

**The role of medial calf perforating veins in the
development of chronic venous insufficiency and
ulceration**

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Abstract

The procedure of open perforator ligation was popularised by Linton and Cockett but became less favoured as it was associated with frequent wound complications, prolonged stay in hospital and mixed results in reported series. Two technological advances have resulted in the impetus to reappraise the indications for surgical interruption of calf perforating veins. Duplex ultrasound is a non-invasive investigation that has allowed anatomical and functional information on blood vessels and flow to be gathered safely and painlessly. Secondly, minimal invasive surgical instrument technology allows interruption of the medial calf perforating veins with expectation of reduced complication rates. The aim of the present work therefore, is to define the role of calf perforating veins in the development of the complications of chronic venous insufficiency.

Deteriorating clinical status of the limb was associated with increasing number and maximum diameter of medial calf perforating veins. The number and proportion of these vessels demonstrating bidirectional flow (incompetence) also increased with deteriorating clinical findings. Incompetent calf perforating veins were found to be associated with main stem venous reflux in the superficial and deep systems, but were rarely found as the sole venous abnormality. Surgical correction of the main stem venous reflux resulted in the correction of the physiology in the majority of incompetent perforating veins (IPV). The minimally invasive approach to the interruption of IPV showed several advantages over the open approach in terms of documented complications and post-operative stay in hospital.

The present work demonstrates associative evidence of a link between the presence of IPV and the development of the complications of chronic venous insufficiency, evidence that saphenous surgery alone will correct IPV physiology without direct intervention to perforators, if the deep system is normal, and also evidence that minimally invasive perforator surgery is associated with few complications over and above those expected for routine varicose vein surgery.

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Finally, I would like to thank the patients and volunteers who so willingly took part in the studies.

Declaration

The work described in this thesis is completely original and all the work was performed by me including the duplex ultrasonography. I also performed the statistical analyses, except those in Chapter 4, which were performed by Dr AJ Lee as indicated.

Dedication

This work is dedicated to my parents Carol and Peter with gratitude for their love and support throughout my education and career.

Abbreviations

ABPI	ankle-brachial pressure index
APG	air plethysmography
AVP	ambulatory venous pressure
CEAP	clinical (a)etiological anatomic pathological (grading system for venous disease)
CVU	chronic venous ulceration
DVI	deep venous insufficiency
DVT	deep venous thrombosis
EVS	Edinburgh Vein Study
ICAM	inter-cellular adhesion molecule
LDS	lipodermatosclerosis
LFVLUS	Lothian and Forth Valley Leg Ulcer Study
LRR	Light Reflective Rheography
LSA	Lothian Surgical Audit
LSV	long saphenous vein
IPV	incompetent perforating vein
MVO	maximum venous outflow
NASEPS (register)	North American Subfascial Endoscopic Perforator Surgery
OR	odds ratio
PAOD	peripheral arterial occlusive disease
PDGF	platelet derived growth factor
PE	pulmonary embolism

PPG	photoplethysmography
PTV	posterior tibial vein
SEPS	Subfascial Endoscopic Perforator Surgery
SFJ	sapheno-femoral junction
SFV	superficial femoral vein
SPJ	sapheno-popliteal junction
SPSS	Statistical Package for Social Sciences
SSV	short saphenous vein
SVI	superficial venous insufficiency
VCAM	vascular cell adhesion molecule
VEGF	vascular endothelial growth factor
VSI	venous sufficiency index
VV	Varicose veins
WBC	white blood cell

Glossary

Atrophie blanche white patches on medial gaiter area of leg, associated with skin changes of chronic venous insufficiency

Cephalad towards the head

Chronic venous insufficiency (CVI) syndrome of failure of the venous system of the lower limb; loosely defined term used by some authors to indicate the underlying venous pathology, by others to suggest the presence of skin changes and by others to indicate both. In the present work, it refers to the presence of venous pathology.

Communicating veins veins connecting two venous systems, mostly muscular venous systems and the deep venous drainage of the leg, but not crossing a fascial plane, as distinct from perforating veins.

Colour-flow Doppler Ultrasound imaging system combining grey scale Ultrasound images with colour Doppler images and spectral Doppler analysis (Synonyms: Duplex, Doppler Ultrasound, Triplex)

Foot Volumetry method of venous haemodynamic assessment in which calf pump function is measured by volume changes

Lipodermatosclerosis skin changes associated with CVI. Palpable thickening of skin, redness, often accompanied by brown pigmentation of haemosiderin deposition.

Main stem veins venous trunks, named veins comprising the long and short saphenous veins and the crural, popliteal, superficial and deep femoral veins.

Perforating vein vein passing from the deep to the superficial venous systems, crossing a fascial boundary.

Pocket Doppler continuous wave Doppler device; produces audible signal of blood flow only, used for assessment of ABPI and assessing veins for reflux.

Post-phlebotic damage following a venous thrombosis, also frequently used to include the skin changes of CVI as the post-phlebotic syndrome

Reflux retrograde flow down a vein

Trendelenberg position supine subject, flat with a head down tilt.

Venous obstruction poorly defined term in frequent use regarding deep vein occlusion, can be used to describe spectrum of disease from functional stenosis to complete occlusion.

Valsalva Manoeuvre, forced expiration against a closed glottis. Used to raise the intra-abdominal pressure, or to increase vagal tone.

Chapter 1.

Introduction, historical perspective and review of the literature

1.1 Introduction

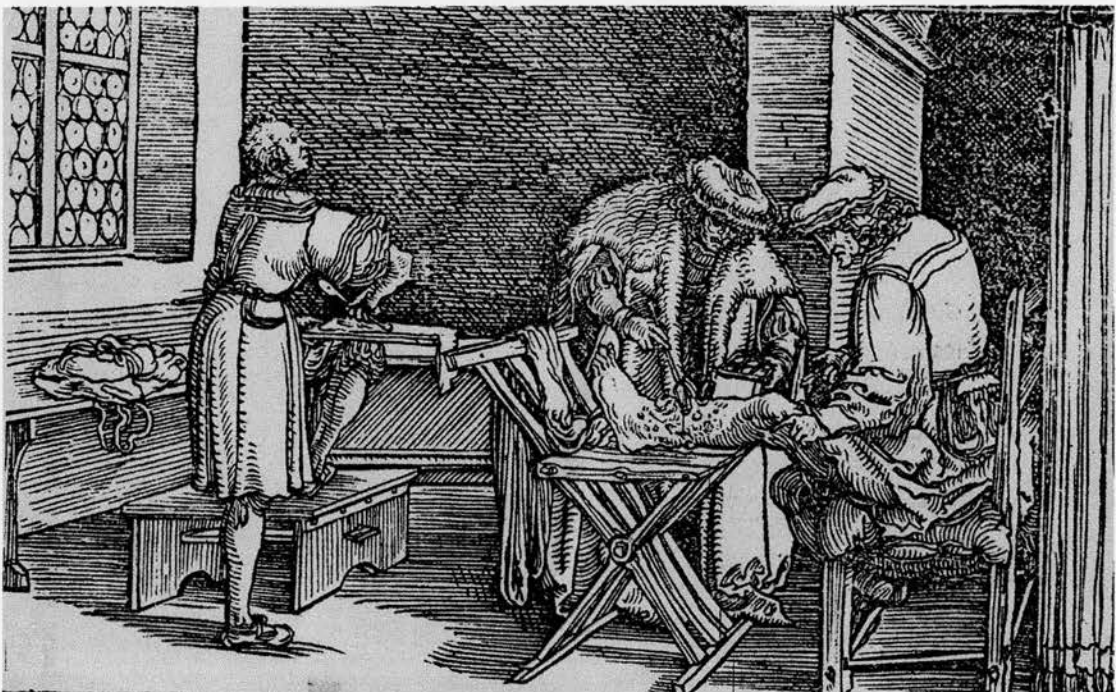
Orwell used a relapsing varicose ulcer to symbolise the wretched state of the captive Winston Smith in 1984 (Orwell 1948). He described in detail the pain and stench associated with a leg ulcer. Smith's ulcer was cured by a soothing balm, the constituents of which Orwell did not divulge. An Old Testament law visited "a sore botch on the leg which cannot be healed" upon those who transgressed (Deuteronomy).

Venous ulceration is a common condition, the cost of which impacts at the level of the patient, the clinician and the health care budget. It is not surprising therefore, that much time and effort has been spent in an attempt to discover the cause(s) and potential cure(s) for this condition. The incompetent (calf) perforating vein (IPV) has enjoyed the reputation of a significant role in the development of venous ulcers. The exact role however remains undefined (Ruckley 1996).

1.2 Historical Perspective

References to simple varicose veins date from as early as 1550 BC (Ebers papyrus), and Hypocrites (460-377 BC) is credited with first noting the association between enlarged leg veins and ulceration. He also went on to describe compression therapy as a remedy.

Figure 1.1 Engraving showing treatment of leg ulceration, source: Trost Spiegel in Glück und Unglück, 1572.



In 1543, Vesalius provided the first description of the anatomy of the venous system (Vesalius 1543). However, the Russian anatomist Von Loder is credited with the first description of perforating veins in 1803. In a Lettsomian Lecture of 1867 entitled "On varicose disease of the lower extremities and its allied

disorders", the London surgeon, John Gay, described perforating veins of the calf and ankle and an association between these and ulceration (Gay 1868). He also recorded that ulcers could occur without the presence of visible varicose veins and he introduced the more accurate term, "venous" ulcer, to replace "varicose" ulcer.

A contribution, which was to have a major influence on the surgical treatment of venous ulceration in the twentieth century, came from the Boston surgeon, John Homans in 1916. In the first of a series of papers, he described ulcers "riding" upon the principal varicose trunk and he advocated a rational management plan to deal with these (Homans 1916). He approached "surface varix" problems with excision of the great saphenous vein from the groin to the mid-calf. If a clinical diagnosis of calf perforator incompetence was made "a thorough exploration of the lower leg" was advocated to ligate varicose perforating veins. Ulcers were to be treated radically with the correction of saphenous incompetence, followed by excision of the ulcer and underlying fascia with skin grafting and, if necessary, the raising of flaps in order to eradicate calf perforators. His first paper alluded to the "more malignant and resistant ulcer" which was associated with less prominent surface veins. He expanded on this in a second paper, dividing the patients into three groups: those with ulcers of surface varix; those with ulcers of surface varix complicated by varicosity of the perforating veins; and those of ulcers of a post-phlebitic type complicated by varicosity of the perforating veins (Homans 1917). This last group, he noted, were the most difficult group to manage and included those patients who developed symptoms after pregnancy or operation. However, to confuse matters for readers accustomed to more modern terminology, he

describes the post-phlebitic vessel as being palpable. Although he appeared to consider the problem of venous ulceration as being primarily due to reflux in the saphenous system, he recognised that the post-phlebitic group of patients were generally incurable by removal of varicose veins alone. This management approach influenced surgical thinking for more than a generation.

In the UK, Dickson Wright, working at St. Mary's Hospital, London, recognised the substantial socio-economic burden of the "gravitational ulcer" and the multifactorial aetiology of the problem (Dickson Wright 1931). His treatment of the ulcer itself was essentially conservative with injection of varices, compression therapy and ultimately skin grafting if necessary. His successor, Cokkinis, recognised the aetiological significance of varicose veins, but also realised that the puerperal white leg or venous thrombosis was a major factor in the development of ulceration (Cokkinis 1933). He added high saphenous ligation to his predecessor's management. Neither of these authors proposed a role for incompetent perforating veins.

Linton's landmark paper in 1938 focused directly on the calf perforator vessel as a cause of ulceration (Linton 1938). He described the venous anatomy of the lower limb in great detail, and advocated ligation of all groups of communicating veins of the calf, both medial and lateral. He described a dissection in the subfascial plane, performed through antero-lateral, postero-lateral and medial incisions. By 1953, faced with a large number of complications, he had changed to a single medial incision to deal with the communicating veins. He added to this the

removal of all varicose veins, division of the superficial femoral vein and partial excision of the deep fascia of the lower leg in an attempt to restore the lymphatic drainage of the lower limb (Linton 1953). He preferred operating after ulcer healing had been achieved, by compression therapy. He did not appear to fully emphasise deep and superficial venous reflux as separate disease processes, nor recognise the need to preserve an adequate venous drainage from the limb, as he stated that “ligation and division of the long saphenous vein [alone], for an unaccountable reason, gave slightly better results.....”.

At the same time that Linton was proposing a role for perforators, European surgeons were also beginning to consider the importance of perforator and deep veins in the development of chronic venous insufficiency (CVI). Gunner Bauer used phlebography to demonstrate the post-thrombotic changes in the deep veins of 33 of 38 ulcer patients, with only five patients having superficial varices alone (Bauer 1948). In particular, he identified the popliteal vein as a key segment in the aetiology of venous ulceration. He speculated that even those patients with clinical evidence of varicose veins could be suffering from post-thrombotic problems. This marked a paradigm shift in the perceived aetiology of venous ulceration and the role of superficial venous reflux. More importantly perhaps, his work also demonstrated a significant improvement in the outcome of DVT resulting from the administration of heparin. Subsequently, he described ligation of the popliteal vein as part of the management of venous ulceration, feeling sure that "in practically all cases with a clear-cut stasis syndrome there is also deep

valvular insufficiency....." (Bauer 1950). Clinically incompetent saphenous veins were also extirpated.

Cockett scrutinised further the role of calf perforating veins. He supported the observation that ulcers were not always cured by ligation of the long saphenous vein alone (Cockett 1953). He sought to distinguish the vast majority of those with varicose veins, who did not develop ulcers, and the relatively few who did. Cockett described a sequence of changes at the ankle region, coining the term "the ankle blow out syndrome". This commenced with the appearance of a dilated mass of subcutaneous vessels and progressed, in some cases, to full ulceration. He suggested that these changes represented the transmission of pressure from the deep system through a perforating vessel to the skin. In a second paper, he described the surgical management of this syndrome (Cockett 1955). The treatment comprised of removal of the main source of venous incompetence, identified as the incompetent perforators and the long and short saphenous systems as necessary. Then going on "to remove the sump of veins in the subcutaneous tissues of the region" and if necessary the ulcer. Furthermore, he advocated the division of perforators by an extrafascial dissection in order to preserve the soleal fascia, which he considered an integral component of a normally functioning calf pump mechanism.

The work of Cockett and Linton had a profound effect on the surgical management of leg ulcers. The emphasis was shifted firmly, almost exclusively in some cases, to the management of calf perforators and, as Cockett was later to

point out, the superficial system was often ignored to the patients' detriment (Cockett 1988). This point is illustrated by an editorial in the Lancet in 1977. The role of superficial venous disease went unmentioned, the paper focusing entirely upon calf perforators (Lancet 1977). Several other authors dismissed the role of the superficial system. Burnand and Browse stated in 1982, "it [ulceration] is rarely produced by simple saphenous incompetence" (Burnand 1982). This view was reiterated in the British Medical Journal in 1983 (BMJ 1983). However, Burnand and Browse did espouse the concept of failure of the calf pump mechanism. This attitude was also apparent in the USA where a review failed to mention saphenous disease as an aetiological factor (Gourdin 1993).

The development of perforator surgery

With growing acceptance of a pathological role for calf perforating veins in the development of chronic venous insufficiency and ulceration, there followed a number of modifications to the techniques described by Linton and Cockett described above. These modifications were primarily aimed at attempting to reduce the number of local calf wound complications associated with incisions through chronically inflamed and indurated tissue. Dodd described a postero-medial subfascial approach, Rob a posterior "stocking seam" incision and DePalma performed multiple small oblique incisions up the medial aspect of the leg (Dodd 1964, Rob 1979, DePalma 1979) (Figure 1.2). However, the problems with wound healing, prolonged hospitalisation and deep venous thrombosis were becoming increasingly apparent. Several studies demonstrated poor results from perforator surgery and many questioned the value of perforator surgery as will be

discussed later. As Fegan popularised injection sclerotherapy for perforators the open surgical approach became less popular in the UK, and only a few centres persisted with the technique (Beesley 1970, Henry 1971).

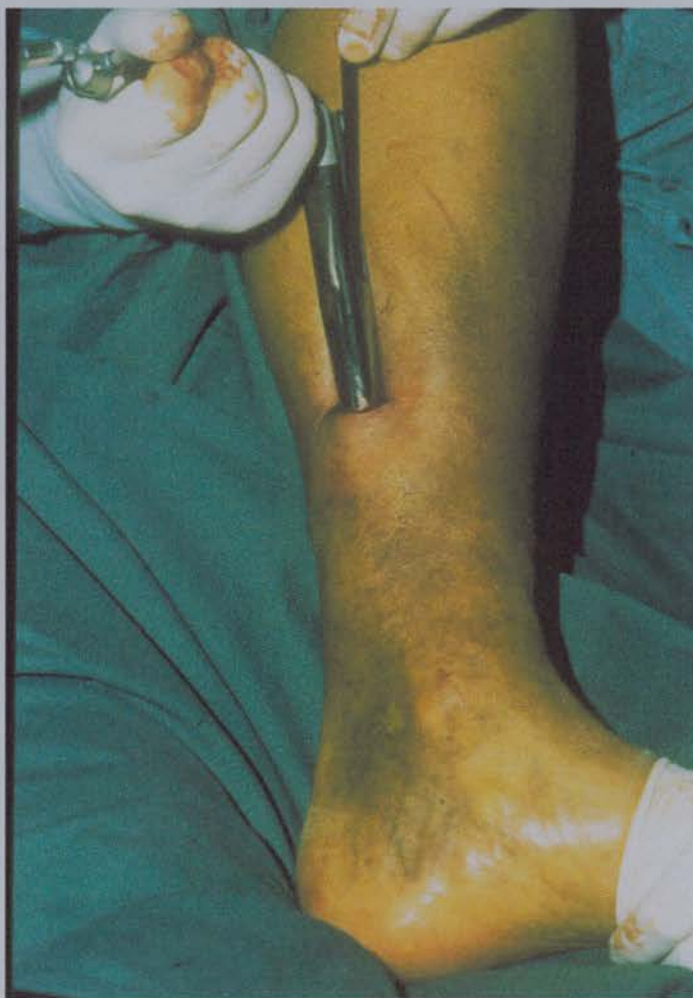
Figure 1.2 Surgical approaches to the medial calf perforating vessels. Left to right: medial approach, stocking seam incision and multiple oblique incisions.



