking. The optimal design and material of a venous stent is presently not known.

In the arterial system, in most cases it is sufficient to use PTA alone. In the venous system, PTA must always be complemented by a stent placement to avoid collapse of the vein.^{26,479,480}

Scientific evidence. Sixteen articles have been identified related to PTA and stenting.^{479–494} Fifteen articles are non-comparative in nature, with only four studies having a prospective design. The methodology is generally moderately clearly described and follow up varies from 2 to 144 months. Often there is no Kaplan-Meier survival analysis performed to assess patency rates; however, some studies with longer follow up report Kaplan-Meier data. Potential confounding factors related to clinical outcome are often not described, frequently additional treatment of the superficial system is performed during follow up. One study is a retrospective, comparative study.⁴⁸² This study has a large proportion of C6 patients, particularly in the intervention group, with a short follow up. There is a possible selection bias, as the inclusion and exclusion criteria are poorly described and it is not clear why patients are included in either the intervention or control groups.

In seven studies with a total of 426 legs there was NIVL, often May-Thurner syndrome, and post-thrombotic pathology present.^{479,480,482,483,489,492} Technical success was achieved in 87–100% of cases, with an average follow up of 45 months (range 4–120 months). Primary* patency was 78% (59–94%), assisted primary patency** 83% (63–90%), and secondary patency*** 93% (72–100%). Ulcer healing rates ranged from 47% to 100%,^{479,482,483,487,492} with 8% to 17% ulcer recurrence rates; patients with patent reconstruction performed generally better.^{479,487} Reduction of pain was observed in 48% of the patients and 61% showed reduction of oedema.⁴⁹⁰ In four studies, with a total of 1,000 lower extremities, NIVL was specifically assessed.^{484,485,487,493} Technical success was achieved in 96–100% of cases, with a follow up of 59 months (6–72 months). Primary* patency was 85% (79–99%), and assisted primary** and secondary

patencies*** were 100%. Rates of ulcer healing ranged from 82% to 85%,^{485,493} with 5% to 8% recurrence.^{485,487} There was statistically significant improvement at all points of the CIVIQ,⁴⁸⁷ and in the VAS and QoL scores.^{487,493} Oedema decreased in 32% to 89% of cases,^{485,487,493} and hyperpigmentation improved in 87%.⁴⁸⁵

In six studies with a total of 921 legs, secondary (post-thrombotic) obstruction was specifically examined.^{481,486–488,490,491} Technical success was achieved in 93–100% of cases, with a mean follow up of 46 months (2–72 months). Primary patency* was 57% (50–80%), assisted primary patency** 80% (76–82%), and secondary patency*** 86% (82–90%). Ulcer healing ranged from 63% to 67%,^{486,490} with 0 to 8% recurrence.^{487,490} There was statistically significant improvement at all points of the CIVIQ⁴⁸⁷ and VCSS⁴⁹¹ scores. Oedema decreased in 32–51% of cases.^{486,487,490}

* Primary patency: the vein is open without any additional intervention.

** Assisted primary patency: the vein is patent, but an additional intervention was needed to keep the vein patent.

*** Secondary patency: the vein is patent after one or more additional interventions were required to treat an occlusion of the vein.

Stent placement is safe with low mortality and morbidity. Stents in the external iliac vein may cross the inguinal ligament to “land” in the common femoral vein. It has been shown that in two thirds of patients with post-thrombotic disease it is necessary to implant stents down to the groin below the inguinal ligament to improve inflow into the reconstructed iliac veins.^{487,491} Interventions distal to the groin, including endophlebectomy or stenting further down into the femoral vein or profunda femoral vein are not yet validated.

4.9.1.2. Open bypass procedures. Scientific evidence. Two studies from the same institution were identified, with

different types of surgical bypasses, that is femoro-femoral bypass (Palma procedure, using GSV or polytetrafluoroethylene bypass), femoro-iliac-inferior vena cava bypass, spiral vein grafts, and femoral vein patch angioplasty.^{495,496} The most recent report also includes the data of the first publication and data about hybrid reconstructions (endophlebectomy, patch angioplasty, stenting).⁴⁹⁵ Both studies are retrospective in nature and often include patients who have already had previous venous interventions, which are not clearly described. A second problem with these studies is that different procedures were performed. Results are not always entirely clear, although Kaplan-Meier analyses were calculated. In these studies with a total of 110 legs and a follow up of 31 to 41 months, there was 89% technical success.⁴⁹⁵ Primary patency of 42% and secondary patency of 56% were achieved at 60 months. Ulcer healing was not registered.

AbuRahma reported a low clinical success and primary patency rate for saphenopopliteal venovenous bypasses (May-Husni procedures) of 56% after 66 months.⁴⁹⁷

New externally reinforced, ringed, grafts with large diameters and coating may affect future results in a positive fashion. Selectively constructing an AV-fistula may also influence patency positively.

4.9.2. Treatment of deep venous incompetence

Introduction. Deep venous incompetence can be divided into primary and secondary forms. In primary incompetence, the structure of the valve sometimes remains intact and is therefore suitable for external or internal repair (valvuloplasty). More commonly there is valvular incompetence caused by DVT. This secondary, post-thrombotic incompetence is caused by a destruction of the valve as a result of the inflammatory response in the thrombus, vein wall, and valve. There are two options for reconstruction. One is to replace the affected valve by transposition or transplantation of a vein segment containing a valve; the second is to create a neovalve from the thickened vein wall.