The mid-eighties saw two technological advances that rekindled interest in the role of the calf perforator in CVI and venous ulceration. Firstly, Subfascial Endoscopic Perforator Surgery (SEPS) allowed the calf perforators to be surgically interrupted with the possibility of a reduction in complications and post-operative stay in hospital. Secondly, colour-flow duplex ultrasound allowed a non-invasive and reproducible method of assessing the deep, superficial and perforating vessels of the lower limb for both reflux and patency.

Hauer in West Germany first described SEPS in 1985. He used a single, one to two-centimetre incision sited on the medial aspect of the calf, just below the knee-joint (Figure 1.3). This was distant from the diseased skin. Access was then gained to the posterior, superficial compartment of the calf. The perforating vessels could be dissected, clipped and then divided between metal clips (Hauer1985, Pierik 1995). Subsequent authors have reported low complication rates. However a number of problems have been encountered (Gloviczki 1997, Nelzen 2000, Whitely 1997).

Figure 1.3 The placement of the endoscope for SEPS.



1.3 Epidemiology and natural history of venous ulceration

The first major epidemiological studies of venous ulceration did not appear until the 1980s. Prior to this, various authors had examined the epidemiology of venous disease as a whole, rather than ulcers in particular. Furthermore, there was a wide variation in reported prevalence venous disease. Study design and method had significant bearing on the results. For example, questionnaire based investigations reported higher rates of varicose veins among women than a study based on physical examination (Evans 1995). The classification of venous disease will be dealt with in Chapter 2.

Reliable and consistent data on venous ulceration are now available. The usual problems encountered when comparing different papers that vary in method and criteria must be borne in mind. The Lothian and Forth Valley Leg Ulcer Study (LFVLUS) group carried out the first major population based study in the UK (Callam 1985). Data were gathered from a community survey of general practitioners, district and occupational nurses and wardens of old people's homes and nursing homes. These were added to data gathered from the hospital-based population seen in out-patient departments, physiotherapy departments and in-patients, in both acute and long-stay wards.

A total of 1477 patients with leg ulcers were identified. Eighty-three per cent of these were managed exclusively in the community, 5% by physiotherapy departments, 7% in hospital out patient departments and 13% were hospital in-patients. The point prevalence was determined to be 1.48 per 1000 of the

population. This reached 2% in the group comprising women over 85 years. To further define the disease process, a group of 600 subjects was randomly selected for more detailed examination. In this population, 76% were venous ulcers as judged by history, clinical examination and continuous wave Doppler assessment of the arterial circulation.

Subsequent work from around the world has demonstrated a similar picture. The prevalence of chronic leg ulcer in the Northwick Park Study (London) was found to be 1.8/1000 (Cornwall 1986). In Skaraborg County (Sweden), it was 3.05/1000 (Nelzen 1991). However the latter figure included all ulcers below the knee. In Perth (Western Australia), the prevalence was 1.05/1000 (Baker 1991) and in Newcastle (UK) it was 1.9/1000 (Lees 1992). The Newcastle study was of the population over 45 years of age. Standing apart from these works, was a Dublin paper putting the prevalence at 15.2/1000 (Henry 1986). The reasons for such a large difference from the other studies are unclear, but could be related to the use of non-medical interviewers.

The natural history of chronic leg ulcer disease indicates a poor prognosis for sufferers. Of the 600 cases (827 ulcerated legs) examined in detail by Callam, 67% were ulcers recurrent at that index episode (Callam 1987). In 22%, the first ulcer had appeared before the patient had reached 40 years. In 35% of cases, there had been four or more episodes of ulceration. Fifty per cent of the ulcers had been present continuously for a period greater than nine months and 8% for five years.

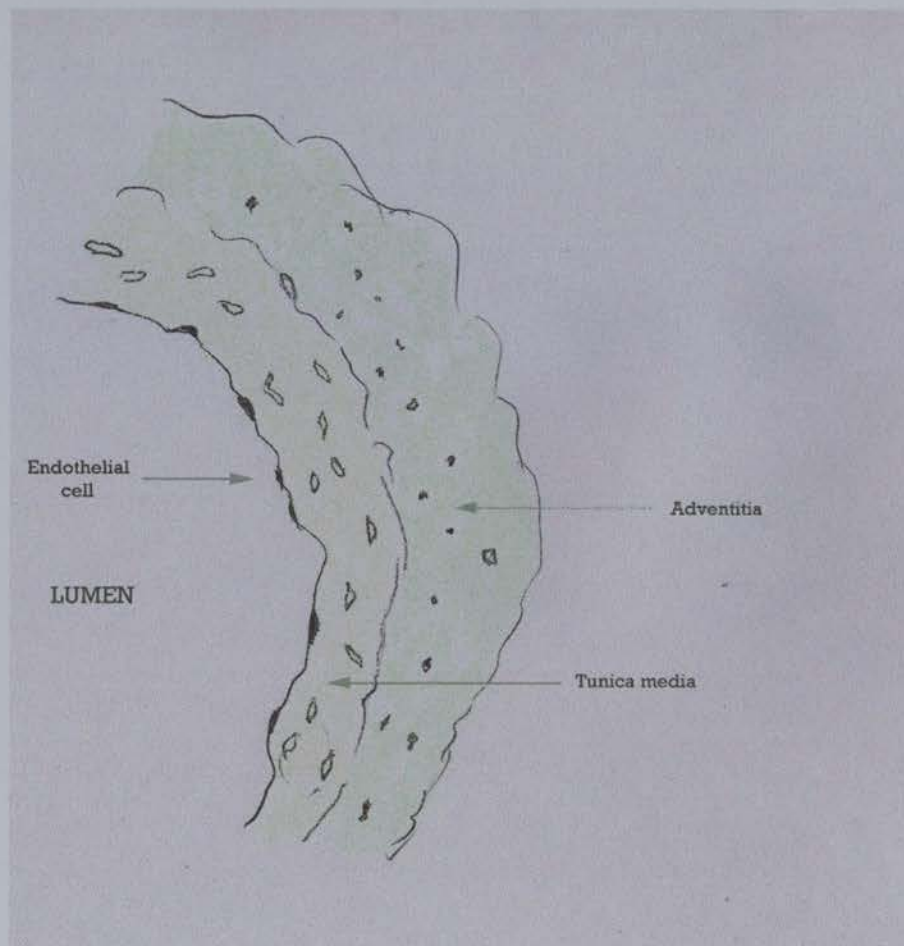
Ten years later Nelzen's work from Sweden showed a similar picture (Nelzen 1997). In a five year prospective study of 382 patients with ulcers (including foot ulcers) 55% survived the full duration of the study. In only 44% of those in the venous ulcer subgroup had the index ulcer healed and the patient remained ulcer-free for the remainder of the study.

1.4 Anatomy of the venous system of the lower limb

Microanatomy

Veins walls are composed of three layers: the intima, the media and adventitia (Figure 1.4). The intimal layer is composed of an endothelial monolayer, an elastic lamina and a basement membrane. The media is comprised of layers of smooth muscle and elastic and connective tissue. This layer is innervated via adrenergic receptors. The adventitia is the thickest layer and contains high levels of collagen.

Figure 1.4 Cross-section of a medium-sized vein showing the wall layers. Note the adventitia is at least as wide as the media contrasting with arterial walls.



The venous valves notionally ensure that blood flows from superficial to deep and caudal to cephalad. Venous valves are generally bicuspid and comprise of a layer of endothelium over a connective tissue skeleton (Figure 1.5). The valves meet along the longest diameter of the elliptical shape that veins take in the body (Edwards 1936) (Figure 1.6).

Figure 1.5 Histological structure of a venous valve.

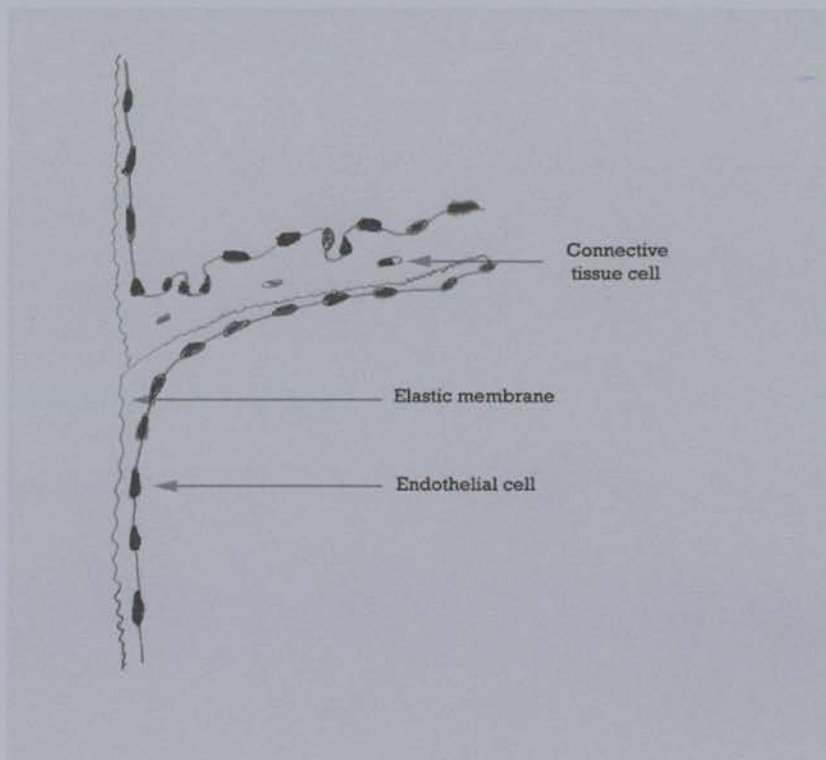
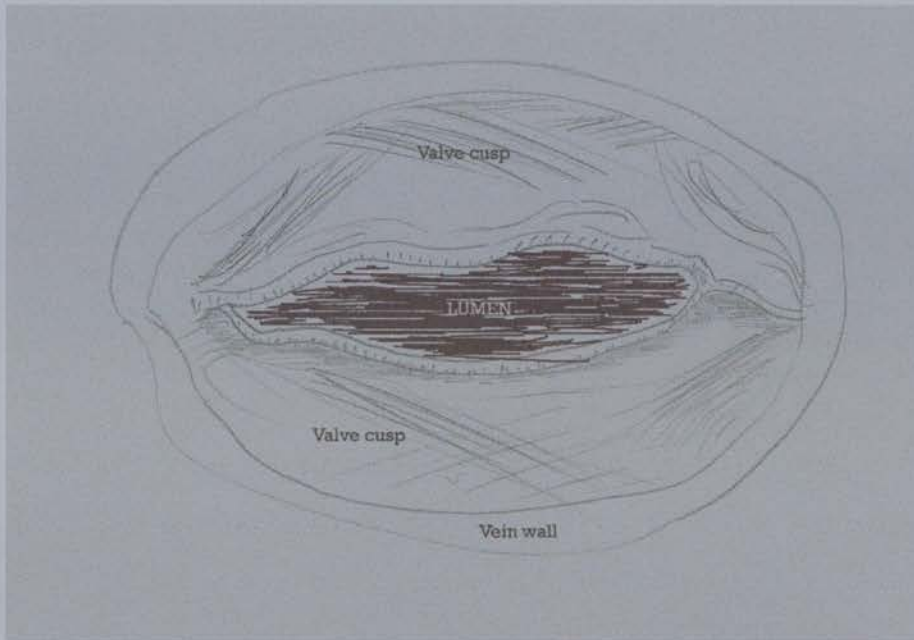


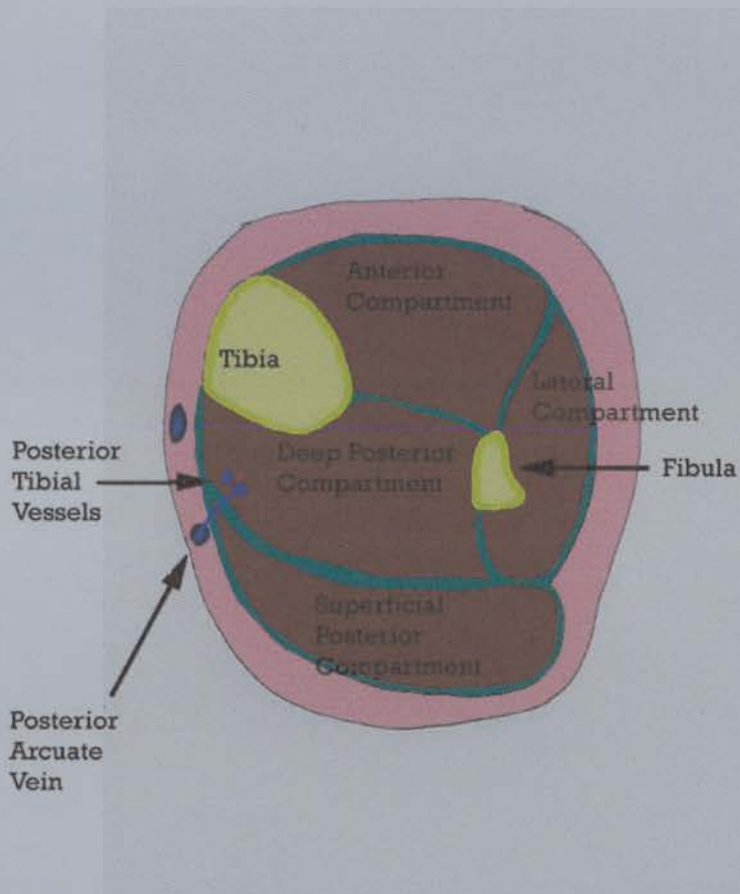
Figure 1.6 The meeting of venous valves along the longest diameter of the elliptically shaped vein.



Gross Anatomy

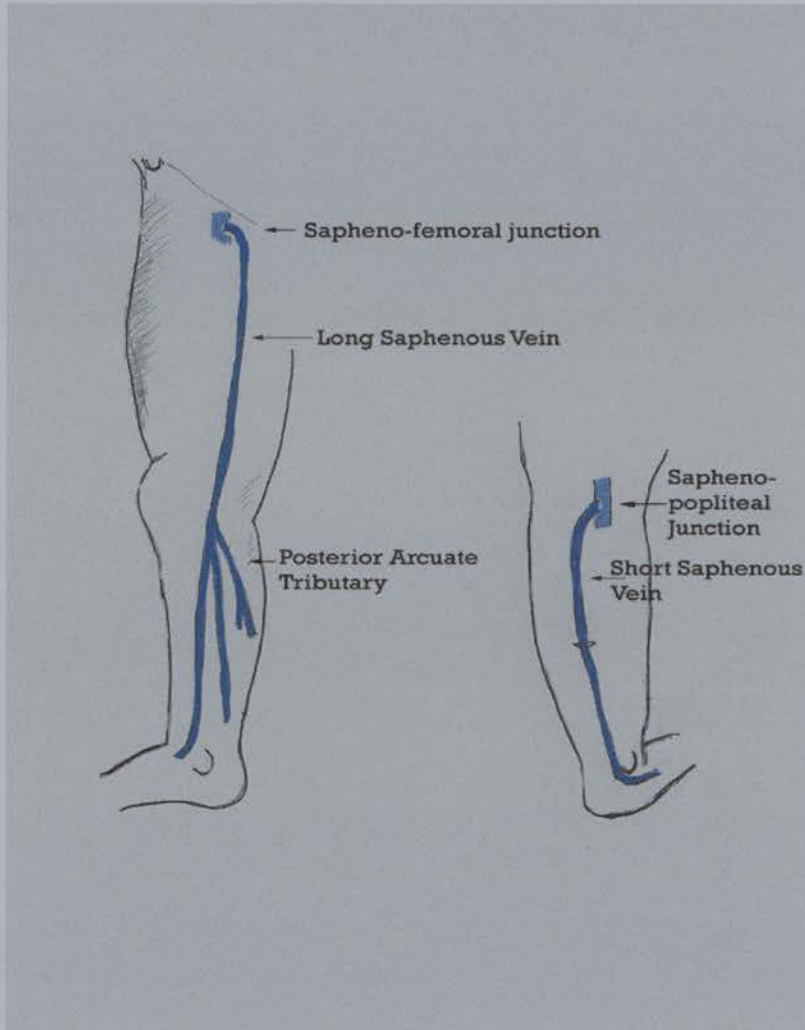
The venous system can be considered in three parts: the superficial system, comprising the long and short saphenous veins and their tributaries, the deep system and the perforating veins (Moneta and Nehler 1996). Fascia divides the calf into deep and superficial compartments, each containing distinct muscle groups. Fascial layers further divide the deep compartment into anterior, lateral and posterior compartments (Fig 1.7). The posterior compartment is subdivided into superficial and deep portions. During Subfascial Endoscopic Perforator Surgery (SEPS), the endoscope is inserted into the superficial posterior compartment of the calf.