Recommendation 56	Class	Level	References
In patients with clinically relevant chronic ilio-caval or ilio-femoral obstruction or in patients with symptomatic non-thrombotic iliac vein lesions, percutaneous transluminal angioplasty and stent placement using large self expanding stents should be considered.	IIa	B	479-483, 485-494
Recommendation 57			
Percutaneous transluminal angioplasty is not recommended as a single treatment for patients with chronic deep venous obstruction.	III	C	26, 479, 480
Recommendation 58			
After percutaneous transluminal angioplasty stent placement should be considered for patients with chronic deep venous obstruction.	IIa	C	479-483, 485-494

Recommendation 59	Class	Level	References
In patients with deep venous obstruction bypass, surgery is not recommended as standard primary treatment.	III	C	495-497

Scientific evidence. A total of 24 articles were identified that describe the non-conservative treatment of deep venous reflux.^{498–520} There were 19 retrospective, one prospective case series, and four prospective cohort studies. In addition, one meta-analysis⁵²⁰ was performed. A wide variety of surgical techniques were described, including: internal valvuloplasty, external valvuloplasty, valvuloplasty through external “banding”, creation of a new valve from the local vessel wall (“neovalve”), transposition of the incompetent vein on to a competent vein, trans-

Most patients with deep venous incompetence can be treated with conservative measures alone. A surgical correction is indicated only when, despite the use of adequate compression therapy and a strict adherence to lifestyle advice, severe symptoms persist, such as leg ulcers. Surgical repair of deep venous incompetence cannot be considered as a replacement therapy, but it is performed in addition to conservative measures and surgical treatment of superficial venous incompetence, and, if necessary, perforating vein incompetence.

Recommendation 60	Class	Level	References
Deep venous obstruction should be treated first, before considering treatment of deep venous reflux.	I	C	513
Recommendation 61			
In the absence of deep venous obstruction and after abolition of superficial venous reflux, surgical correction of deep venous axial reflux (proven by duplex ultrasound and descending venography) may be considered in patients with severe and persistent symptoms and signs of chronic venous disease.	IIb	C	498-504, 506-520
Recommendation 62			
Surgical treatment of patients with deep venous reflux, but without severe clinical symptoms and signs of chronic venous disease, is not recommended.	III	C	

plantation of an autologous valve bearing vein segment to an incompetent vein in the leg, and other less common techniques of valve repair. Often, these operations were combined with surgical treatment of incompetent superficial or perforating veins during or just before or after deep venous surgery, which makes the interpretation of the results rather difficult. In general, very heterogeneous populations, often with only small patient numbers (between 20 and 50), were described or patient history and demographics were simply not mentioned. Outcome measures used were heterogenous. In conclusion, it can be stated that the durability of all of these techniques cannot be derived from the available literature.

Summary. In general, good short-term results are described in all the above mentioned studies for all techniques. Technical success of the operation is close to 100%, when it is described. Competence of the replaced or repaired valve during follow up is variable between 35% and 100% at a follow up of up to 144 months.^{498–520} There seems to be a trend in the literature, that valvuloplasty and creating a neovalve leads to better results than transposition or valve transplantation. Success rates of 70% are reported after valvuloplasty in primary incompetence versus 50% after transposition or transplantation in post-thrombotic patients at 60 months.⁵²¹ Overall, ulcer healing varies between 54% and 100% up to 5 years.

As no comparative studies have been performed, it is not possible to indicate which valve (re)construction techniques or other invasive treatments should be performed and at what timing, in patients with deep venous incompetence.

In addition to all invasive treatment options, compression therapy is mandatory, presumably lifelong. Patients with post-thrombotic changes may continue to suffer from venous reflux (e.g. calf veins) and/or obstruction. Compression therapy improves venous outflow and may enhance the patency of the reconstruction.

Therapeutic anticoagulation (AC) with coumadins or LMWH is necessary after PTA and stenting, at least for patients with chronic obstruction after DVT. The duration of AC is unclear and should last at least 3 months. Some authors recommend lifelong AC. LMWH and antiplatelet drugs are recommended by some authors for treatment after PTA and stenting of the deep venous system in NIVL patients.

CHAPTER 5: RECURRENT VARICOSE VEINS

Introduction

Varicose vein recurrence following surgical intervention is a common problem for both patients and clinicians. Whether after open surgery or endovenous intervention, mid-term recurrence rates remain in the region of up to 35% at 2 year follow up, and 65% at 11 year follow up.^{423,522–524}

According to an international consensus meeting held on recurrent varices after surgery (REVAS), the definition of recurrent varicose veins is as follows: “the existence of varicose veins in a lower limb previously operated on for varicosities, with or without adjuvant therapies, which includes true recurrences, residual veins and new varices, as a result of disease progression.”^{107,525,526}

In the more recently published “Vein Term Update,” a new acronym has been introduced to describe both

recurrent varices (i.e. those presenting de novo in an area previously treated successfully) and residual varices (i.e. those remaining after treatment).¹ PREVAIT stands for PREsence of Varices (residual or recurrent) after InTervention and defines recurrent varicosities following both surgery and endovenous intervention (thermal, ultrasound guided foam sclerotherapy [UGFS]).

Recurrence can be classified according to clinical criteria and duplex ultrasound (DUS) examination. Clinical recurrence has to be further defined by DUS examination.

5.1. Etiology

The etiology of recurrent varicose veins is still poorly understood. It was originally thought that these were largely tactical and technical errors resulting from poorly planned or completed procedures.^{107,168} There is, however, evidence suggesting that factors such as neovascularization may be involved in recurrence.^{167,524,527}

The sources of reflux feeding recurrent varicosities, assessed by venous DUS, can be multiple, but have been reported most commonly at the SFJ.¹⁰⁷ A multicentre study identified incompetence at the level of the junction in 47% of their patients: 10% had no identifiable source of reflux; 75% of legs assessed had incompetent perforator veins, whereas in 17% it was of pelvic or abdominal origin.

Pelvic vein reflux has been identified as an important contributing factor to varicose vein recurrence.⁵²⁸ It is particularly common in multiparous women, having been reported in 44% of parous and 5% of nulliparous asymptomatic women.⁵²⁹ Pregnancy increases blood volume and causes compression of the pelvic veins secondary to the gravid uterus, resulting in pelvic vein incompetence.⁵³⁰ In addition to mechanical compression, hormonal effects may also be implicated in the development of varicose veins in pregnancy, with both oestrogen and progesterone receptors present in normal and varicose vein walls.^{531–533} Venous obstruction, secondary to DVT, or direct compression, secondary to pelvic pathology, may also contribute to varicose vein recurrence.

A prospective study of 113 limbs identified four main causes of recurrence (Table 13).¹⁶⁶

Tactical error. Tactical error refers to errors in pre-operative planning. This includes erroneous identification of the refluxing segment. With the advent of improved pre-operative imaging in the form of venous DUS examination and with minimally invasive ultrasound guided techniques providing targeted treatment, human error should play a lesser part in the development of recurrence.⁵³⁴ Pre-operative DUS imaging has been shown to improve the results of varicose vein surgery, based on correct identification of incompetence in the GSV, AASV, and/or SSV system.⁵³⁴ Tactical errors also include decisions regarding the surgical approach by the treating physician that may result in recurrence.

There is evidence that stripping or ablating the GSV, as opposed to performing high ligation only, results in reduced recurrence rates. A randomized trial of SFJ ligation ± GSV stripping revealed recurrence rates at 2 years of 43% in the ligation group and 25% in the ligation + stripping group.⁵²²

Table 13. Causes of recurrent varicose veins (least to most common).

Tactical error — 4%	Persistent venous reflux in a saphenous vein secondary to inadequate preoperative evaluation and inappropriate surgery
Technical error — 5.3%	Persistent venous reflux due to inadequate or incomplete surgical technique
Neovascularisation — 13%	Presence of reflux in a previously ligated SFJ or SPJ caused by development of incompetent tortuous veins linked to thigh (or calf) varicosities
Disease progression — 15%	Development of venous reflux secondary to the natural evolution of the disease

In endovenous intervention, the persistence of a below knee refluxing GSV segment (i.e. ablation of the above knee segment only) was found to be associated with recurrence, reflux, and the need for further intervention.⁵³⁵ However, the increased risk of paraesthesiae and saphenous nerve damage following treatment of the below knee GSV should be taken into account.⁵³⁶

When planning intervention in CVD, it is of paramount importance to carefully discuss the risks and benefits of each option with the patient.

Technical error. Technical error refers to inaccurate treatment at the time of surgery or endovenous intervention. This may be related to poor access, poor visualization of the target vein segment and the SFJ or SPJ (in ultrasound guided endovenous procedures), or inexperience.

Historically, a lack of experience by the operating surgeon has been blamed for high recurrence rates. However, there is evidence against this, suggesting that human, or technical error, plays a lesser role in the development of recurrence compared with neovascularization and disease progression.^{166,537}

Neovascularization. Neovascularization refers to the formation of new veins, typically at the site of the previous ligation of the GSV or SSV. This results in reconnection of the deep vein with a residual main saphenous trunk (if not stripped) or with superficial tributaries, eventually resulting in clinical recurrence.⁵³⁸ After GSV stripping, revascularization of the saphenectomy track has been observed, seen as multiple tortuous venous channels in the track of the previously stripped GSV.⁵³⁹

On DUS examination, neovascularization is visualized as a network of complex, tortuous vessels, connecting the end, or stump, of the GSV or SSV to a tributary in the thigh or calf.^{148,164} It is important to note that different degrees of DUS-detected neovascularization exist; neovascularization is present in 25–94% of recurrent varicose veins.^{540,541} However, assessment of neovascularization on DUS examination can be challenging.

The mechanism for the development of angiogenesis and neovascularization is still unclear.⁵²⁴ Mediators such as growth factors (e.g. vascular endothelial growth factor), matrix metalloproteinases, and angiopoietin are involved.¹⁶⁴ A number of theories have been postulated to explain why neovascularization develops post-operatively. It may be part of the physiological healing process after venous surgery. In the track where the original vein was stripped, the post-operative haematoma may organize, with development of capillaries, venules, and finally tortuous recurrent veins. Altered venous haemodynamics may lead to its development. Or finally, it may be a physiological response to venous disconnection.

Either way, neovascularization has been found to account for a considerable proportion of recurrences and there is evidence suggesting it plays a greater role in open surgery than in endovenous therapy.¹⁶⁶ DUS examination detected neovascularization in 18% of the surgery group and 1% of the Endovenous Laser Ablation (EVLA) group, while clinical recurrence rates were similar.¹⁶⁷

However, the presence of DUS detected recurrence does not necessarily mean a new intervention is needed. The rate of re-operation following varicose vein surgery was shown to vary according to the nature of the recurrence.⁵³⁴ DUS detected neovascularization seldom required re-intervention, whereas patients with recurrent or residual varicose veins because of tactical or technical failure had more re-operations during a follow up period of 7 years.

Disease progression. Disease progression accounts for a large proportion of recurrences.¹⁶⁶ The progression may be multifocal, ascending, or descending. According to the ascending pathophysiological principle, superficial veins may dilate and become varicose over time. According to the descending principle, ongoing reflux at the SFJ or SPJ and/or saphenous trunks may cause superficial tributaries to dilate and become varicose. As a result of disease progression, incompetence can also develop in a previously untreated saphenous trunk, for instance in the SSV, after previous treatment of the GSV, or in perforating veins.

Recurrent varicose veins remain a poorly understood entity with several proposed etiologic factors. Their incidence and severity may be related to the original treatment modality; however, disease progression may also play a major role. Further studies are required to increase

understanding of their development at a molecular level to enable the development of effective prevention and treatment strategies for recurrent varicose veins.

5.2. Risk factors

In addition to the aforementioned four factors, there is evidence suggesting that the original intervention has an impact on the likelihood of recurrence, although recurrence rates are largely comparable among treatment modalities.^{166,542}

5.3. Diagnosis of recurrent varicose veins

DUS is the preferred diagnostic approach to investigate recurrent varicose veins (see 3.2.3.3).

5.4. Treatment of recurrent varicose veins

The management of recurrent varicose veins is a challenge for the clinician. Repeated intervention is associated with reduced patient satisfaction.^{166,543,544} Therefore, a less invasive approach, consisting of multiple phlebectomies or alternative techniques, has been advocated to replace invasive redo surgery including re-exploration of the groin or popliteal fossa.^{545,546} Extensive redo surgery should be performed only in selected cases.