Figure 1.7 The fascial compartments of the calf.



(a) The superficial vessels lie superficial to the investing layer of fascia of the leg. The long saphenous vein (LSV) forms from the medial side of the superficial dorsal arch of the foot. From anterior to the medial malleolus it runs over the medial aspect of the calf to pass a hands-breadth posterior to the patella. It ascends the medial aspect of the thigh, pierces the deep fascia through the foramen ovale and joins the common femoral vein 3cm below and lateral to the pubic tubercle in the groin.

Figure 1.8 a&b. The anatomy of the superficial venous system.

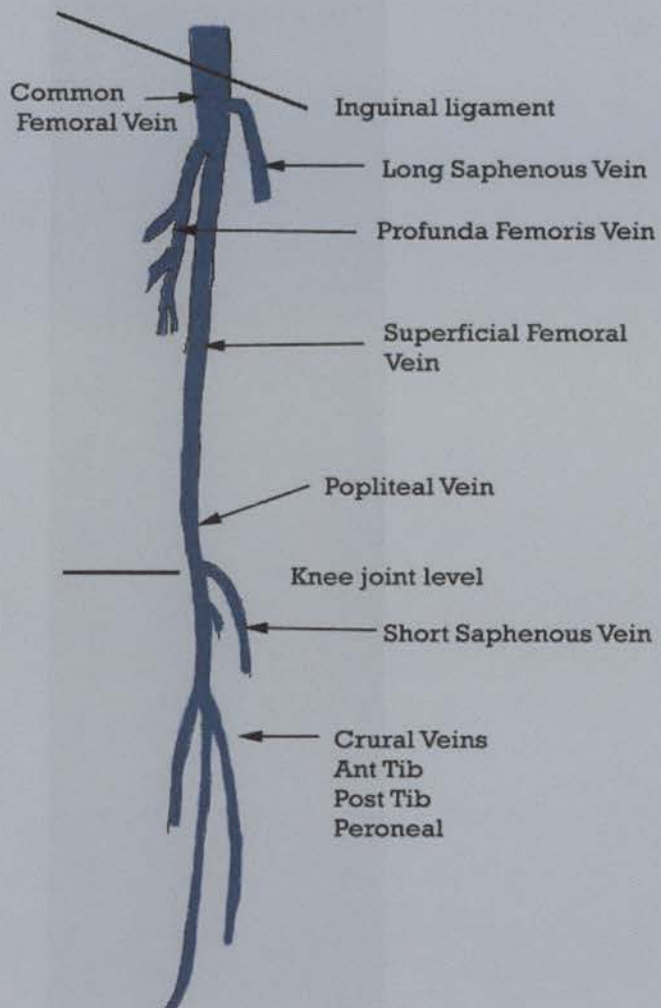


Named tributaries of the LSV in the calf include the posterior and anterior arcuate veins of the leg. The posterior arcuate vein is of particular relevance as this vessel communicates with the perforating veins of the calf and then carries blood cephalad to feed the LSV below the knee (Figure 1.8a). The short saphenous vein forms from the lateral end of the superficial venous arch of the foot in the midline of the calf. This vessel penetrates the investing fascia at a variable point on the posterior of the calf. Typically this is one third of the way down the calf. It joins the deep system at the sapheno-popliteal junction (Figure 1.8b).

(b) The deep system forms as venae comitantes around the three calf arteries (the posterior and anterior tibial and the peroneal vessels). These converge around the popliteal artery as, usually, two popliteal veins. The vessel changes its name to the superficial femoral vein as it passes through the adductor hiatus and becomes the common femoral vein as it is joined by the profunda femoris vein in the groin, at a point just inferior to where the LSV penetrates the fascia (Figure 1.9).

Various muscular veins and sinuses feed the deep system. The gastrocnemius veins in the popliteal fossa are particularly large tributaries. These can cause confusion when performing a duplex scan of the popliteal fossa, reflux in the gastrocnemius vein can be misinterpreted as short saphenous reflux (Vasdekis 1989) (Figure 1.9).

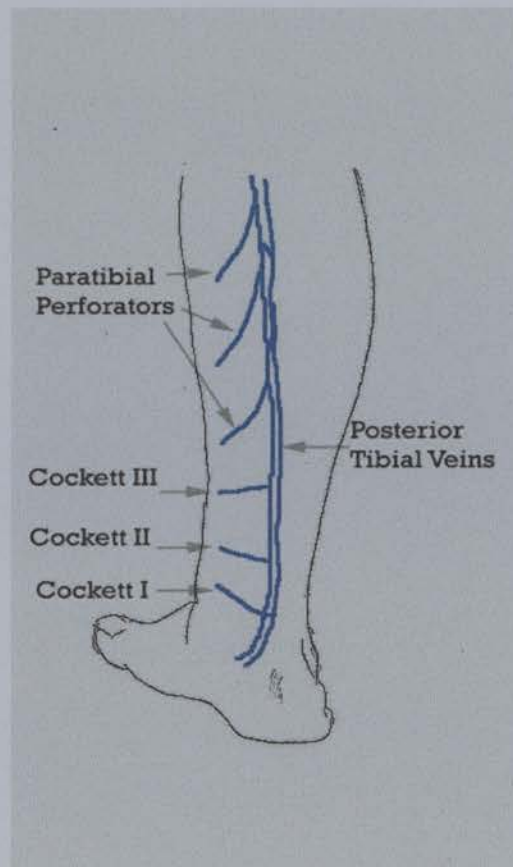
Figure 1.9 The anatomy of the deep venous system of the lower limb.



(c) Various perforating vessels are named and described in various anatomical texts. Perforating veins can be considered to be those connecting the deep and superficial systems, as opposed to communicating veins, which form connections within a system e.g. deep vessel to deep vessel. The Hunterian or mid-thigh perforator and Dodd's perforator just above the knee provide communication between the deep systems and the LSV. Just below the knee are Boyd's

perforators and on the medial aspect of the calf are the three Cockett perforators. These connect the posterior arcuate vein of the calf with the deep vessels. Also described is an infra-malleolar perforator (Figure 1.10). In Last's anatomy textbook the blood flow is described as being from superficial to deep through the perforators except on the foot. Here the blood flows in a deep to superficial direction (McMinn 1990).

Figure 1.10 The locations of named perforating vessels connecting to the long saphenous system of the calf.



More recently, perforating vein anatomy was re-examined by Moses et al (Moses 1996). Forty limbs from cadavers with no clinical evidence of venous disease were studied. Medial calf perforators were described as “direct” if connecting the

superficial veins to the deep system and “indirect” if connecting superficial veins to muscular venous sinuses. The total number of perforators identified was 552, giving a mean of 13.8 per limb. Of these 137 (25%) were greater than 2mm in diameter and 287 (52%) were direct perforators. By plotting the distances between perforators and bony landmarks on a chart, the perforators were described as being grouped in five clusters in various locations the calf. The lower perforators were found to communicate with the posterior arcuate vessels. Farther up the calf, they were observed to communicate with the other, unnamed tributaries connecting with the LSV. Sixty-three per cent of the medial calf perforators identified, were found to be accessible through the superficial posterior compartment of the calf. Wittens and colleagues confirmed this finding operatively (Pierik 1998). Access to the other, more distal perforators required division of the inter-muscular fascial septum to enter the deep posterior compartment (Figure 1.7).

1.5 Venous physiology

Traditional teaching ascribes three functions to the body's venous system. Firstly, the return of blood to the heart, secondly, a storage or capacitance space for sixty per cent of the blood volume and thirdly, a thermoregulatory role for the superficial veins.

Considering the first function, the principle force to be overcome in maintaining the venous return is gravity. The normal pressure of the right atrium is 0 mm Hg in an erect subject, falling to -3 to -5 mm Hg during respiration and with the cardiac cycle. The normal physical formulae governing fluid dynamics and rigid tubes cannot apply to the highly compliant veins. Although the resistance of a distended vein is negligible, a siphon effect cannot occur and despite a negative right atrial pressure, blood cannot be drawn back into the heart as the veins simply collapse. Therefore the venous return must be actively pumped back into the right side of the heart. The situation thus arises that in a subject standing still, the pressure of the veins foot level will rise to approximately 90 mm Hg (depending on the height of the subject) in less than a minute. If the subject remains still after this, the veins will engorge to the point that 10% of the blood volume is pooled within the leg venous system and therefore lost to the circulation within ten minutes (Gardner & Fox 1989), rising to 20% at fifteen minutes (Guyton 1991).

The calf muscle pump is the principle method of venous return from the lower part of the body. However, Gardner and Fox, describe in detail this pump as only one in a series of pumps from the sole of the foot right up to the thigh.

The foot pump

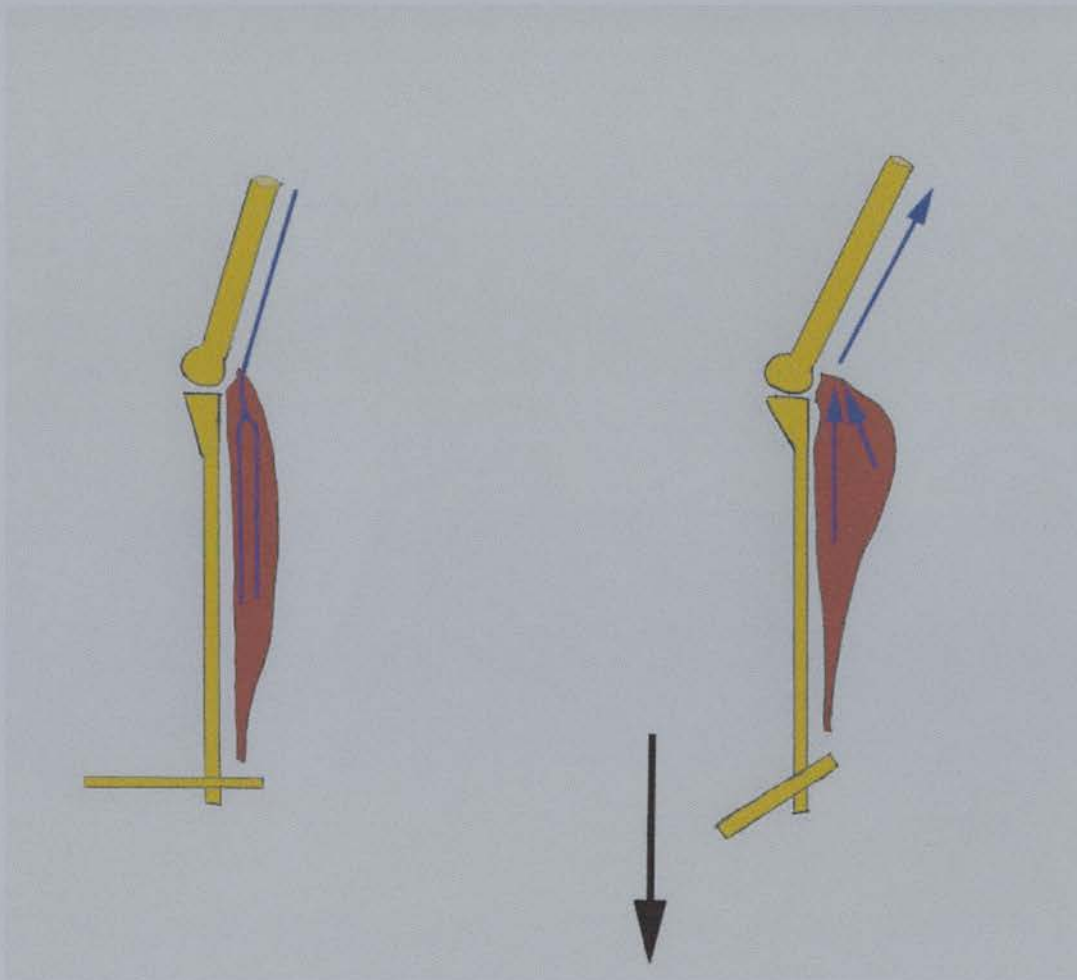
Simple planting of the foot will expel blood into the posterior tibial veins. One paper suggests that despite the absence of valves within the deep arch of the foot, blood is prevented from passing to the superficial system by tension in the plantar aponeurosis and interosseous muscles which kink or occlude the veins of the foot, channelling the blood in to the deep venous system of the calf (Gardner and Fox 1989). This cephalad flow is further facilitated during the walking cycle by relative relaxation of the calf muscles when the foot is first planted. Muscular tension within the calf is developed only as the "toeing off" process is initiated. Thus, the foot provides an atrial systole function to the calf muscles' ventricular diastole. The foot pump is reported to generate up to 100 mm Hg pressure on walking (Gardner and Fox 1989).

The muscle pumps

The calf muscle pump generates a positive pressure gradient, and therefore venous flow, by squeezing on both the venous sinuses, within the muscles, and the venae comitantes that surround the named arteries as they pass through the calf (Figure 1.11). The calf muscle pump action has two phases. First, the posterior muscle groups contract. Then, as these relax, the anterior muscles dorsiflex the ankle joint providing a second surge of blood. Furthermore, the contraction of the muscle, shortening along its length provides not just a squeeze, but also a piston-like push on the blood. The distal popliteal vein is emptied by the approximation of the two heads of the gastrocnemius muscle (Hach 1976). Further up into the thigh other muscle pumps act in sequence, including the sartorius and quadriceps

compression of the superficial femoral vein, the adductor compression of the profunda system and the gluteal squeeze of blood into the iliac system.

Figure 1.11 Schematic representation of the calf pump mechanism. Blood pools in the veins and muscular sinuses of the posterior muscle group. Plantar flexion of the ankle results in the blood being driven out of the muscles and up the leg.



The role of the superficial vessels is less clear. The LSV in particular has curious properties suggesting an important conduit role. This vessel is very thick walled. Perhaps this is due to the lack of a muscle group around it to support a distended vessel, but it indicates a limited role as a capacitance vessel, but possibly an

important role in flow none-the-less. A more important role of the superficial venous system may be thermoregulatory.

1.6 Calf perforating vein anatomy and physiology

The common sites of calf perforators have been outlined above. Conventional teaching states that blood flows from the superficial to deep, the direction being controlled by the presence of valves within the perforating veins (Guyton 1991). However this concept is not without challenge. Work by Barber and Shatara (1925) and Hadfield (1971) suggest that not only are valves absent from the smaller calf perforating veins, but the valves present are rudimentary and incapable of adequate closure. A dissection study by Mozes refers to the presence of unidirectional valves in perforating veins but offers no supporting data (Mozes 1996).

Understanding of perforator physiology is further complicated by work from the Middlesex group (McMullin 1991). They examined 56 perforators on 25 limbs with clinical evidence of venous disease using duplex. On distal compression, only one perforating vessel demonstrated outward flow, but local compression around the site of the perforators could induce outward flow in 38 vessels. They demonstrated outward flow at 13 cm/s and inward flow of 15 cm/s. The discussion section of this paper speculated on the possibility that outward flow is physiologically normal, but in the absence of normal limbs as controls, this idea remains unsubstantiated.

Further work from the Middlesex Hospital reported a larger series comprising ten normal control limbs, 19 limbs in patients with venous disease on the contralateral limb and 60 limbs with superficial venous incompetence (SVI). Of the last group,

29 limbs demonstrated LDS. There were a further 15 limbs with deep venous incompetence (with or without SVI), all of which had LDS and two had active ulceration (Sarin 1992). The aim of this study was to demonstrate the effects of different sites of stimulation on the direction of blood flow through calf perforators. They found that on distal calf compression (a) blood flowed in an inward direction in 85% of perforators, (b) blood flowed outwards in 15% of perforators, including an unspecified number perforators found in limbs with no evidence of venous disease and (c) reverse flow on distal compression occurred only in limbs with other venous disease but this was not correlated to the severity of venous disease. However, on compression proximal to the perforator in question, a significant number of perforators demonstrated outward flow and this correlated with the clinical severity of the venous disease (Table 1.1). The authors suggested that an ideal technique to study perforator function would be ambulant duplex scanning, but they also added that this might not, in fact, be possible.

Table 1.1 Direction of perforator blood flow on proximal calf compression and relaxation.

Venous Status	Compression		Relaxation	
	<i>Inflow %</i>	<i>Outflow %</i>	<i>Inflow %</i>	<i>Outflow %</i>
Normal	76	24	10	31
Normal-CVD	55	45	20	15
SVI	54	46	26	26
SVI + LDS	57	43	34	7
DVI	19	81	52	26

CVD, SVI, Superficial venous incompetence; LDS, lipodermatosclerosis; DVI, deep venous incompetence. (From Sarin et al 1992)

1.7 The Aetiology of Venous Ulceration

Leg ulceration encompasses a heterogenous group of disorders. Furthermore, the aetiology of any single ulcer must be considered to be multi-factorial.

(a) The role of non-venous disease

The Lothian and Forth Valley Leg ulcer Study (LFVLUS) group found that 11% of the 660 patients assessed in detail had impalpable pulses in the ulcerated limb (Callam 1987a). Furthermore, 21% had an ankle brachial pressure index (ABPI) of 0.9 or less and 10% had an ABPI less than 0.7. Fifty-two per cent of the limbs with arterial impairment also had clinical evidence of venous disease. A further 9% of the patients had rheumatoid disease and 5% diabetes.

However, further work by Fowkes and Callam demonstrated that these prevalences of arterial disease were similar to those of the population in general (Fowkes 1994). This suggests that perhaps those patients with peripheral arterial occlusive disease are at no greater risk of ulceration due to venous reflux or obstruction than the population with venous disease alone. However, the presence of arterial disease does have major implications for the conservative management of those with ulcers, namely compression bandaging (Figure 1.12).

Figure 1.12 Mixed venous and arterial ulcer. The main ulcer area (yellow arrow) was treated with compression bandaging and the unrecognised arterial component has resulted in pressure necrosis over bony prominences of the foot (red arrows).



A similar picture to the LFVLUS was painted by the Northwick Park study (Cornwall 1986). One hundred and ninety-three limbs were selected at random for detailed study from a population of 424 limbs. As defined by pocket Doppler examination and ankle-brachial pressure index, 9% of the limbs were affected

solely by an ischaemic problem and 22% in combination with venous disease. A more detailed study from Sweden, again using the pocket Doppler to examine the venous system, reported similar findings (Nelzen 1991). Venous disease was present in 72% of ulcerated limbs. An ABPI of 0.9 or less was found in 40% of the subjects, 0.7 or less in 22% and 0.5 or less in 6%. Other factors deemed contributory were diabetes (26% of limbs), ischaemic heart disease (26%), hypertension (28%), rheumatoid disease (19%) and arthroses (31%).

Other important aetiological factors include obesity, ankle joint immobility, localised and generalised neurological conditions and haematological dyscrasias.

Co-morbidity can be viewed as playing three significant roles: firstly, as a significant and potentially reversible aetiological factor, secondly, as an impediment to successful conservative and operative management, and thirdly, as a marker of the degree of debility of this group of patients.

(b) Venous (reflux and occlusive) disease and ulceration

During the 1980s the concept of calf pump failure as the major aetiological factor in venous ulceration gained favour. Initially, the actual site of failure of the calf pump was considered to be in either the deep system (due to the effects of DVT) or the calf perforators (Burnand 1976 Burnand 1982a, Browse 1983). Relatively little attention was paid to the superficial venous system.

(i) Distribution of disease in the superficial and deep venous systems

Understanding of the anatomical and physiological aspects of lower limb venous return changed dramatically with the advent of colour-flow Doppler imaging. This technology allowed the examiner to gather data on the patency and anatomy of vessels, together with images and spectral analysis of blood flow direction and velocity.

Two basic abnormalities of the venous system occur in association with the chronic venous insufficiency: reflux and obstruction. Reflux can affect the deep, superficial and/or perforator venous systems of the lower limb. The complications of chronic venous insufficiency can be associated with reflux disease in any or all of these systems. Obstruction, on the other hand, only appears to be associated with CVI if it occurs in the deep system.

Table 1.2 shows the distribution of venous disease demonstrated by a variety of investigative techniques. The anatomical patterns of distribution of venous disease are grouped in a variety of ways by the different authors. Authors differ

with respect to the anatomical sites for which data are provided. Furthermore, some of the figures quoted on table 1.2 could only be derived by estimation from graphs and figures in the original papers.

The values shown on Table 1.2 vary widely, but it is now clear that a strong association exists between reflux in either the deep or superficial main stem vessels and ulceration. A change in the understanding of the importance of venous reflux alone (as distinct from post-phlebotic venous obstruction) in the pathogenesis is also apparent. In, 1988 Raju and colleagues, using descending phlebography and ambulatory venous pressure to detect reflux, found that only 0.9% of ulcer patients had reflux limited to the superficial system (Raju 1988). By contrast, Shami et al in 1993 using duplex scanning, found isolated superficial venous disease in 53% of subjects with ulceration (Shami 1993).

Another important observation is that clinical examination alone is inadequate in the diagnosis and assessment of superficial venous disease (Shami 1993, Scriven 1997). The importance of this is further underlined by Labropoulos' observation that 92% of patients with venous ulceration demonstrate a segment of superficial reflux (Labropoulos 1996). Furthermore, the same author had previously demonstrated that 14.3% of 217 limbs with a history of radiologically proven DVT, had venous reflux affecting the superficial system alone, the deep systems having, it would appear, recovered completely (Labropoulos 1994). Forty seven per cent of this cohort had mixed deep and superficial disease. Seventeen (13%) of the 129 limbs with ulcer disease in this study demonstrated superficial system

disease in isolation, emphasising once more the importance of adequate investigation of patients with CVU.

We are therefore able to conclude the following regarding venous reflux and obstruction and the development of LDS and ulceration.

- (1) Reflux, rather than obstruction, is the important venous aetiological factor.
- (2) In a large proportion (up to 50% by duplex ultrasound assessment) the reflux may be limited to the superficial system (and therefore easily corrected by surgery).
- (3) Proper assessment of the superficial venous system requires duplex ultrasonography.
- (4) The role of IPV cannot be determined from these data, nor must it be considered in isolation from the effect of venous reflux elsewhere in the limb.

To summarise therefore, it would appear that up to 40% of venous ulcers occur associated with superficial system reflux only. A further 40-50% occur with mixed deep and superficial disease. The remainder are those occurring with deep system reflux or obstruction.

Table 1.2 The distribution (%) of venous reflux in patients with venous ulceration.

<i>Author year</i>	<i>Meth</i>	<i>N</i>	<i>Gd</i>	<i>S</i> <i>only</i>	<i>D</i> <i>only</i>	<i>P</i> <i>only</i>	<i>S&P</i>	<i>D&P</i>	<i>S&D</i>	<i>S,D&P</i>	<i>Total</i> <i>S</i>	<i>Total</i> <i>D</i>	<i>Total</i> <i>P</i>
Cockinis '33	Cl	144	III								63		
Cockett '55	Cl	182	III		47						53		
Schanzer '82	AVP & Tourn.	52	III	6		40	22						36
Ruckley '82	Cl & PD	827	III								68		
Sethia '84	PD	60	III		33	8	28	30					
Gooley '88	PD & PPG										67		
Raju '88	Desc. Phleb.	139		0.9	71	3			28				
McEnroe '88	LRR & Tourn.	142	III	21	65				14				
VanBemmelen 90	Dup	25	III	8	8					84			
Hanrahan '91	Dup	95	III	17	2	8	19	4	12	32	79	50	63
Nelzen '91	PD	463	III	34	8				30			38	46
Mastro-roberto '92	Dup	51	III	4	2	6	22	16	22	29	76	47	73
Nicolaides '93	AVP & Dup	236	0-III	65									35
			III	49									51
Shami '93	Dup	79	III	53	15				32				
Neglen '93	APG & Dup	31		6	29				65				65
Weingarten '93		148	III	20	25				55				
Lee '93s	Dup	98	II/III	19	1	2	37	1	12	24	93	38	55
		25	III	16			36	12	24	12	88	84	60
Labropoulos '94	Dup	217	0-III	14	39				47				
		129	III	13	26				64				
Van Rij '94	Dup	120		40	8				28				28
Myers '95	Dup		I	55	2				18				
			II	39	7				39				
			III	38	8				48				
Labropoulos '96	Dup	416	0-III	31	3	0.5	8	0.6	10	17	66	25	31
		120	III	18	4	1	19	1.5	13	39	90	58	61

No. number of limbs studied; Gd. grade of venous disease (Rutherford); S only, superficial disease only; D only, deep disease only; P only, perforator disease only; S&P, D&P, S&D, SD&P, combinations of superficial, deep and perforator disease. CL, clinical; AVP, ambulatory venous pressure; Tourn, tourniquet; PD; pocket Doppler; Dup, duplex; LRR, light reflective rheography; APG, air plethysmography; Desc Phleb, descending phlebography.

(ii) The proximal and distal distribution of venous reflux

A number of authors have attempted to attribute importance to the distribution of reflux in the proximal and distal venous segments, both deep and superficial. The understanding of where the important sites of venous reflux occur in relation to venous disease was similarly changed by the introduction of duplex scanning. The previous mainstay of investigation, descending phlebography, has a critical flaw as a technique. The process of injecting contrast medium through a femoral vessel and then looking for reflux using a Valsalva manoeuvre fails to identify reflux distal to the first competent valve encountered by the bolus of contrast medium. This problem can be partially overcome by combining both ascending and descending phlebographic techniques, but this method provides little or no information on the superficial system disease since tourniquet placement is required to ensure adequate concentration of contrast medium in the deep veins.

Using phlebographic techniques, Strandness et al examined the deep venous systems of patients with radiologically proven DVT (Strandness 1983). Over a follow-up period of 39 months, the segments with radiographic evidence of damage that held the greatest prognostic significance for the development of grade II and III skin changes were the more distal vessels, particularly the calf veins. Only 8% of the subjects with normal deep calf vessels developed the skin changes of CVI, compared with 40% of those with deep distal vessel occlusion or reflux.

Shull et al looked at a similar group of 51 patients (55 limbs) with venographically proven DVT (Shull 1979). Using ambulatory venous pressure (AVP) combined with venous Doppler velocity measurements and ascending phlebography, they concluded that the most important prognostic factor for deteriorating AVP values, and the subsequent development of ulceration, was the condition of the popliteal vein. This was independent of the presence of persisting obstruction elsewhere in the venous system.

Moore et al, also using Doppler velocities to detect reflux in patients with skin changes, identified the sites of venous pathology in the deep and superficial systems (Moore 1986). They demonstrated a strong association between the skin complications of CVI and distal reflux disease, occurring either in isolation (14% of limbs) or in combination with proximal disease (66%). However, a figure of 11% was reported when looking at ulcerated limbs with proximal vessel reflux in the deep system in isolation. The discussion section of the paper did not refer to this finding, emphasising instead the importance of deep distal disease. Furthermore, there was no “denominator” to the putative associative link as the number of patients with distal reflux and no skin changes was unknown.

Gooley and Sumner employed a combination of Doppler studies and photoplethysmography (PPG) to investigate limbs with suspected “post-phlebotic” syndrome (Gooley 1988). They demonstrated a correlation between venous refill times and the competence of the distal vessels and the saphenous systems. The ulcer group in this study demonstrated a significantly higher incidence of below-

knee popliteal reflux. The authors did however report that proximal disease in isolation could be associated with skin changes.

Rosfors et al considered that the most important segment was the posterior tibial vein, finding that ulceration could occur if reflux was present in this vessel even if the below-knee popliteal vessel was competent (Rosfors 1990). In this study foot volumetry and strain-gauge plethysmography were used to give a functional value to the venous disease.

The preceding studies were all performed without duplex ultrasonography and the identification of exact sites of reflux must have been problematic at the very least. The first investigators to employ duplex encountered significant problems imaging the crural vessels and often these vessels were not commented upon. However, with time and experience data on the distal vessels were reported.

Hanrahan et al reported the duplex assessment of the veins of ulcer patients and found that 72% demonstrated popliteal vein incompetence (Hanrahan 1991). The same proportion of patients had reflux in the common femoral vein, but only 26% of subjects had superficial femoral vein reflux, suggesting that in the majority of cases in this cohort the segments of venous reflux were discontinuous. They did not report on the status of the posterior tibial vein, but did include data on the superficial system. The authors did not enable readers to correlate the distribution of the superficial system reflux with that of the deep, but it would appear that

proximal superficial system reflux alone rarely, if ever, caused ulceration in this series. Reflux in either system must extend to below the knee to cause ulceration.

Neglen reported similar data, demonstrating that in the ulcer population, there was a 77% probability that the deep system reflux would extend to the below-knee popliteal segment (Neglen 1993). In this paper, posterior tibial vein reflux was present in 42% of the patients with grade II or III skin changes (using the ISVCS classification). Three-quarters of these patients also had common femoral vein reflux.

An association between non-healing ulcers and below knee reflux was reported by Brittenden et al although in this series the popliteal vein was implicated rather than the PTV (Brittenden 1995). The same group also demonstrated that following venous surgery on the perforator and saphenous systems, incompetence in the popliteal segment was a strong predictor of ulcer recurrence (Bradbury 1993a). In this study, the nine patients, of an original 43, in whom ulcers recurred had popliteal segment reflux. In this series, only one patient with popliteal vein reflux did not develop a recurrent ulcer during the follow-up period.

Further work from Edinburgh examined the differences between an ulcerated limb and its non-ulcerated fellow (Brittenden 1996). The significant differences between the two limbs lay in the competence of the above and below knee popliteal segments and the PTV. Further evidence implicating the PTV came from Myers et al who reported a rise in the incidence of grade II and III skin

changes associated with increasing frequencies of PTV incompetence rather than the popliteal vein segment alone (Myers 1995).

Labropoulos published work from St. Mary's Hospital, London implicating the distal vessels. Eighty per cent of limbs with LDS or ulcer disease had distal reflux. Furthermore, in cases where the reflux was confined to the superficial system, ulcers only occurred only if the full length of the long saphenous vein was diseased (Labropoulos 1994).

It would therefore seem reasonable to conclude that there is strong evidence, from both duplex scanning and non-duplex studies, that distal venous reflux in both the deep and superficial systems has an important role in the development of ulcers. The reliability of crural vessel imaging can be questioned and perhaps accounts for the variance in reported incidence of reflux in these segments.

(c) The impact of surgery on the natural history of venous ulceration

Before examining the evidence for the potential role of IPV in the development of ulcers, it is important to assess the impact of venous surgery in general on the natural history of CVU. Much of the evidence concerning IPV and CVU is presented in the context of surgery on these vessels. It would therefore seem sensible to examine the effects of main stem vessel surgery on CVU.

At present, there exist no published data from a trial of venous surgery, randomised or otherwise using conservative or non-surgical therapy as the control.

However, there are large series published which report the long-term outcome of surgery.

Darke and Penfold divided 232 limbs (213 patients) with active ulceration into four groups on the basis of the findings on pocket Doppler examination and ascending and descending phlebography (Darke 1992). The details of follow-up are given in Table 1.3.

Table 1.3 Darke and Penfold's data on follow-up and recurrence rates of patients operated for venous ulcer disease.

	Venous disease	% of cohort	Follow-up*	Recurrence
Group I	IPV alone	4		
Group II	SVI + IPV	39	3.5 years	9%
Group III	DVI (non-phlebotic)	35	4 years	60%
Group IV	DVI (post-phlebotic)	22		

*mean value, following surgery. IPV, incompetent perforating veins; SVI, superficial venous insufficiency; DVI, deep venous insufficiency.

The main follow-up reported was the outcome of the group II patients. They underwent saphenous system surgery as required, but not perforator surgery. Only 54 limbs were available for long-term follow-up. Of these 48 (91%) had complete healing after a mean duration of 3.4 (range 1-8) years. Of the five in whom there was a recurrence, there were other factors identified to explain this: one developed chronic lymphocytic leukaemia, one had diabetes mellitus, two

were found subsequently to have short saphenous reflux previously undiagnosed and the other was found to have popliteal vein incompetence.

The conclusion drawn was that at least 40% of venous ulcer patients will obtain medium to long-term ulcer healing following surgery to the saphenous system surgery alone. Saphenous surgery alone, it is possible to surmise, may lead to a major improvement to abnormal venous haemodynamics. The findings of this paper are supported by evidence from several other studies (Hoare 1982, Sethia 1984, Wright 1988).

The role and fate of the incompetent perforating veins were never fully explored by the authors but this paper did provide important evidence of the potential benefits of surgery for ulcer patients.

(d) What is the relationship between incompetent calf perforating veins and CVI?

The evidence regarding IPV will be considered in three sections: firstly, the results of surgery on IPV; secondly, associative evidence linking IPV to ulceration and thirdly, haemodynamic evidence of the effects of perforator incompetence.

(i) Results of perforator surgery

From a surgical perspective, the first question remains, does perforator surgery alter the natural history of venous ulceration? The results from many published series are given in Table 1.4.

The results vary widely. The reported recurrence rates range between two and 34%. Similarly, complication rates range between 1 and 44%.

Table 1.4. Published outcomes of perforator surgery.

<i>Author (year)</i>	<i>Patients (n)</i>	<i>Limbs (b)</i>	<i>Wound comps (%)</i>	<i>Recurrence (%)</i>	<i>Follow-up period</i>
Silver (1971)	28	31	13	10	64% > 5y
Field (1971)	51	57	-	2	1-8y (mean 6y)
Thurston (1973)	89	102	12	13	3-84m (mean 3y)
Bowen (1975)	55	71	44	34	6m-15y (48% > 3y)
Burnand (1976)	41	41		DVI 100% no DVI 1/17	up to 5 years
Blumenburg (1978)	16	25	4	4	6m - 6years
DePalma (1979)	53	68	1	6	6m-12 years
Almgren (1982)	57	41 ulc 16 LDS	19	(48 ulcer free) 22%	?
Hyde (1981)	83	-	13	33	Mean 10 y
Negus (1983)	77	108	19	13	6m -6 y (76% > 3y)
Cheung (1985)	32	31 ulc	22	34	5m - 4y
Johnson (1985)	37	47	11	22% at 1 year 41% at 3 years 51% at 5 years	
Wilkinson (1986)	108	134	24	2	6m-9y (80% > 5y)
Szostek (1988)	148	148	17.5	14.5	6m-10y (105 cases)
Cikrit (1988)	32	-	-	22	6m-10y (4y mean)
Nash (1991)	90	-	-	18	3y
Robison (1992)	17	18	56	37	42m (life table)
Bradbury (1993)	53	53	-	26	med 60m (3-144m)

m, months; y, years; ulc, ulcer; LDS, lipodermatosclerosis; DVI, deep venous insufficiency; med,

median

These studies have a number of flaws. They are retrospective series rather than randomised controlled trials. The ulcer groups are poorly defined, particularly

with respect to confounding aetiological factors. Most of these studies pre-date duplex ultrasonography, therefore the anatomical descriptions of the disease must be open to question. Furthermore, and for the same reason, the completeness of the perforator surgery and concomitant venous surgery has undergone little or no quality control. It is not possible, in most series, to disentangle the effects of perforator surgery from accompanying surgery to the superficial veins. The ulcer status at the time of surgery was often not stated and similarly, the definitions of the complications were far from precise. There was no standard post-operative management even within series. The series were incomplete with cases missing from follow-up. There was no life-table analysis on any of the data.