RFA and EVLA have been described as safe and effective options for treatment of recurrent varicose veins.^{377,547,548} The pattern of reflux feeding the recurrence can be from multiple origins, and the SFJ is often involved as a source.¹⁰⁷ Recurrence may also be secondary to incompetent perforators or pelvic vein incompetence. If a truncal vein segment is involved, this may be suitable for endovenous ablation, which may re-establish competence in previously incompetent perforating veins.⁵⁴⁷ Ablation of the refluxing axial segment has been reported to re-establish competence in previously incompetent perforator veins.⁵⁴⁷

When compared with conventional surgery in the treatment of SSV recurrence, EVLA was found to have a higher technical success rate and lower complication rate, particularly with respect to sural nerve neuralgia (20% vs. 9%).⁵⁴⁹ RFA was also found to be superior to redo groin surgery, with significantly lower pain scores, bruising, and procedure times.³⁷⁷

UGFS has also been used successfully in the treatment of recurrence,³²³ although with lower success rates compared with laser ablation.

Recommendation 63	Class	Level	References
Endovenous thermal ablation, ultrasound guided foam sclerotherapy, or phlebectomies should be considered for the treatment of symptomatic recurrent varicose veins.	IIa	B	323, 377, 547-549
Recommendation 64			
Extensive redo surgery (including re-exploration of the groin or popliteal fossa) is not recommended as a first choice treatment in patients with recurrent varicose veins.	III	B	377, 545, 549

CHAPTER 6: CONGENITAL VENOUS MALFORMATIONS

Introduction

CVD describes visual and functional abnormalities in the peripheral venous system, affecting most commonly, but not exclusively, the lower limbs. Classification systems, such as the CEAP classification,¹⁰⁹ have been employed to differentiate between congenital, primary, secondary, and unknown causes of CVD.

Congenital vascular malformations (CVMs) are present in a very small proportion of patients. However, despite a limited incidence, the magnitude and severity of their clinical manifestations can be striking. Congenital venous malformations are disorders resulting from abnormalities in the development of the venous system. Depending on the developmental aberration, venous, arterial, and/or lymphatic channels may be involved, resulting in heterogeneous clinical presentations.⁵⁵⁰

In this chapter, the classification of CVMs is discussed, paying particular attention to congenital venous malformations, as well as syndromes affecting the venous system, such as Klippel-Trenaunay (KTS) and Parkes-Weber syndrome (PWS).

6.1. Pathophysiology

The pathophysiology of CVMs is unclear and may be secondary to sporadic mutations or a possible hereditary component, although familial inheritance is rare. CVMs are non-degenerative and non-inflammatory in origin and can appear anywhere in the body.

Development of the circulatory and lymphatic systems begins in the third gestational week, with the formation of peripheral and central blood islands from mesoblastic cells. In the first developmental stage, proliferation and fusion of these cells results in the creation of a primitive capillary network. This is followed by retiform and plexiform stages as the foetus develops. Ultimately, specific vessels enlarge to contribute to the definitive circulatory system, while others that are present only in the embryonic stages regress.⁵⁵⁰

Aberrant development at any of these stages can result in CVMs. Importantly, if this occurs during the primitive capillary stage, the abnormal embryonic vessels remain in the form of clusters and do not differentiate into definitive vessels.

Furthermore, they are separate from the main venous trunk and are therefore defined as extratruncular.⁵⁵⁰ If the defect occurs at a later stage, it may lead to abnormalities in “named” vessels, with resulting hypoplasia, aplasia, obstruction, or dilatation. These are directly involved with the truncal venous system, and are therefore classified as truncular. This distinction is important in the classification of CVMs.

6.2. Classification

Introduction. CVMs are challenging to understand and define. A number of contributors have attempted to classify these lesions, aiming to develop a universal system to standardize their diagnosis and description, as well as to improve communication among specialists reporting in the literature. Different contributors have employed differing

Table 14. Haemangiomas and Vascular Malformations.

Haemangiomas
Vascular Malformations
- Capillary
- Venular
- Venous
- Lymphatic
- Arteriovenous
- Combined
○ Venous-lymphatic
○ Venous-venular

standards for their classifications, including embryological, anatomical, clinical, and haemodynamic criteria, resulting in heterogeneous classification systems.⁵⁵⁰ The International Society for the Study of Vascular Anomalies (ISSVA) aims to further increase knowledge of the pathogenesis, diagnosis, and treatment of patients with CVMs. Among its roles is review of specific classification systems.⁵⁵¹

6.2.1. International Society for the Study of Vascular Anomalies classification

Mulliken and Glowacki first introduced a biological classification based on pathological characteristics of the endothelium and the natural course of the vascular lesion.⁵⁵² This system made the distinction between vascular tumours (of which haemangioma is the most common) and vascular malformations (Table 14).

This classification was redefined⁵⁵³ and adopted by the ISSVA. Again, the distinction was made between haemangiomas and vascular malformations, which were subdivided into single system and combined lesions (e.g. arterial and/or venous, and/or lymphatic; Table 15).

6.2.2. Hamburg classification

The Hamburg classification was developed in 1988⁵⁵⁴ and approved by the ISSVA. This classification system described CVMs in terms of their anatomical and clinical characteristics (i.e. arterial, venous, shunt, or combined) and the embryological stage during which the malformation began to develop (truncular or extratruncular).

This classification system does not take into account haemangiomas or lymphatic malformations, but adequately describes lesions according to clinical and anatomical characteristics and facilitates communication between different specialties as a result of its descriptive nature (Table 16).

6.2.3. Puig classification

A new classification system was also developed by Puig, describing the subgroup of venous malformations (VMs) in terms of their anatomical characteristics and pattern of venous drainage (Table 17).⁵⁵⁵ The authors used this classification system as a basis for interventional therapy, particularly in assessing the suitability of paediatric patients for sclerotherapy.