Despite these criticisms however, it is fair to say that longer follow-up periods are associated with higher ulcer recurrence rates and that concomitant deep venous reflux or obstruction has significant bearing on long-term outcome.

It would also be reasonable to conclude from Sethia and Darke's work, that a large proportion of these patients might have benefited long-term from adequate saphenous surgery alone (Sethia and Darke 1984). It would also appear that, from the evidence of Burnand and Bradbury, patients suffering from post-phlebotic damage to the popliteal system have a very poor prognosis with either medical or surgical treatment (Burnand 1976, Bradbury 1993).

(ii) Association between incompetent perforating veins (IPV) and clinical status

Evidence of association between IPV and clinical status has become clearer with the introduction of duplex ultrasonography. Using this technique, Hanrahan sought to identify the nature of venous reflux in the region of ulceration on an affected limb (Hanrahan 1991). He found that in 46% of cases there was no duplex evidence of any venous abnormality in the ulcer bed itself i.e. within 2cm of the ulcer margin. More specifically, although he identified a mean of 2.43 IPV per limb in the ulcer group, he found that only 27% of the limbs had IPV in the ulcer base itself.

Myers et al studied a much larger group of subjects, 1114 limbs, with a range of severity of venous disease (Myers 1995). 776 had uncomplicated primary varicose veins, 70 LDS and 96 an ulcer history. The main stem vessels were examined in a standard manner. The patient was examined erect and a pneumatic cuff was used to induce blood flow. Pathological reflux was defined as $\geq 0.5s$ of retrograde flow. However, the description of the actual perforator examination was scanty and the method of inducing blood-flow not mentioned. Criteria defining incompetence were not stated explicitly. However, from the results section it would appear that the presence of outward flow was the practical definition of pathological perforator function.

Medial calf IPV were seen in 57% of limbs with simple varicose veins, 67% of limbs with LDS and 66% of limbs with an ulcer history. The authors examined

the relationship between SVI and DVI and incompetent perforators. The results are in Table 1.5.

Like Hanrahan they demonstrated that an IPV could be imaged in two thirds of patients with an ulcer but incompetent perforators did not increase in frequency with a deterioration of clinical status.

Table 1.5 The percentage of patients demonstrating IPV in association with reflux in the deep, superficial and neither systems.

Limbs examined	Simple VVs	LDS	Ulceration
All limbs	57%	67%	66%
SVI present	63%	76%	68%
DVI present	69%	69%	72%
No main stem reflux	10%	10%	2%

After Myers et al 1995

A similar study was performed by the St. Mary's group (Labropoulos 1995). Thirty-four limbs in patients with a history of venous ulceration were examined using duplex ultrasonography. This study reported that only 17% of limbs failed to demonstrate a segment of venous reflux within 2cm of the ulcers. In only 12 of 43 ulcers (28%) could an IPV be seen in the base or within 2cm of the ulcer edge. IPV could be demonstrated in 15 of the 34 limbs (44%). Taking these two studies together it would be possible to argue that there is a poor correlation between local IPV, or indeed any IPV on a limb and venous ulceration. Certainly, there seems little to support the concept of an IPV feeding every ulcer crater as proposed by Robert Linton (Linton 1938).

Later work by Labropoulos et al, however, suggests a stronger link between the presence of IPV and venous ulceration (Tables 1.6 & 1.7)(Labropoulos 1996). These authors stated that flow was considered bi-directional when “net” or summated flow was in the deep-to-superficial direction on distal calf compression. A method of for this calculation was not given. Dividing 594 limbs into four clinical groups according to severity of venous disease, they demonstrated an increasing burden of venous reflux in the limb associated with deteriorating clinical status. In particular, they demonstrated an increase in the number of limbs demonstrating IPV and an increase in the mean number of IPV per limb. These numbers were the total IPV for the limb, not just the medial calf perforating veins. In 174 disease-free limbs there were no IPV. In 145 limbs with varicose veins only, 2% demonstrated IPV. Seventy-five of 155 limbs with lipodermatosclerosis demonstrated IPV (a mean of 1.8 per limb) and 73 of 120 limbs with ulceration demonstrated IPV (2.1 per limb).

Table 1.6 Labropoulos’ data regarding the number of perforators per limb by clinical status.

Clinical grade (limbs n)	Limbs with IPV (n)	Total IPV (n)	AK IPV (n)	BK IPV (n)	Mean IPV per limb	Range of IPV
0 (174)	0	0	0	0	0	0
1 (145)	3	3	0	3	1	0-1
2 (155)	75	135	44	91	1.8	1-6
3 (120)	73	157	49	108	2.1	1-7
All limbs	151	295	93	202	1.9	0-7

Table 1.7 Labropoulos' data regarding sites of reflux against clinical group (total incidence)

Clinical grade (limbs n)	Superficial veins n (%)	Deep veins n (%)	Perforators n (%)
0 (174)	13 (7)	4 (2)	0
1 (145)	131 (90)	15 (10)	3 (2)
2 (155)	138 (89)	93 (60)	75 (48)
3 (120)	108 (90)	70 (58)	73 (61)
Total (594)	390 (66)	182 (31)	151 (25)

Tables 1.6 & 1.7. AK, above-knee; BK, below-knee; Grade 0 - disease-free limb, 1 – varicose veins only, 2 – lipodermatosclerosis, but no ulcer history, 3 – ulcer history.

Two observations can be made from these data. Firstly, the number of perforators imaged per limb increases with deteriorating clinical status. Secondly, the number of patients with SVI does not increase between grades 1, 2 and 3. The number with DVI does increase between grades 1 and 2, but not grades 2 and 3. The only difference, in terms of distribution of reflux, between grades 2 and 3 on these data is the presence of incompetent calf perforators.

The evidence indicates an association between the presence of incompetent calf perforators and chronic venous insufficiency. However, the published data are divided on the issue of a specific link with ulceration and, most certainly, a causal link cannot be made. The contribution of IPV to the haemodynamics of the limb cannot be quantified using duplex ultrasonography. This method gives qualitative anatomical information only. However, incompetent calf perforators are placed at the scene of the crime with some consistency. Perforators are present on limbs with ulceration between 60 and 66% of occasions. Whether they are a guilty party or simply innocent bystanders remains not proven.

(iii) Haemodynamic evidence of the role IPV

Two groups of experiments will be considered here. Firstly, basic physiological work, mainly carried out in Scandinavia in the nineteen-sixties and seventies, and, secondly, studies of venous function following surgical intervention will be examined.

Arnoldi sought to determine the pressures in the deep veins of the lower leg with the subject nearly upright, in both static and dynamic conditions (Arnoldi 1966). He wanted to study the effect of incompetence in the superficial, deep and perforating vein systems on distal deep vessel intra-luminal venous pressures. He investigated 22 patients divided into two groups. In both groups there was saphenous disease and perforator incompetence as well as CVI. The venous valves of the deep system of those in Group A had been demonstrated by phlebography to be competent. However, in Group B the valves were absent, presumably destroyed by thrombus. Catheters were inserted into the popliteal, posterior tibial and saphenous veins and pressures obtained. Significant technical problems appear to have been encountered with this procedure. At rest, the pressures, not surprisingly, were proportional to the height of the column of blood from the point of measurement to the heart, but did seem to be a little higher in the group with deep venous insufficiency. The subject was instructed to perform four powerful calf contractions. During exercise, in both groups, the pressure in the posterior tibial vessel was highest during calf muscle systole and in the saphenous vein it was highest during diastole.

The preceding year Arnoldi had published work on subjects with normal venous systems (Arnoldi 1965 a&b). He had shown that there was a drop in the pressure recorded in the posterior tibial vein on commencement of a stepping action. This fall in pressure continued for four steps and then plateaued in a state of dynamic equilibrium. This paper essentially demonstrated ambulatory venous pressure measurement.

This 1966 paper demonstrated that in patients in Group A (saphenous reflux with intact deep systems), the posterior tibial vein pressure fell with the first stepping action but this decline did not continue with successive steps, the initial drop in pressure simply being maintained. However, in the Group B subjects (saphenous and deep system reflux), the pressure in the PTV fell with the first step but then rose with subsequent steps. The time for the venous pressures to return to the pre-exercise level was significantly shorter in the Group B subjects.

Arnoldi drew the following conclusions. The pressure at rest appears to be the same regardless of the degree of pathology. The large calibre incompetent perforators allow a free transmission of the high contraction pressures in the distal posterior tibial veins to the subcutaneous tissues. The high pressures in the subcutaneous tissues were constantly maintained in patients with long saphenous or deep system reflux, as long as these patients remained upright. The flow of blood through the perforators acted like a "hydraulic ram" on the tissues.

Bjordal published a series of papers examining the pressures in the distal venous system together with the volumes of flow through perforating veins. He inserted catheters connected to pressure transducers into the calf veins. First he demonstrated that in patients with saphenous system disease alone, the raised ambulatory venous pressure of the calf was not corrected by blocking the perforators, but was corrected by occlusion of the saphenous vein (Bjordal 1970). He then repeated the experiment comparing a group of 11 patients with primary varicose veins with a group of 18 patients with varicose veins and a definite history of DVT (Bjordal 1971). All the patients had one or more dilated calf-perforating veins on phlebography or clinical examination. The patients with varicose veins behaved as before, the AVP dropping on saphenous occlusion. The patients with a history of DVT fell into two groups. Firstly, there was a group in whom the AVP fell to normal levels on saphenous occlusion. Secondly, there was a group in whom the pressure remained high on saphenous occlusion. Bjordal concluded that post-phlebitic ulcer patients could therefore be divided into two groups: those who would benefit from superficial and perforator system surgery, and those who would not. He also felt that the high pressures in the saphenous system were due to saphenous reflux rather than perforator pathology.

Bjordal published a third paper in this series the following year, specifically addressing the haemodynamics of perforators (Bjordal 1972). In six patients, he used electromagnetic devices placed around calf vessels in anaesthetised patients to measure flow in the saphenous and perforating veins and simultaneously measured the venous pressures during rest and ambulation. All the patients had at

least saphenous disease and an incompetent perforator on clinical examination and ascending phlebography.

There was no flow through the perforators at rest. During calf diastole the flow was inwards and during calf systole it was outwards. However, the net or summated perforator flow was in fact inwards. However, if the saphenous vein is occluded proximally by tourniquet the outward perforator flow during calf systole is increased, producing a net outward flow. Authors often misquote this last finding.

He further observed that on occlusion of the LSV the AVP fell by 17mmHg, but occlusion of the perforating veins only produced a fall of 2mmHg in the AVP.

Criticisms of this final experiment are as follows. Firstly, the sample size was small. Secondly, the patency of the deep system vein was not stated and given the period during which the experiment was performed, probably not reliably known. The author uses the expression "mean flow in perforators". I have interpreted this to mean the net or summated blood flow. How he actually calculated this value is not clear as the data are presented as a continuous flow trace. The magnitude and direction of flow through the saphenous vein, when patent, is not made clear.

The other aspect demonstrated in Bjordal's studies is the blood flow rate in each direction. Calculated from his graphs, the flow rate approaches 500 ml per minute in both directions, compared with only half that in the isolated and presumably

much larger proximal saphenous vein. This means that although the net flows are relatively small, the actual velocities through these incompetent vessels must have been astonishingly high.

Bjordal referred rather critically to previous work by Sturup and Hojensgard (Sturup 1950). These investigators had measured the catheter transducer pressures in varicose veins during rest and walking in patients with varicose veins and with post-phlebitic limbs. The diagnosis of a post-phlebitic state had been made by phlebography and the diagnosis of perforator incompetence was made as a result of a Trendelenberg test.

The pressures measured at the ankle when the patient was static were similar in the two groups. However, on ambulation the pressures fell dramatically in the primary varicose vein group if the saphenous vein was occluded by tourniquet, but in the six post-phlebitic limbs this was not the case. In one case the pressure fell by 40 cm of water. However, in the other five cases there was no change or an indefinite rise on walking with the saphenous vein occluded. They also observed that the increased pressure registered at the ankle on raising intra-abdominal pressure, by coughing, could not be prevented by occluding incompetent calf perforators, but could be prevented by occluding the saphenous vein in patients with competent perforators.

Bjordan made the suggestion that the investigators had simply failed to occlude the saphenous vein adequately in those patients with deep system disease. In the present day this could be quality-controlled by duplex ultrasound.

The results of the above studies are somewhat confusing but a few points should be considered. Firstly, the disease patterns may have been considerably different from the ones we encounter today. The diagnosis and treatment of DVT has changed radically over the last fifty years with anticoagulation now routine. This may have reduced the number of chronically occluded segments and increased the proportion in which reflux in the main pathology. Indeed, in other work, Sturup and Hojensgard report extensive collateralisation on phlebography (Hojensgard 1950). Secondly, the patients did not have the deep veins imaged in the manner that would now be routine prior to such experiments i.e. using colour-flow Doppler. If the deep vessels were occluded or significantly stenosed as the pressure at the ankle would rise on exercise as reported by Sturup and Hojensgard. However, if the veins merely demonstrated reflux, the pressure would remain the same or may even show a modest decrease.

To summarise, Arnoldi's work demonstrated the pressure changes now seen as part of ambulatory venous pressure measurements. The pressure in the veins of the calf at rest is dependent on the subject's height. A stepping action reduces pressure in the calf veins. This pressure drop is at its greatest after four steps in health but in the presence of venous reflux disease there is no further drop after the first step. The dynamic equilibrium is established sooner at a higher level.

Bjordal demonstrated that at rest there is no blood flow through the calf veins. During ankle flexion and extension blood flows both ways through in competent calf veins but the net flow is from superficial to deep. Occlusion of the incompetent LSV in patients with deep venous reflux results in increased flow from the deep to superficial systems.

More recently, McMullin et al investigated 49 patients with signs and symptoms of CVI (McMullin 1990). They felt unable to determine on duplex whether perforators were competent or not. Patients with no named-vessel venous reflux on duplex were investigated with ascending venography. Forty limbs had an ulcer history, 13 LDS only and 15 with varicose veins only. There were 18 limbs with no clinical signs of venous disease. 28 limbs had DVI and 32 SVI, with 14 others diagnosed on ascending venography to have at least two incompetent perforators, in the absence of main stem disease. They calculated the venous sufficiency index (VSI), for each of the groups based upon anatomical distribution of reflux and for the separate clinical groups. VSI was a quotient based upon the proportional drop in venous pressure on walking and the venous return time. There was considerable overlap of results between the groups.

The VSI increased with improving clinical status. The anatomical group with the poorest VSI were those with DVI, next were those with SVI and then with very nearly the same values as the SVI group were those with perforator disease in isolation. From these data it would appear that perforator disease alone is not capable of producing a significant deterioration in venous function. Furthermore,

it is not possible to identify the contribution of IPV to the dysfunction of the DVI and SVI groups. Other authors since have reported isolated IPV reflux in a limb to be extremely rare. It is therefore possible that the authors failed to detect deep and/or superficial reflux in the group supposedly representing “IPV only”.

Zukowski et al studied 221 limbs from a group of 149 patients with skin changes varying from simple varicose veins alone to ulcers (Zukowski 1991). The patients were assessed for the anatomical extent of the disease (venography and ultrasound) and for the functional contribution of the various sites of reflux / incompetence using AVP (ambulatory venous pressure) measurement. The sites of deep-to-superficial incompetence were sequentially occluded using tourniquets at the below-knee level and at the ankle level. The patients were divided into three groups: Group A, varicose veins only with no evidence of incompetent perforating veins, Group B, varicose veins with incompetent perforating veins and Group C, deep venous disease, regardless of the state of the superficial system. Further sub-grouping of the Group B limbs was performed by repetition of the 90% venous refill times (VR 90) and ambulatory venous pressures after the placement of tourniquets (T) at the below knee (bk) and ankle levels (ank) (Table 1.8). The normal value of VR 90 were considered to be >15s.

Table 1.8 The effects of tourniquet on group B patients

Variable	Subgroup I	Subgroup II	Subgroup III
VR 90	>15 s with bk-T	>15 s with ank-T	>15 s with ank-T
AVP	<45 mmHg with bk-T	<45mmHg with ank-T	<45 mmHg with ank-T
Skin changes	Nil	17 (68%)	25 (100%)
Ulceration	Nil	Nil	7 (28%)

VR 90, venous return time to 90% of resting pressure; bk-T, below-knee tourniquet; ank-T, ankle tourniquet. After Zukowski 1991.

The following conclusions were drawn. In subgroup I, the placement of a below-knee tourniquet normalised the haemodynamics of the leg, the incompetent perforating veins were not haemodynamically compromising the limb. In subgroup II the ankle tourniquet, but not the below-knee tourniquet normalised the haemodynamics of the leg and the perforators were responsible for a proportion of the haemodynamic compromise of the limb. Subgroup III represented undiagnosed deep system pathology.