6.3. Venous malformations

Venous malformations (VMs) are a subtype of CVMs. They have an estimated incidence of 1–2/10,000 births, a

Recommendation 65	Class	Level	References
The Modified Hamburg Classification system may be considered for the classification of vascular malformations.	IIb	B	⁵⁵⁴

prevalence of 1%, and are the most common type of CVM.⁵⁵⁶

Etiology. The majority of isolated VM's appear on a sporadic basis with no hereditary component,⁵⁵⁷ although rare autosomal dominant conditions such as familial cutaneo-mucosal VM or glomuvenous malformation exist.⁵⁵⁶

Clinical characteristics. VMs may not be apparent from birth, developing in later childhood or adulthood. Often rapid growth occurs in puberty. The location of VMs is relatively equally distributed: 40% occur in the head and neck area, 40% in the extremities, and 20% in the trunk.⁵⁵⁸

VMs present as soft, compressible, blue-tinged masses that, like veins, may change in size according to position or expand with the Valsalva manoeuvre.⁵⁵⁸ Superficial ecchymoses, teleangiectasiae or varicosities may be present. There is no evidence of pulsatility, thrill, raised temperature, or hyperaemia, differentiating them from arteriovenous malformations (AVMs). VMs are most commonly found in the skin and subcutaneous tissues; however, they can involve the

underlying muscle, bone, and viscera. If large in size, they may cause pressure effects on surrounding structures and planes, including bone, muscle, and subcutaneous tissue.

Importantly, VMs may be located intraorally and may cause bleeding, speech impediments, and airway obstruction. VMs are also at risk of thrombosis and there is evidence that the presence of VMs is associated with localized intravascular coagulopathic features.⁵⁵⁹

Diagnosis. DUS examination is the preferred initial imaging modality in the examination of VMs. It is safe, widely available, rapid, non-invasive, and low cost. Patients with VMs are young, so avoiding ionizing radiation is paramount. DUS allows differentiation between high flow (AVMs) and low flow (VMs, lymphatic malformations) CVMs. VMs are usually compressible, heterogeneous masses, and appear as hypoechoic, heterogeneous lesions in the majority of cases (82%). In a study of 51 soft tissue VMs, 16% had an identifiable pathognomic phlebolith on DUS.⁵⁶⁰

VMs may be difficult to differentiate from adjacent fatty structures. Fat suppression techniques, such as inversion recovery sequences (Short Inversion Recovery, STIR), may be helpful in characterizing lesions.

CT is of limited use because it requires ionizing radiation and because of its poor lesion characterization, particularly in cases where the VM is deep and adjacent to underlying structures.⁵⁵⁶ In addition, the use of contrast CT may underestimate the true lesion extent.⁵⁵⁸

MR imaging, with its superior soft tissue and lesion characterization, is the preferred imaging modality to define lesion extent and the relationship with adjacent

Table 15. Tumours and Vascular Malformations.

Tumours	
Haemangiomata	Superficial (capillary of strawberry) Deep (cavernous) Combined
Others	Kaposiform haemangioendothelioma Tufted angioma Haemangiopericytoma Spindle-cell haemangioendothelioma Glomangiomas Pyogenic granuloma Kaposi sarcoma Angiosarcoma
Vascular Malformations	
Single	Capillary (C) (port wine stain, naevus flammeus) Venous (V) Lymphatic (L) (lymphangioma, cystic hygroma) Arterial (A)
Combined	Arteriovenous fistula (AVF) Arteriovenous malformation (AVM) Capillary Lymphatic Venous Malformation (CLVM) [(associated with Klippel-Trenaunay Syndrome (KTS)) - Capillary Venous Malformations (CVM) - Lymphatic Venous Malformation (LVM) Capillary, arteriovenous malformation (CAVM) Capillary, lymphatico - arteriovenous malformation (CLAVM)

Table 16. Modified Hamburg Classification.

Type of defect	Truncular	Extratruncular
Predominantly arterial	Aplasia	Infiltrating
	Obstruction	Limited
	Dilation	
Predominantly venous	Aplasia	Infiltrating
	Obstruction	Limited
	Dilation	
Arteriovenous shunting	Superficial AV fistula	Infiltrating
	Deep AV fistula	Limited
Mixed defects	Arterial and venous	Infiltrating
	Haemolympathic	Limited

Table 17. Puig Classification.

Type I	Isolated malformation without peripheral drainage
Type II	Malformation that drains into normal veins
Type III	Malformation that drains into dilated veins/venous ectasia
Type IV	Malformation that represents dysplastic venous ectasia

structures.⁵⁵⁶ Fat suppression techniques, such as inversion recovery sequences (Short inversion Time Inversion Recovery, STIR), may be particularly helpful in characterizing lesions difficult to differentiate from adjacent fatty structures.⁵⁶¹

Direct percutaneous phlebography entails fine needle puncturing of the VM and contrast injection under fluoroscopy. It is the imaging modality of choice to diagnose VMs in situations where previous imaging has been equivocal⁵⁵⁶ and is used during sclerotherapy procedures as an initial diagnostic evaluation.

Management

The management of VMs involves a number of disciplines, including surgery, dermatology, medicine or paediatrics, and radiology. Clear communication between members of these disciplines and a true multidisciplinary approach are extremely important in the assessment and management of patients with VMs.

Conservative. VMs can be a chronic, non-life threatening condition with a potentially variable clinical picture. Mild symptoms are successfully managed with conservative measures, including limb elevation during sleep and avoidance of activities that may exacerbate symptoms. Patients can have localized intravascular coagulopathy, which may lead to thrombosis and paroxysmal pain.⁵⁵⁹ Aspirin and prophylactic treatment with LMWH have been used in selected cases as an adjunct to conservative treatment,⁵⁵⁶ while elastic compression garments have been employed to provide symptomatic relief.⁵⁶²

Sclerotherapy. The rationale for using sclerotherapy to treat VMs is the same as for treating varicose veins: to cause damage to the venous endothelium. A sclerosing agent (e.g. ethanol, sodium tetradecyl sulphate [STS] or polidocanol), in liquid form or aerated to produce foam, is directly delivered into the venous lumen via fine needle injection under image guidance (e.g. ultrasound, phlebography), allowing the agent to directly interact with the endothelium.⁵⁵⁶

QoL measures following sclerotherapy to VMs have revealed improved symptoms following therapy.⁵⁶³ Patients with localized VMs did better than those with diffuse malformations affecting whole muscles or compartments.