There have been several attempts to quantify the effects of perforator surgery on the haemodynamics and function of the leg. To do so it was necessary to separate the effects of perforator interruption from those of interruption of the long and short saphenous systems.

In two papers, Burnand addressed the role of perforators in ulceration from a post-perforator surgery perspective. In the first paper he studied a group of patients who developed recurrent ulceration following perforator surgery (Burnand 1976). Of 41 patients followed-up, 17 were ulcer-free. 23 of the 24 with recurrences had

deep system disease on phlebography. The author's conclusion was that the calf perforators that were incompetent were a manifestation of DVI and not themselves the cause of ulceration. In the second paper 107 limbs from 77 patients with ulceration were compared with 30 healthy volunteers (Burnand 1977). All limbs were assessed clinically and the sites of incompetent perforators were determined by localisation using a tourniquet and finger compression method. The abnormal limbs underwent phlebography during which the sites of incompetent perforating vessels were noted. A slight modification to the technique of ambulatory venous pressure measurement was made. The foot pressure measurement was made and followed by a repeat measurement after a cuff around the thigh and then calf had been inflated to the point where it raised the resting pressure by 1-5 mmHg. This usually required an inflation pressure of 60-90 mmHg. The patients then underwent long and short saphenous surgery and perforating vein surgery as indicated on the basis of all the investigations. AVP measurements were repeated three months after the initial venous surgery. The results of segmental AVP measurement are given in Table 1.9.

Table 1.9 The effect of tourniquet application on AVP measurements and surgery.

Subjects	ak-tourniquet	bk-tourniquet	Effect of surgery
SFJ incompetence	better	better	Improved AVP
SPJ incompetence	same	better	Improved AVP
Perforator incompetence	same	same	minimal AVP improvement
SPJ incomp. & IPV	better	same	Improved AVP
DVI	same	same	no effect on AVP

ak, above-knee; bk, below-knee; SFJ, sapheno-femoral junction, SPJ, sapheno-popliteal junction; DVI, deep venous incompetence; AVP, ambulatory venous pressure. (After Burnand 1977).

The conclusion was drawn that the only measurable benefit from venous surgery was to be gained from superficial system surgery. It was noted that none of the AVP measurement changes returned to normal after venous surgery.

Akesson et al employed staged venous surgery in an attempt to separate the component improvements in venous function (Akesson 1990). All subjects had recurrent ulceration and DVI (30 limbs from 25 patients). They were extensively assessed using ascending and descending phlebography, occlusion strain-gauge plethysmography, foot volumetry and AVP. Any superficial venous insufficiency was corrected first (12 limbs) and then at a later date, a subfascial ligation was performed by means of a Linton's procedure (Table 1.10).

Table 1.10 The results of staged venous surgery on the superficial venous system (procedure 1) and calf perforating vessels (procedure 2).

Functional modality	Procedure 1	Procedure 2
MVO	Improvement, NS	Deterioration, NS
Foot Volumetry		
(a) Ejection fraction	Improvement, NS	No change
(b) Reflux / expelled vol	Improvement, sig.	No change
AVP		
(a) Ambulatory Pressure	Improvement, sig.	No change
(b) 90% refill time	Improvement, sig.	No change

(MVO, maximum venous outflow; sig, statistically significant; NS, non-significant; AVP, ambulatory venous pressure). After Akesson 1990.

Either the calculated maximum venous outflow value is a test of insufficient sensitivity to detect changes caused by saphenous and perforator surgery or it is

inappropriate in these circumstances. After saphenous surgery AVP may also be an inappropriate as the perforators may no longer be in continuity with the dorsal veins of the foot.

Nonetheless, the conclusion drawn by the authors from this evidence was that in the wide range of assessment modalities used, the benefit from the Linton's component is minimal. However, it would appear that in the presence of mixed superficial and deep venous disease there is a potential benefit correcting the superficial system disease as measured in the short-term on venous function tests. It must be mentioned that, for a variety of reasons, the entire group was not retested using all modalities, indeed some of the numbers were quite small.

The Edinburgh group performed a study predicting the group of patients in whom recurrent ulceration was likely to occur following subfascial perforator surgery (Bradbury 1993b). Fifty-three patients who underwent subfascial ligation, with saphenous system surgery as indicated, were assessed pre-operatively using foot volumetry, repeated one month after operation and then regularly thereafter. The follow up was over a median period of 60 months (range 3-144) during which time recurrent ulceration appeared in 14 (26%) of the study group. The median period to recurrence was 48 months (range 10-72).

The pre-operative ejection fraction was significantly lower and the half venous refill time was significantly shorter in the recurrence group compared to the non-recurrence group. There was improvement in the venous refill time in both

groups post-operatively, but only the recurrence group showed an improved ejection fraction at one month. At recurrence both parameters had deteriorated in the recurrence group to a level close to the pre-operative value. The group at particular risk of recurrence were those with deep venous reflux and especially those with popliteal segment reflux (Table 1.11).

Table 1.11 Venous function test in patients before and after Linton's procedure and saphenous surgery for venous ulcer.

Modality	Pre-op value	One month	At recurrence	Final value
Ejection fraction				
(%)				
(a) Recurrences	0.95	1.65	1.1	1.0
(b) No recurrences	1.8	1.9	-	1.9
Half venous refill				
time				
(a) recurrences	1.75s	4.75s	2.25s	2.75s
(b) no recurrences	4.5s	9.0s	-	7.5s

After Bradbury 1993b.

The question as to what actually happens to incompetent calf perforators after correction of superficial system disease has been addressed to limited extent only. However, these limited data indicate a possibly crucial element in explaining the benefits of superficial system surgery. Campbell and West have presented data in abstract form only suggesting a partial restoration of perforator competence (Campbell 1995). They performed a prospective audit of the effects of long and short saphenous surgery examining completeness of surgery and changes in calf perforators. At pre-operative duplex scan assessment they found 226 incompetent

calf perforators in 164 of the 185 limbs examined. At follow-up duplex examination, 182 (80.5%) had become competent or showed no flow at all. The mechanism of return to competence is open to speculation. Were the perforators cut or avulsed during the phlebectomy stage of the procedure, or did the removal of the long saphenous pressure allow the veins to return to a normal size? Did perforators remain incompetent because the saphenous incompetence had not been effectively corrected, or were they being fed by deep venous reflux?

1.8 The process of ulceration

As already described, leg ulcers represent a heterogenous group of conditions linked by anatomical site. While venous ulceration probably represents a more discrete pathological entity, with defined microscopic changes, the initiating event leading to an ulcer occurring is far from certain, but is probably minor trauma. The association between venous ulceration and failure of the calf pump mechanism and resultant rise in ambulatory pressure venous is clearly documented (Pollack 1949, Nicolaides 1986). However, the actual reason for raised AVP leading to not just ulceration, but also to the failure of ulcers to heal is far from established.

Three theories have enjoyed favour, namely tissue hypoxia, the fibrin cuff hypothesis and the white cell trapping hypothesis.

Tissue hypoxia

There is no clear evidence that hypoxia plays any significant part in development of CVU. In fact, a large body of work indicates that tissue oxygenation is in no way an aetiological factor (Clyne 1985, Scott 1990).

Fibrin cuff hypothesis

The initial work for this hypothesis came from Browse and Burnand in the 1980's (Burnand 1982b). Microscopic observations lead the discovery of an association between raised venous pressure and the presence of a peri-capillary cuff in the

skin of the calf. It became clear that these cuffs consisted of fibrinogen and its polymers. The proposed mechanism suggested that under the circumstances of a constantly raised capillary venous pressure, plasma proteins were exuded from the microcirculation and, in the peri-capillary region, fibrin polymerisation occurred. The build-up of this material in turn leads to hypoxia, tissue damage and ultimately, ulceration. However, as indicated above, subsequent work has failed to demonstrate a fall in tissue oxygen tension.

White cell trapping hypothesis

White blood cells (WBC) are central to the processes of acute and chronic inflammation. WBC are implicated in the destructive processes associated with ischaemic, inflammatory and autoimmune diseases (Lin 1988, Yamakawa 1984, Blaide 1986). During the process of a normal inflammatory or immune response, the intra-vascular WBC are transferred to the extra-vascular space by a well-defined series of steps. The first step, margination, is followed by WBC emigration from the intravascular space, WBC activation and ultimately the release of the destructive free radicals, proteolytic enzymes and further chemotactic substances which mediate and escalate the response process. The process of margination has been the particular focus of much work by the Middlesex group among others.

Briefly, the white cell surface ligand, L-selectin interacts with endothelial cell adhesion molecules ICAM-1, ELAM-1 and VCAM-1. A rolling interaction progresses to a firm adhesion. Studies have demonstrated WBC being lost to the

circulation during periods of dependency; a rise in haematocrit being accompanied by a fall in WBC counts on samples taken from the ankle (Thomas 1988, Moyses 1987). The interpretation suggested was that these "lost" WBC were trapped within the microcirculation of the leg.

Capillary proliferation is evident on histological examination. This appears to be derived from a single capillary loop system described as having a glomerular appearance (Haselbach 1986). Furthermore, the capillary endothelium expresses increased levels of Factor VIII related antigen and adhesion molecules, suggesting a disruption to the normal endothelial function (Wilkinson 1993, Veraart 1993). The presence of a vascular proliferation around the skin changes associated with CVI was previously ascribed to the now disproved notion of tissue hypoxia. This proliferation appears to be induced by an increased expression of angiogenic factors, in particular, Platelet Derived Growth Factor (PDGF) and Vascular Endothelial Growth Factor (VEGF) (Haselbach 1986).

Further work from the Middlesex group has demonstrated evidence of increased WBC activation in blood samples taken from the limbs of patients with the skin complications of CVI compared with healthy controls and patients with simple varicose veins (Coleridge Smith 1999). However, it is probably not possible to determine from the published data whether this is cause or effect with respect to ulceration. It would be easy to envisage the establishment of a positive feedback loop. The abnormalities of capillaries and increased levels of adhesion molecules combined with the presence of active ulceration lead to increased WBC

margination and chemotaxis. What is not clearly understood is the process(es) by which venous hypertension initiates the above sequence and why the calf skin is affected far more frequently than the dorsum of the foot, for instance.

1.9 Summary and plan for present work

(1) First and foremost, there is no proof, in the form of a randomised controlled trial, that venous surgery of any kind alters the natural history of ulcer disease nor that venous surgery is superior to conservative treatment. However, there are reports of uncontrolled series in which saphenous surgery appears to confirm long-term benefit for selected patients.

(2) There is little evidence to support Homan's assertion that a perforator feeds every venous ulcer, but there does appear to be evidence of an association between incompetent calf perforators and venous ulcer disease. Limited data exist regarding the number, size and physiology of perforators in diseased and healthy states.

(3) The evidence on the haemodynamic effects of incompetent perforators is unclear and conflicting. This situation is summed up by the conflicting findings of the Zukowski and Akesson papers.

(4) There exist conflicting data from Bjordal and Campbell regarding the potential effects of saphenous surgery alone on perforator physiology.

(5) SEPS appears to be a safe procedure that effectively divides medial calf perforating vessels but there are no data demonstrating an advantage over the open procedure in terms of efficacy, morbidity and post-operative stay in hospital.

The present work, therefore, has the following aims:

(1) To examine the characteristics of calf perforating vessels in healthy and diseased states and to correlate the properties of these vessels with clinical status of the limb in terms of the severity of venous disease.

(2) To examine the effects of superficial venous surgery alone (i.e. without intentional perforator interruption) on the physical characteristics and function of calf perforating vessels.

(3) To describe the Edinburgh Vascular Unit's experience of open and minimally invasive perforator surgery.

Chapter 2

Development, Justification and Validation of Duplex Ultrasonography, Recruitment of Subjects and Classification of Venous Disease

2.1 Background

As indicated in the previous chapter, colour-flow duplex scanning technology has offered a radical new approach to the assessment of the venous system of the lower limbs. Older techniques of phlebography and varicography have largely been replaced for reasons of practicality, patient acceptability and radiation exposure under the assumption that duplex ultrasound is a satisfactory investigation.

Inevitably, the requirements and constraints of a research tool are different from those of an investigation to plan a surgical intervention. The present work represents a series of observational studies on subjects and patients. These volunteers may or may not require venous surgery, but the medical, and therefore ethical, justifications for performing invasive investigations with exposure to radiation are not present. Duplex ultrasonography was therefore an attractive investigation technique.

The aims of imaging the venous systems of the subjects were as follows:

- (1) Definition of the venous anatomy of each limb, especially in patients with anatomical variations and following surgery.
- (2) Definition of the sites of occlusion and reflux affecting the deep and superficial venous systems.
- (3) Detection of evidence of previous DVT.
- (4) Images of the medial calf perforating veins, both healthy and diseased.

The question to be answered was therefore whether duplex ultrasound could reliably give this information.

2.2 The principles of duplex ultrasound

Duplex ultrasonography has largely replaced phlebography for the routine examination of the venous system. Largely because it is non-invasive, it has good patient acceptability and therefore the potential for frequent, repeated examinations.

Ultrasound is defined as the frequency above human hearing (approximately 20kHz) and is emitted in short bursts from the transducer. The images are compiled from the returning echoes. Ultrasound is produced by a reverse piezo-electric effect, the echo reception itself results from the piezo-electric generated by returning sound striking the receiver and recording a signal in the form of electrical charge. The same crystals transmit and receive the sound waves.

Duplex ultrasonography or colour-flow Doppler ultrasound combines B-mode ultrasound with a superimposed colour image generated by the pulsed Doppler effect. Using complex calculations the colour image is combined with the greyscale image on the monitor.

The Doppler effect occurs when there is a relative movement between a sound source and a sound receiver. The observed frequency increases in proportion to relative velocities if the two objects are moving relatively towards each other and decreased if they are moving apart. (Meiere and Farrant 1995).

The Doppler principle is summarised by a mathematical form:

$$f_D = 2f_0 v \cos\theta / c,$$

where f_D is the Doppler frequency shift, f_0 is the incident frequency, v is the flow velocity, c is the speed of sound in tissue and θ is the angle between the ultrasound beam and the flow direction. This formula suggests that the frequency of an ultrasound echo from a moving object is not equal to the frequency of the incident sound wave. The calculated Doppler shift (f_D) is therefore dependent upon the velocity and direction of the reflector object.

Several factors impinge upon and limit the reliability of Doppler ultrasound: the transducer performance is limited; the ultrasound signal attenuates in tissue and red blood cells scatter the signal to a significant degree. These can be compensated for to some extent but there is an inherent compromise within the system (Taylor 1990).

2.3 The development of Duplex ultrasound for use in the assessment of venous disease. The derivation of “normal” values.

Following the development of colour flow duplex scanning, there was a significant change in the perceived importance of deep and superficial venous reflux with respect to the development of the skin changes of CVI. This topic has been discussed in the opening chapter. In summary, the role of superficial venous reflux alone as a cause for ulceration became clear and the concept of the so-called “post-phlebotic” limb has become one of a limb affected by chronic venous insufficiency of the deep and/or superficial venous systems. Over a ten-to-fifteen year period duplex was examined against phlebography, quoted as the “gold standard”, and then used to explore the pathophysiology of the lower limb venous system.

Much of the work on venous duplex was done in St. Mary’s hospital, London. Szendro et al published a comparison between duplex scanning and ambulatory venous pressure (Szendro 1986). The upper limit of normal for venous reflux was defined at 0.5s. Unfortunately, this value is not referenced. A reference is made to work by David Sumner, but upon review of this chapter the figure of 0.5s normal venous reflux is not quoted (Sumner 1984). Nonetheless this value appears entrenched in subsequent literature. Szendro et al examined 23 patients and six healthy volunteers. DVI was assumed to be present if the minimum pressure was more than 50mmHg on AVP, with a 90% venous return time of greater than 15s. This examination was taken as the “gold standard” against

which duplex was compared. Duplex scanning demonstrated a sensitivity of 84% and a specificity of 88%. The authors reported this as satisfactory. The biggest flaw in this paper seems to be the use of AVP as the evidence-based or reference standard for the detection of deep venous reflux. In particular, the use of tourniquets to “exclude” the contribution of superficial reflux has subsequently been shown to be an inadequate manoeuvre for the control of saphenous reflux.

In 1989, Van Bemmelen et al published a paper that has been cited frequently (Van Bemmelen 1989). The authors scrutinised the often-quoted 0.5s reflux time for normal veins. They measured the duration of venous reflux in the deep veins of 32 subjects. Their stated aims were the quantification of the duration of reflux at various sites in the deep venous system, a comparison of the recorded times when erect or in the 10⁰ reverse Trendelenberg position and the effects of proximal versus distal compression. The subjects were described as being in good health without history suggesting potential venous disease. The reflux times were found to be shorter in the upright position than recumbent ($0.69 \pm 0.83\text{s}$ vs. $1.79 \pm 0.95\text{s}$ at the common femoral vein on performing a Valsalva manoeuvre). Using a pneumatic rapid inflation cuff, the reflux times at the popliteal vein level were compared for proximal and distally sited compression. The reflux induced by proximal compression was considerably longer than that for the distal compression ($0.96 \pm 0.47\text{s}$ vs. $<0.5\text{s}$). This last value is now frequently taken to be a “normal” for popliteal vein reflux. 95% of values for venous reflux time at the common femoral, superficial femoral, profunda and popliteal vein levels were

less than 0.5s when measured following distal compression with a pneumatic rapid inflation cuff.