The choice of sclerosant agent is an important variable in both the efficacy and complication rate profile of the different agents. A large series reporting the use of ethanol in 87 patients over 399 sessions has revealed initial success rates of 95%, with no recurrence at follow up (average 18.2 months).⁵⁶⁴

Minor and major complication rates were 12.4%: erythema, blistering, and localized skin ulceration or necrosis, as well as DVT and pulmonary embolism (reported in 1.25% and 0.25% of sessions, respectively) have all been reported.

Sodium tetradecyl sulphate (STS) has a more favourable side effect profile. A large series of 72 patients over 226 sessions revealed no major complications. Minor complications were present in approximately 3% of the sessions, including ulceration, skin necrosis, and transient sensory deficits.⁵⁶⁵ According to this series, after treatment, 15% of

patients became asymptomatic, 28% rated the therapy as good, 24% were improved, 28% unchanged, and 5.6% felt worse. Again, patients with infiltrative lesions reported poorer outcomes than those with localized lesions.

Polidocanol has the lowest side effect profile, with pain and swelling being the most common complications.⁵⁵⁶ A retrospective series of 19 patients with VMs found that, after treatment, patients reported a decrease in pain and significant reduction in the size of the lesion.⁵⁶⁶

A prospective study compared use of UGFS with ultrasound guided liquid sclerotherapy in treatment of symptomatic VMs. UGFS required a significantly smaller volume of sclerosant and had improved treatment outcomes compared with liquid sclerotherapy.⁵⁶⁷

Surgical. The decision to treat VMs surgically should be multidisciplinary. The main indications for treatment are persistent pain, functional impairment, or cosmetic implications in head and neck lesions, as well as location posing a realistic risk to the patient (e.g. lesions affecting the airway).⁵⁵⁸

Surgical resection is appropriate in patients with focal, well-defined VMs that are thrombosed and limited to a specific area. However, many VMs are infiltrative and involve more than one muscle group or fascial plane, resulting in extensive debulking. In these cases, sclerotherapy can be used as an adjunct.⁵⁵⁶ Truncular VMs with deep venous abnormalities may require resection and deep venous reconstruction. Extratruncular, diffuse VMs are best treated with sclerotherapy.

Patients with VMs should be treated conservatively or with sclerotherapy where possible.

6.4. Syndromes

Some forms of combined congenital vascular malformations have been previously described as syndromes. The two most important syndromes are KTS and PWS, and both will be discussed in this chapter.

6.4.1. Klippel-Trenaunay syndrome

Maurice Klippel and Paul Trenaunay first described this condition in 1900, referring to it as “naevus vasculosus osteohypertrophicus” after observing two patients with skin lesions associated with asymmetric soft tissue and bone hypertrophy.⁵⁶⁸

Vascular malformations can be single or combined depending on the components of the circulatory system that are involved in the lesion.⁵⁵³ KTS is a syndrome characterized by capillary, venous, and lymphatic abnormalities, without significant arteriovenous shunting. It is a rare condition, occurring in 1:20,000-1:40,000 live births with an unclear cause.⁵⁶⁹ Patients with this condition are characterized by the clinical triad of port wine stain, varicose veins, and soft tissue and/or bone hypertrophy (occasionally hypotrophy).

6.4.1.1. Etiology. The genetic origin of KTS is still unclear. The literature on the subject is heterogenous, varying from sporadic cases⁵⁶⁸ to single gene defects.⁵⁶⁹

With regards to the development of clinical signs and symptoms, several theories have been proposed. It is thought that KTS presents as a consequence of a

mesodermal abnormality during foetal development, resulting in the maintenance of microscopic arteriovenous communications in the limb bud, leading to the development of naevi, hypertrophy, and superficial varices.⁵⁷⁰

Other developmental theories include primary obstruction or atresia of the venous system (leading to increased venous pressure, chronic venous hypertension, limb hypertrophy, and varicose veins)⁵⁷¹ and increased angiogenesis during development.⁵⁷²

6.4.1.2. Clinical characteristics. Clinical findings are usually present at birth, but in some cases they may not be fully apparent.⁵⁷³ Clinical features are variable, ranging from minimal disease to disfigurement with a significant cosmetic impact.

Clinical signs: capillary malformation (naevus flammeus). In KTS patients typical capillary malformations are seen, often described as “naevus flammeus.” There are characterized by reddish pink macules that are present from birth but may not be visible until a few days after delivery.

Capillary malformations are present in KTS in up to 98% of patients, making them the most common associated clinical abnormality.⁵⁷⁴ They are usually multiple, affecting the lower limb in 95% of cases, and can spread to the buttock or chest. Rarely, the entire side of the body may be affected.

Clinical signs: varicose veins. Varicose veins are another clinical feature associated with KTS. Abnormal veins can manifest as anomalous lateral veins or persistent embryonic veins. These are dilated and tortuous secondary to valvular incompetence or deep venous abnormalities. In the Mayo Clinic series, 72% of patients had atypical veins, the most common abnormality being the persistence of a lateral embryonic vein.⁵⁷⁵ The authors advised that the presence of a large, persistent, superficial vein in the lateral thigh that does not join the deep system should alert the clinician to the possibility of KTS. A smaller proportion of patients had an anomalous medial vein or, more rarely, a suprapubic vein.

In addition to superficial venous abnormalities, the deep venous system also may be anomalous. Venous ectasia, hypoplasia, aplasia, or the persistence of an embryological sciatic vein are all manifestations of deep venous abnormalities in KTS.

Clinical signs: lymphatic hyperplasia. Lymphatic hyperplasia is found in a large number of patients. This presents as vesicles containing clear fluid and may be associated with marked lymphoedema, resulting in soft tissue hypertrophy and leg length discrepancy. In a large series from the Mayo Clinic, lymphatic hyperplasia was present in 67% of their patients.⁵⁷⁵ Importantly, the presence of this triad was variable. In 63% of patients, all three features were present, while the remaining patients had two or fewer. Furthermore, most had lower limb malformations, mainly unilateral. Only 30% suffered from upper limb malformations.

Patients with KTS are at increased risk of developing superficial vein thrombosis, DVT and pulmonary embolism.⁵⁶⁹

Symptoms. The diagnosis of KTS is made according to the presence of physical signs. However, patients may present with symptoms, most commonly swelling, pain, bleeding from superficial varicosities, and superficial thrombophlebitis.⁵⁷⁵

Pain is a significant complaint, with up to 88% of patients experiencing varying degrees of discomfort.⁵⁷⁶ A number of factors causing pain and discomfort in patients with KTS have been identified, including varicose veins, CVI (C3–C6), cellulitis, superficial vein thrombosis, DVT, vascular malformations, arthritis, and neuropathic pain.⁵⁶⁹

6.4.1.3. Diagnosis. The diagnosis of KTS is largely clinical. As for CVD, DUS examination is the gold standard to assess the superficial and deep venous systems in these patients. This enables assessment of aberrant venous anatomy, as well as confirming the absence of any clinically significant arteriovenous shunting.

Plain radiographs are used to measure limb length in the first instance. Other helpful imaging modalities to assess for venous abnormalities include MR imaging (useful to differentiate between bone, fat, muscle hypertrophy, and lymphoedema), MR angiography and/or venography, CT imaging (helpful in assessing bony anatomy), and contrast studies (arterial and venous), which allow delineation of the deep venous system and collaterals, as well as revealing localized vascular malformations.⁵⁷⁴

6.4.1.4. Management. KTS is a rare, complex disorder requiring a multidisciplinary approach to its management.⁵⁷⁷ This involves a number of specialties, including paediatrics, general medicine, orthopaedic, plastic and vascular surgery, interventional radiology, cardiology, and physical therapy.⁵⁷⁸

The disorder is a mixed vascular malformation, with capillary, venous, and lymphatic components. There is no cure for the syndrome, and treatment is directed towards symptomatic management, secondary prevention of venous hypertension, and preservation of functional integrity of the legs.⁵⁷⁹

Patients often do well without intervention; however, absolute indications for treatment exist. These include haemorrhage, infection, acute venous thromboembolism, and refractory ulceration.⁵⁷⁸

Conservative treatment. The treatment of VMs is similar to that of other forms of CVD. Limb elevation, compression therapy (stockings or compression bandaging), and decongestive physical therapy, in the form of massage, all can be beneficial in the management of the hypertrophied limb affected by lymphoedema and CVI (C3–C6). Skin care is paramount in patients at risk of developing cutaneous manifestations of CVD, including ulceration.⁵⁸⁰

Because of the increased risk of venous thromboembolism, AC may be considered in patients with recurrent episodes of superficial or deep vein thrombosis.⁵⁷⁸

TCL therapy has been used in the treatment of naevus flammeus to lighten or, where possible, remove the cutaneous abnormality.

Surgical treatment. Surgical intervention is limited to those patients who are not candidates for conservative treatment. It is important to fully assess both the superficial and deep venous systems by DUS to evaluate the extent of VMs and the patency of the deep venous system prior to performing any surgical procedures.⁵⁸⁰

The Mayo Clinic has published the largest reported series of patients with KTS.⁵⁷⁵ According to their experience, the most common operations performed in these patients were

epiphysiodesis (i.e. fusion of the epiphyseal, or growth, plate, in a child to slow or halt the growth of a limb), stripping of refluxing truncal veins, debulking procedures, and amputations. Nonetheless, they advised that patients with KTS should be treated conservatively where possible.

Abnormal veins and obvious varicosities can be removed where the deep venous system is competent and functional. Otherwise, compression therapy has been used successfully to reduce swelling and signs of venous disease.⁵⁸⁰

Incompetence of the main superficial trunks in KTS patients may not only be addressed by stripping, but also with more modern technology in the form of endovenous thermal (laser or radiofrequency) ablation or foam sclerotherapy.^{551,581}

UGFS with STS and polidocanol has been used to treat superficial varicose tributaries with good cosmetic and functional results, with a reduction in pain levels and in the size of varicosities.^{566,579}

Endovascular RFA has also been employed to treat venous insufficiency in patients with this syndrome. Patients reported decreased leg pain, oedema, and varicose vein prominence after intervention.^{551,582} In selected cases, both treatment modalities can be used together for the treatment of superficial venous disease.⁵⁸¹

Open surgery is not only limited to ligation and stripping, but also includes deep venous reconstructions or entrapped popliteal vein release in those cases where embryological abnormalities have left the patient with significant deep venous anomalies. Recurrence rates for treatment of VMs can be up to 15%, but clinical improvement in patients is significant and further interventions may be performed if required.⁵⁸⁰

Limb hypertrophy, resulting in leg length discrepancy, may be treated by epiphysiodesis in the growing child where the difference is predicted to exceed 2 cm. Very rarely, amputation is required where the size of the limb affects the patient's day to day functioning.⁵⁸³

6.4.2. Parkes-Weber syndrome

PWS presents similarly to KTS but has a distinct pathophysiological mechanism. It was first described in 1907 by the physician Frederick Parkes Weber. The incidence is sporadic, with no apparent racial or gender predilection.

6.4.2.1. Etiology. Unlike KTS, which is a low flow malformation involving the capillary, venous, and lymphatic systems, PWS is characterized by fast flow arteriovenous abnormalities. It is present from birth and most commonly affects the lower limbs. Persistent lateral thigh vein is uncommon, and lymphatic and soft tissue malformations do

not usually occur.⁵⁵¹ The presence of a fast flow fistula can increase cardiac preload, leading to cardiac failure, and even cutaneous ischaemia.

Originally thought to be a sporadic disease, there is evidence that the *RASA1* gene on chromosome 5 plays a significant role in the development of PWS. This gene mediates growth, differentiation, and proliferation of several cell types, including vascular endothelial cells.^{584,585} Mutations result in multifocal capillary malformations with fast flow vascular lesions.⁵⁸⁴

6.4.2.2. Clinical characteristics. PWS is characterized, like KTS, by capillary cutaneous malformations and limb hypertrophy, in addition to AVMs. The connections between arteries and veins are high flow, and can result in skeletal or soft tissue hypertrophy. Local effects of arteriovenous fistulae are prominence and dilatation of the superficial veins secondary to increased pressure. A bruit or machinery murmur is audible and palpable throughout the cardiac cycle.