The authors conceded that the pressures generated by these passive methods were probably considerably different from those occurring in normal activities. However they felt that distal compression gave a closer approximation to a physiological stimulus than proximally induced flow. They went on to outline some of the pitfalls of phlebography. If the dye is injected proximally in the groin, the presence of a competent proximal valve will mask the effects of reflux more distally. Secondly, there is a paradoxical “trickle down” effect of contrast creeping down past the semi-closed valves of a patient in the recumbent position. Furthermore, phlebography gives little or no information on leakage from the calf muscle pump during the diastolic component of the pump cycle.

Further evaluation of duplex scanning, comparing it with both ascending and descending phlebography, was performed by Neglen and Raju in 1992 (Neglen 1992). The authors examined 52 limbs from 32 patients with venous disease of varying clinical severity. The “gold standard” was taken to be the axial scoring system devised by Kistner (Kistner 1986). The grade of reflux is determined by the distal extent reached by a contrast bolus injected into the groin vessels. The patients were examined in the semi-erect 60^o reverse Trendelenberg position. Criticism was made regarding the reliability of the Valsalva manoeuvre for examining groin vessels. Once more the authors were concerned with the potential inaccuracies associated with phlebography, namely, the effect of a

competent proximal valve, the effects of heavy contrast media, the natural open position of valves in the relaxed, recumbent limb and the potential for proximal obstruction to hide distal reflux disease. These problems accounted for the 36% discrepancy rate between duplex ultrasound and phlebography. Duplex was found to have the highest specificity (93% for patients examined in the erect position) and sensitivity (77%) when clinical grade was used as the disease-defining standard. This paper highlights the difficulties encountered when the evidence-based standard is demonstrated to be inadequate and is greatly superseded by a newer technology.

Baker et al confirmed the difficulties encountered with descending phlebography when comparing the findings duplex ultrasound (Baker 1993). Once more the problems of identifying isolated deep venous reflux with a descending contrast technique were exposed. The authors did however express a preference for the use of ascending phlebography to define anatomical variations and abnormalities in the most distal calf vessels.

In 1994, Masuda, Kistner and Eklof produced a paper performing a similar comparison to that performed by van Bemmelen (Masuda 1994). On this occasion however, the limbs examined were mainly diseased, 19 of 22 subjects had LDS or chronic venous ulcer disease. They concluded that in diseased limbs, the Valsalva manoeuvre produces the most consistent results when performed with the patient in the 15° reverse Trendelenberg position, but the pneumatic cuff was more effective in the standing position. The results of examination of the

proximal segments demonstrated similar results by either method. However, there was a high level of variability observed when the results for the popliteal vein examination were analysed on a case-by-case basis. The authors concluded that there was little to choose between any of the methods of examination of the popliteal and distal vessels, especially in symptomatic limbs. The authors expressed concern regarding the reliability of assessment of popliteal and calf veins. Of further note was the finding that in otherwise healthy limbs, up to 1.5s of reflux in the common femoral vein could be induced by a Valsalva manoeuvre in the reverse Trendelenberg position.

As preliminary work towards the Edinburgh Vein Study, a reproducibility study was performed (Evans 1997). The subjects were patients with severe venous disease. While good levels of concordance were observed, both inter- and intra-observer, certain sites and venous abnormalities produced discrepancies. Variation in observations were particularly evident on examining the critical popliteal vein segments. Potential sources of intra-observer were considered to be differences in anatomical knowledge (vascular surgeon vs. public health trainee vs. radiologist) and the crucial value of 0.5s to define pathological reflux.

Several investigative techniques for locating and assessing calf perforating veins have been described. These include continuous wave "pocket" Doppler (Miller 1974), thermography (Patil 1970), phlebography and duplex ultrasound (Labropoulos 1996, Sarin 1992). However, there remains little in the literature to describe duplex ultrasound methods for identifying and defining calf perforator

reflux. The Middlesex group described the results of several procedures as referred to in the opening chapter (McMullin 1990, Sarin 1992). However, they, like several other authors, did not describe their technique at all (Campbell 1995 and Labropoulos 1996).

2.4 Development of a protocol for the present work

For the present studies, a standard examination technique was devised based partially upon the literature cited above, and partially upon common practice within the radiology department of the Royal Infirmary of Edinburgh. The deep and superficial systems were examined with the patient virtually upright on a tilted table. Venous flux was induced by a Valsalva manoeuvre and manual calf squeeze and release. An initial general examination of the venous anatomy was performed, followed by detailed examination of specific segments by both the colour-Doppler and the spectral Doppler analysis functions of the machine. Examples of the screen images of these examinations are given on figures 2.1-8. Pathological reflux was defined at the 0.5s level for the popliteal segments (Van Bemmelen 1989). The following segments were assessed: the common femoral vein (CFV), the sapheno femoral junction (SFJ), the superficial femoral vein (SFV) at its origin and at the mid-thigh segment, if visible, the above and below knee segments of the popliteal vein and the posterior tibial vein (PTV). The last segment was the most difficult to identify and examine. This was often most easily found when searching for the perforating veins on the calf, the method for which is described below. The PTV was easily identified at ankle level and then traced back up the calf to the popliteal end. The presence of reflux was sought at the mid-calf level and just above the ankle.

Medial calf perforating veins were defined as vessels situated between the medial subcutaneous border of the tibia and the posterior midline of the calf, which were

seen to cross the deep fascia and to connect the deep (usually posterior tibial) vein with the superficial venous systems. Medial calf perforators were sought with the subject seated on a couch with the legs dependent, hanging freely. The examining technician sat on a low chair with the subject's foot perched on the chair edge. This minimised the relative movements between examiner, subject and probe. Venous flux was induced by a calf squeeze and release manoeuvre. The calf was squeezed distal to the subject vessel. The most distal perforators were examined after a foot squeeze and release.

Each perforator was examined using the colour flow Doppler, and where possible, the spectral Doppler analysis functions of the machine. A vessel was determined to be competent if it exhibited only inward flow, and to be incompetent (IPV) if it was seen to allow deep to superficial (venous) flow, whether or not flow was unidirectional outward or bidirectional. The maximum diameter of the vessel (mm) was also recorded. The lower limit of resolution of the duplex scanner allowed detection of perforators down to 1mm in diameter.

Figure 2.1 (a&b). Just below the sapheno-femoral junction in B-mode and colour flow. ALT, antero-lateral tributary, LSV, long saphenous vein, CFV, common femoral vein.

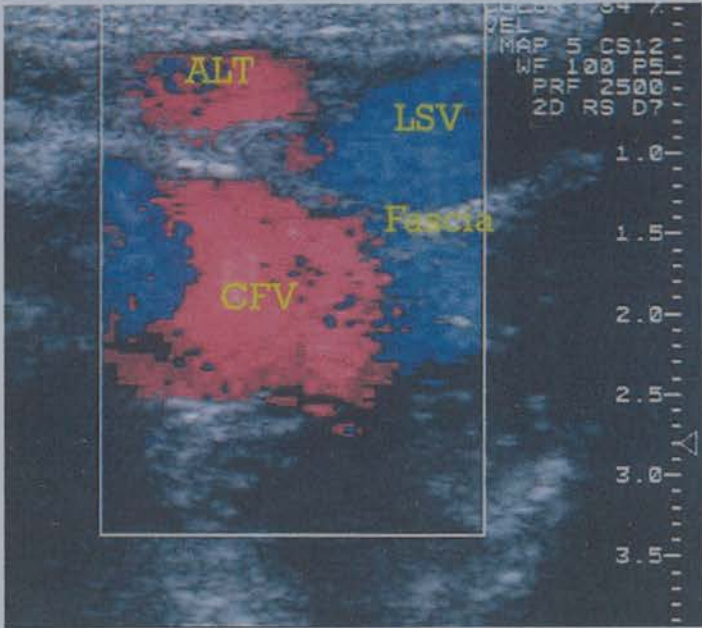
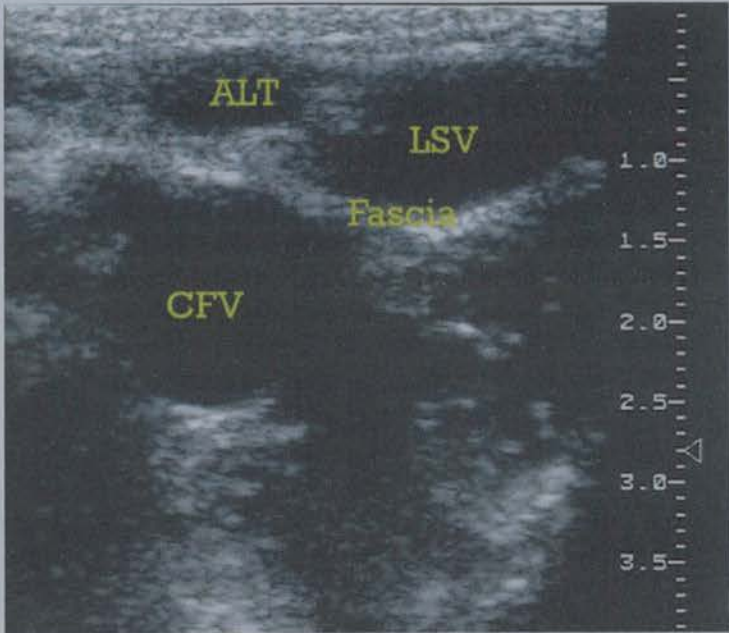


Figure 2.2 Hunter's (mid-thigh) perforator. LSV, long saphenous vein, MTP mid-thigh perforator, F, fascia.

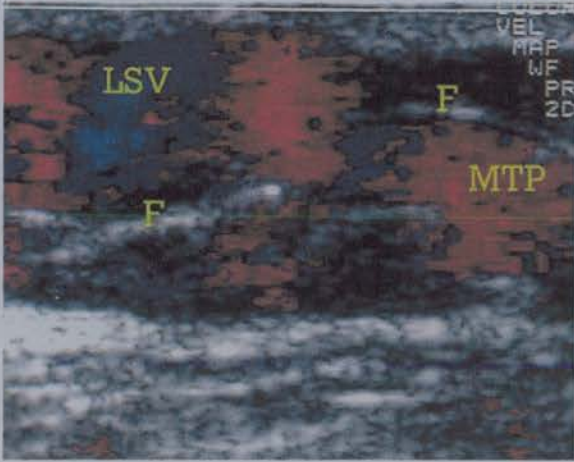


Figure 2.3 (a&b). Incompetent short saphenous vein (SSV) and a competent popliteal segment.

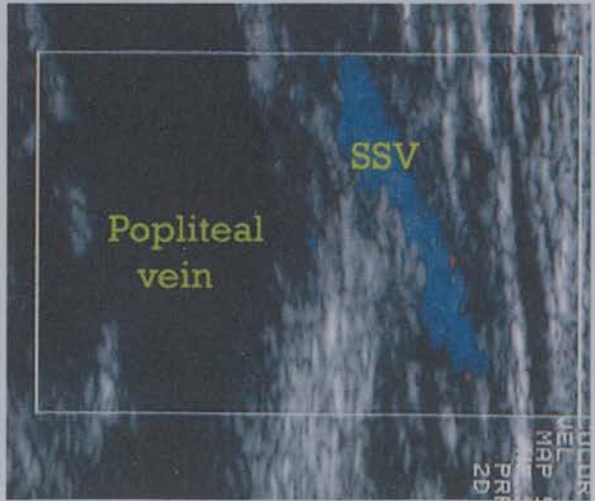
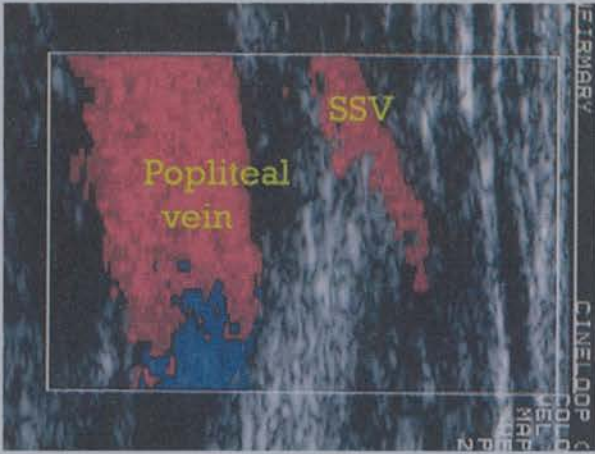


Figure 2.4 (a&b). Incompetent perforating vein (IPV) crossing the fascia and communication with a superficial vein (sup vn).

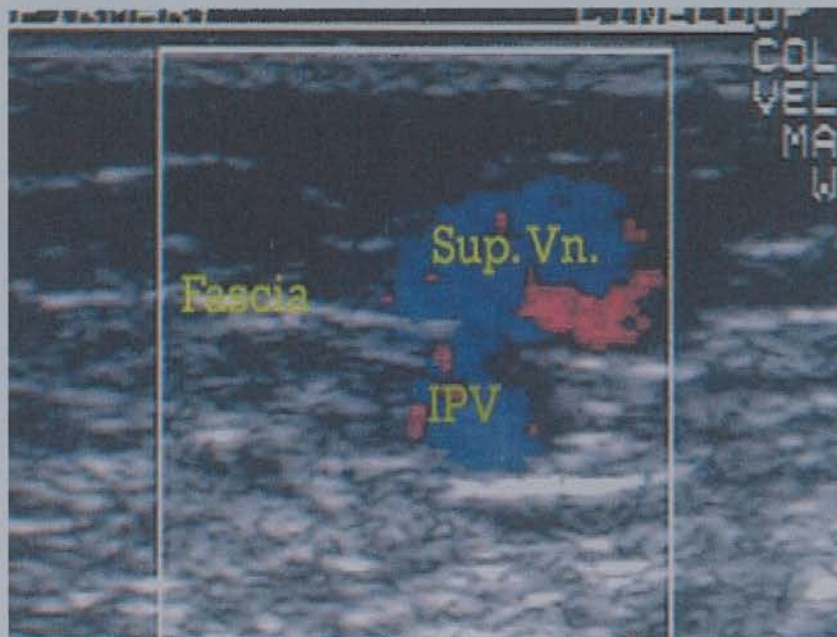
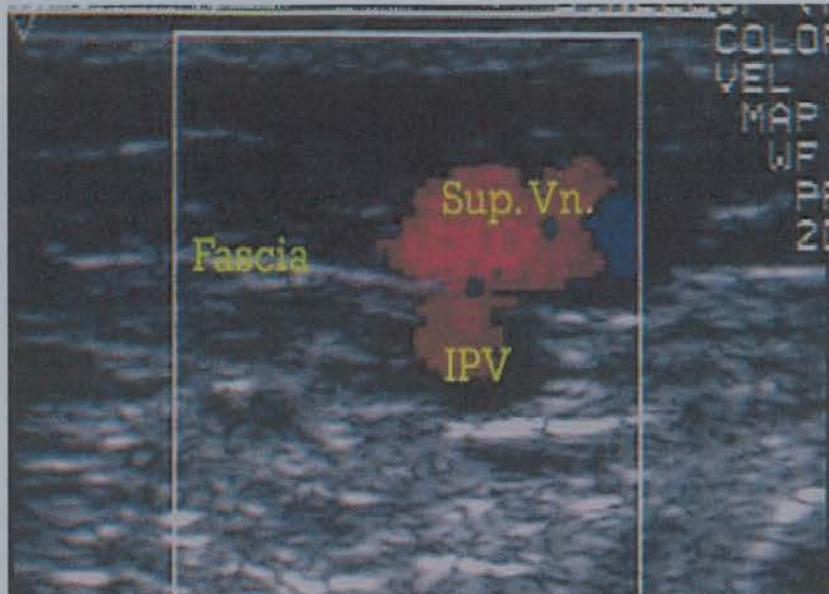


Figure 2.5 (a&b). Incompetent calf perforating vein in communication with an incompetent segment of posterior tibial vein (PTV).

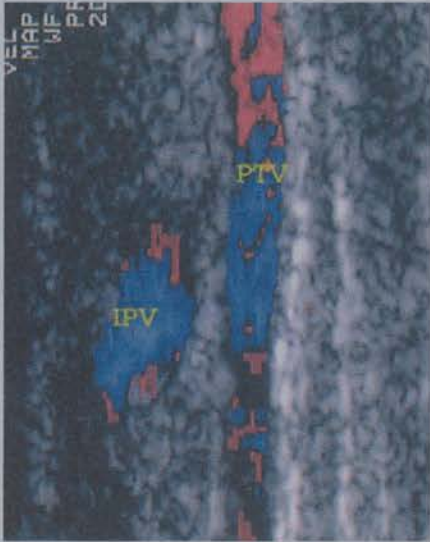
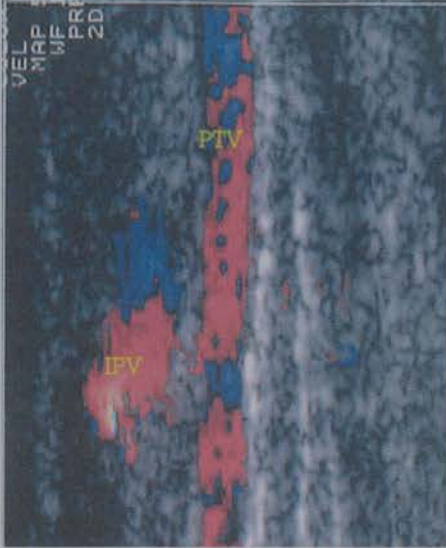


Figure 2.6 (a&b). Incompetent calf perforating vein in communication with a competent segment of posterior tibial vein (PTV).