The presence of high flow fistulae prior to epiphyseal union results in regional effects, including increase in bone length, girth, and in the temperature of the affected limb.

Systemic effects are the result of the large flow of blood travelling from the arterial to the venous system. This can result in a marked increase in cardiac preload, leading to congestive cardiac failure.⁵⁸⁶

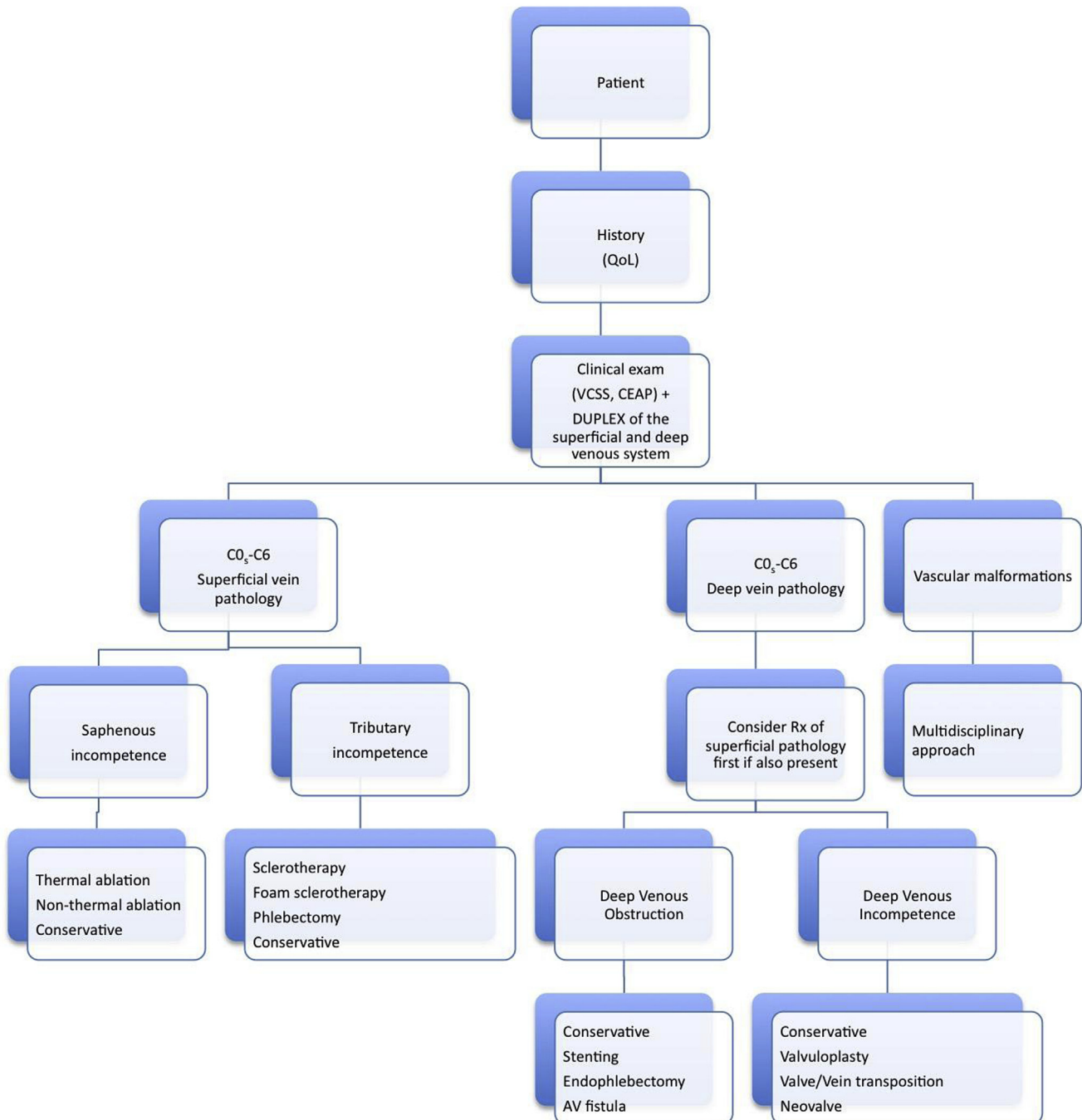
6.4.2.3. Diagnosis. Similar to KTS, DUS examination can be very helpful in characterizing arterial and venous anatomy, as well as in differentiating between high and low flow anomalies. Plain radiographs and MR imaging are helpful in assessing the hypertrophied limb. MR studies also provide assessment of lymphatic, venous, and soft tissue components of the affected limbs.⁵⁸⁷ Arteriography and venography can assess the circulatory anatomy and characterize arteriovenous fistulation.

6.4.2.4. Management. Conservative management, where possible, is preferred. This includes prevention of trauma and damage to the affected limb as healing may be impaired and the patient is at an increased risk of bleeding in the presence of AVMs. Lower limb swelling may be managed with limb elevation and compression therapy. Limb growth, similar to KTS, can be addressed with epiphysiodesis where marked.

Fast flow, significant AVMs associated with clinical signs (e.g. ulceration or congestive cardiac failure), are a potential indication for intervention. This is in the form of arterial embolization or surgical resection of the lesion.^{585,588} In extreme cases, amputation may be required where the affected limb is markedly impinging on a patient's QoL.

Recommendation 66	Class	Level	References
Symptoms and signs of chronic venous disease secondary to congenital venous malformations should be treated conservatively where possible.	I	C	551, 563, 566, 579, 585, 588
Recommendation 67			
Potential interventions in severe cases of congenital venous malformations, Klippel-Trenaunay syndrome, and Parkes-Weber syndrome should be decided by a multidisciplinary approach in a specialised centre	I	C	

Flowchart 'Management of chronic venous disease'



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