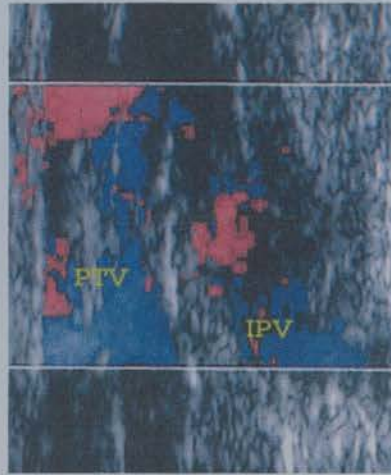


Figure 2.7. Paratibial calf perforator.

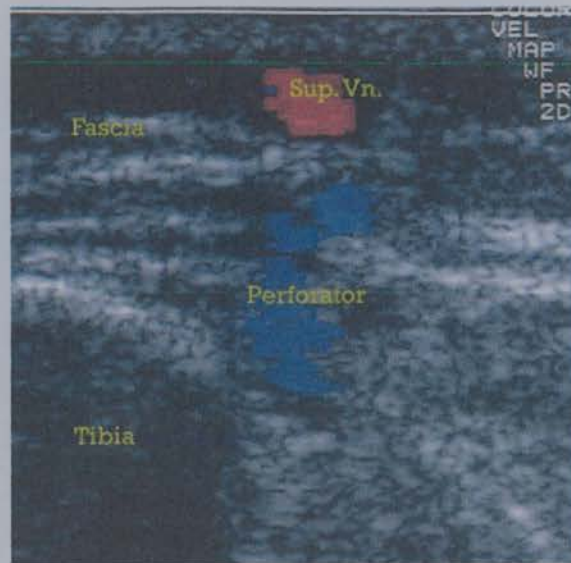
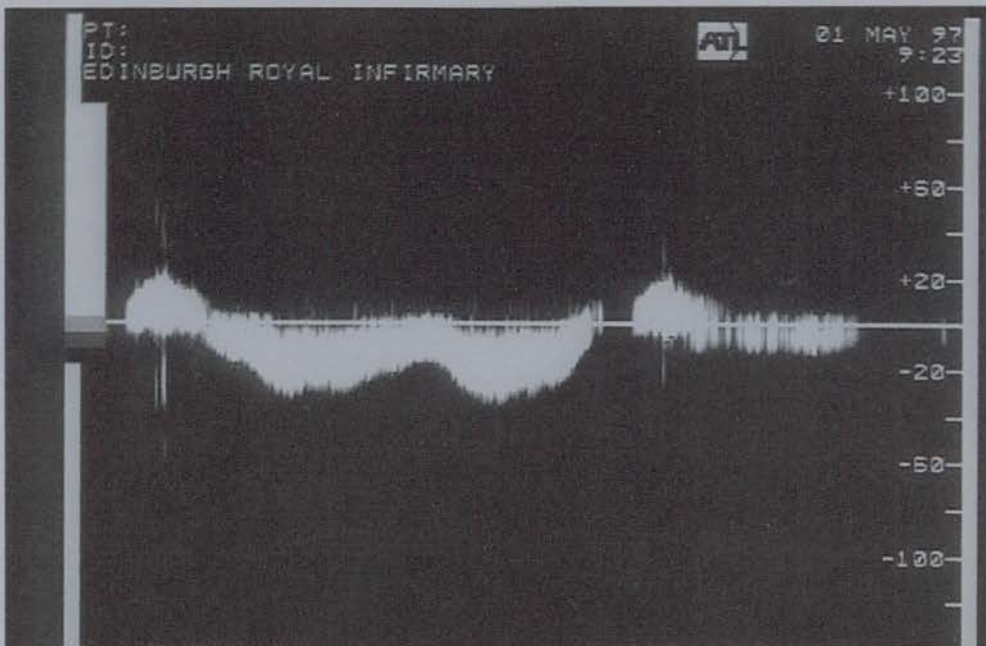


Figure 2.8. Spectral analysis of blood flow through calf perforating vein during foot squeeze and release. Note bidirectional flow.



2.5 Validation

The data were crosschecked in a number of cases where patients with lipodermatosclerosis or ulcers proceeded to SEPS. Twenty-four limbs underwent surgery. Seventy perforators were identified pre-operatively by duplex. 59 perforators were confidently identified by the surgeon at operation. This leaves a discrepancy of 11 perforators. In two cases the marked perforator was too distal to be reached by the scope and the structure taken to be the perforator could not be dissected confidently enough to be allow clipping. The dissection was therefore discontinued. In three procedures bleeding caused the procedure to be abandoned after interrupting the first perforator leaving a total of eight perforators that were unverified. In two cases, there was no evidence of the perforator at the marked site. Two unmarked perforators were found operatively. This means that in the cases where the duplex detected site of a perforator was adequately examined by the surgeon (60 places), a perforator was found in 58 cases within 2 cm of the mark. Two marks had no perforators at them and two additional perforators were identified. These results compare well with published series (Pierik 1998).

The present work would have been considerably strengthened by a validation study to confirm inter and intra-observer in standard duplex technique for main stem pathology.

2.6 Reporting Standards and the classification of venous disease

Classification provides functions essential to research. Subject groups can be compared and researchers are enabled to communicate with each other. In medicine, a further function is to facilitate a comparison before and after intervention. The classification system should be simple and easy to use, repeatable and consistently reproducible and comprehensive.

The basis of a classification system for venous disease should take into account the key questions asked of clinician and researcher. Where is the disease? What is the nature and aetiology of the disease? How bad is it? How does it impact upon the patient?

The earliest classifications were based upon clinical findings, in particular anatomical distribution of abnormalities. Widmer devised a system for the well-known Basle study (Widmer 1978). This has subsequently provided the starting point for other classifications. He graded the veins themselves as being trunk varices defined as dilated tortuous trunks of the long or short saphenous vein and their major branches of the first or second order, reticular varices, defined as dilated subcutaneous veins, not belonging to the main trunk or its major tributaries, and hyphen webs, defined as intradermal venectasis. Porter et al on behalf of the International Consensus Committee on Chronic Venous Disease produced a similar series of definitions (Porter 1995). Varicose veins were defined as dilated, palpable subcutaneous veins generally larger than 4mm, reticular veins were, dilated, non-palpable subdermal veins 4mm in size or less

and telangiectasis was defined as dilated intradermal venules less than 1mm in size. Both of these classifications only give information on the superficial manifestations of venous disease.

Some attention must also be given to the severity of venous disease. The Society for Vascular Surgery and the North American Chapter on the International Society for Cardiovascular Disease produced a document in 1988 grading the clinical severity of venous disease. The limbs were graded as Class 0, asymptomatic, Class 1, mild CVI, with mild to moderate swelling or discomfort, with dilated subcutaneous veins, locally or generalised, Class 2, moderate CVI, including hyperpigmentation of the gaiter area, brawny oedema and subcutaneous fibrosis (lipodermatosclerosis), but without ulceration, and Class 3, severe CVI, comprising pain, ulcerative changes, eczema, and/or severe oedema (Porter 1988).

Further classification can be performed according to site and aetiology of the venous disease. However, there are inherent difficulties associated with this. The patient does need to be investigated using radiological imaging in order that this can be done with accuracy.

A consensus statement regarding the classification of venous disease was issued following the annual meeting of the American Venous Forum in Maui, Hawaii in February 1994 (Porter 1995). A bold attempt was made to devise a classification system which defined venous disease according to Clinical, (A)Etiological, Anatomical and Pathological criteria, the so-called CEAP classification (Table

2.1). To this was added an anatomical score, which was the sum of the anatomical segments involved, each scoring one point, a clinical score and a disability score. The clinical score was obtained by summing the values (0, 1 or 2) given for each of the following aspects: pain, oedema, venous claudication, pigmentation, lipodermatosclerosis, the size of the largest ulcer, the duration of the ulcer, ulcer recurrence and ulcer number. The disability score was from 0 to 3, 0, asymptomatic, 1, symptomatic, but can function without support device, 2, can work 8-hour day with support device and 3, unable to work even with support device. There was no place given to haemodynamic venous function.

The CEAP classification provides data on venous disorders to a fine level of detail together with a structure to present the data. However, the process of classification is laborious and does not lend itself to easy interpretation of the data. For example, a patient with ulceration, due to deep venous reflux and obstruction following a DVT, combined with varicose veins, a common presentation, will have a disability score of C3A5D2 and a CEAP classification of C₅E_SA_{2R,3R,13RO,14RO,16R,17R}P_{RO}. A further difficulty occurs when reviewing a patient either post-intervention or as part of a follow-up study. The patient remains in (a minimum of) clinical class 5 even if the skin improves dramatically.

For the purposes of the present work the patients were originally classified by the clinical grading system suggested in the 1988 Reporting Standards Paper (Porter 1988). This is a neat system that, in practice, has produced little clinical overlap between the groups. Furthermore, the classification produces groups that are

immediately clinically relevant to both the patient and the clinician. When the data were published in peer-reviewed journals, the referees suggested adopting the CEAP system and where possible this was done (Appendix, Published Papers).

Table 2.1. Summary of CEAP Classification.

Criteria		Groupings
Clinical	Class 0	No evidence of venous disease
	Class 1	Telangiectesiae or reticular veins
	Class 2	Varicose veins
	Class 3	Oedema
	Class 4	Skin changes
	Class 5	Healed ulcer
	Class 6	Open ulcer
(A)Etiological	E _C	Congenital
	E _P	Primary, undetermined cause
	E _S	Secondary, known cause
		Post-thrombotic Other
Anatomical	Superficial veins (A _S)	
	Segment 1	Telangiectasis/reticular veins
	Segment 2	LSV, above knee
	Segment 3	LSV, below knee
	Segment 4	Short saphenous vein
	Segment 5	Non-saphenous
	Deep veins (A _D)	
	Segment 6	Inferior vena cava
	Segment 7	Common iliac
	Segment 8	Internal iliac
	Segment 9	External iliac
	Segment 10	Pelvic (gonadal, broad ligament)
	Segment 11	Common femoral
	Segment 12	Deep femoral
	Segment 13	Superficial femoral
	Segment 14	Popliteal
	Segment 15	Crural
	Segment 16	Muscular
Segment 17	Thigh perforating veins	
Segment 18	Calf perforating veins	
Pathophysiological	P _R	Reflux
	P _O	Obstruction
	P _{R,O}	Reflux and obstruction

2.7 Patients and volunteers

Royal Infirmary of Edinburgh in-patients and healthy volunteers were the subjects for investigation of the association between perforator properties and clinical status. Fifty healthy volunteers were recruited to act as controls. These subjects were drawn from colleagues, friends and patients undergoing elective non-vascular general surgical procedures. All had palpable distal pulses and gave no history to suggest peripheral vascular occlusive disease (PAOD). It was felt that diminished arterial flow through the lower limb due to PAOD might significantly alter the venous flow characteristics. This was demonstrated to be likely in a small group of patients scanned for saphenous vein mapping prior to lower limb revascularisation in whom the perforators were also assessed. In these limbs perforators were almost entirely absent and long refill periods were required between calf/foot squeeze manoeuvres to allow blood flow in calf perforating veins to reappear on the display.

The controls gave no history of venous surgery, injections for varicose veins or DVT. They had no clinical evidence of venous disease, in the form of trunk varices, reticular varices or hyphen webs as defined by Widmer (see below) (Widmer 1978). In each limb the main venous trunks, superficial and deep, were examined for reflux or occlusion using duplex ultrasound and the data for that limb were not used if either were present. The number, diameter and competence of perforators in each limb were recorded. The scanning techniques are described below. The patients with varicose veins were recruited from the elective

admissions to the Edinburgh Vascular Unit for varicose vein surgery. The patients with ulcers were recruited from Professor Ruckley's venous clinic.

The patients were categorised in to clinical grades according to the 1988 reporting standards recommendation as suggested by the Journal of Vascular Surgery (JVS) (Porter 1988) and later the CEAP guidelines when these were published Porter (1995) (see above).

Chapter 3

The relationship between the number, competence and diameter of medial calf perforating veins and clinical status in patients with lower limb venous disease.

3.1 Background and aims

As outlined in the opening chapter, the relationship between perforator anatomy and physiology and the clinical status of the lower limbs has not been completely elucidated. The aim of this study therefore, was to explore this relationship and establish any associative link between incompetent calf perforating veins (IPV) and the clinical status of the limb.

3.2 Patients and methods

The subjects and patients were divided into four clinical groups. In Group 1 (50 limbs) were subjects without evidence of venous disease on history, examination or duplex scanning of the superficial and deep systems (CEAP clinical grade 0). Group 2 (95 limbs) comprised patients with varicose veins but no skin changes except oedema (CEAP grades 2&3). In Group 3 (58 limbs) were limbs affected by lipodermatosclerosis, with no history of ulceration (CEAP grade 4). The Group 4 (108 limbs) cohort consisted of patients with a history of venous ulceration, either active or healed (CEAP grades 5&6).

The demographic features of the four groups are outlined in Table 3.1. The differences between the proportions of patients of each sex did not reach statistical significance, even when calculated on the basis of limbs rather than number of subjects. The increase in age across the clinical groups reaches the statistical significance at the level of $p < 0.01$ (Kruskal-Wallis).

The subjects underwent duplex ultrasound scanning as described in Chapter 2.

Table 3.1. Demographic characteristics of subjects in relation to Clinical Group and CEAP grade.

CEAP clinical grade and Group	0 Group 1	2/3 Group 2	4 Group 3	5/6 Group 4	P value
Subjects/patients	28	71	46	87	
Male: female ratio	14:14	24:47	24:22	41:46	ns*
Limbs	50	95	58	108	
Median age (range) (years)	49.5 (23-81)	54 (19-77)	58 (39-76)	64.5 (29-87)	<0.01†

ns, not significant; * χ^2 test; † Kruskal-Wallis one-way analysis of variance.

The relationship between number, flow characteristics and diameter of the medial calf perforating veins, superficial and deep main stem venous reflux and the clinical severity of chronic venous insufficiency are summarised in Table 3.2.

3.3 The relationship between main stem disease and clinical status

Deteriorating clinical status was associated with a significant increase in the prevalence of short saphenous and deep venous reflux (Table 3.2, Figure 3.1). In particular, a history of open or healed ulceration was strongly associated with reflux in the popliteal and posterior tibial veins. Six patients had a history of radiologically proven DVT. However, duplex findings of thickened vein walls, strictures and deformed, immobile valvular cusps suggested that (perhaps) a higher proportion had suffered a sub-clinical or undiagnosed DVT. Eleven limbs in the group of patients with and ulcer history demonstrated deep venous obstruction on duplex.

Figure 3.1 Graphical representation of data in Table 3.2. The distribution of venous reflux on duplex by clinical group. Note, group 1 subjects have no disease.

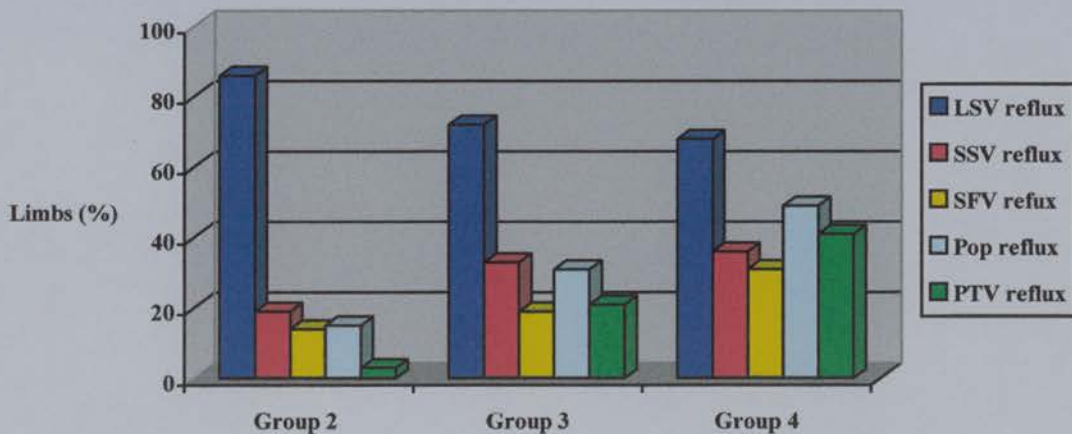


Table 3.2. The relationship between clinical grade and duplex ultrasonography findings of main stem venous pathology.

	Group 1	Group 2 n (%)	Group3 n (%)	Group4 n (%)	p value
LSV reflux	-	82 (86%)	42 (72%)	74 (68%)	NS
SSV reflux	-	18 (19%)	19 (33%)	39 (36%)	0.046*
SFV reflux	-	13 (14%)	11 (19%)	34 (31%)	0.014*
Pop V reflux	-	14 (15%)	18 (31%)	53 (49%)	0.002*
PTV reflux	-	3 (3%)	12 (21%)	44 (41%)	<0.001*
Deep occlusion	-	-	-	11 (10%)	

LSV, long saphenous vein; SSV, short saphenous vein; SFV, superficial femoral vein; PopV, popliteal vein; PTV, posterior tibial vein; IQR, inter-quartile range; IPV, incompetent perforating veins; * χ^2 test; † Kruskal-Wallis one-way analysis of variance; ns, not significant

3.4 The relationship between the number of medial calf perforators, IPV and clinical grade.

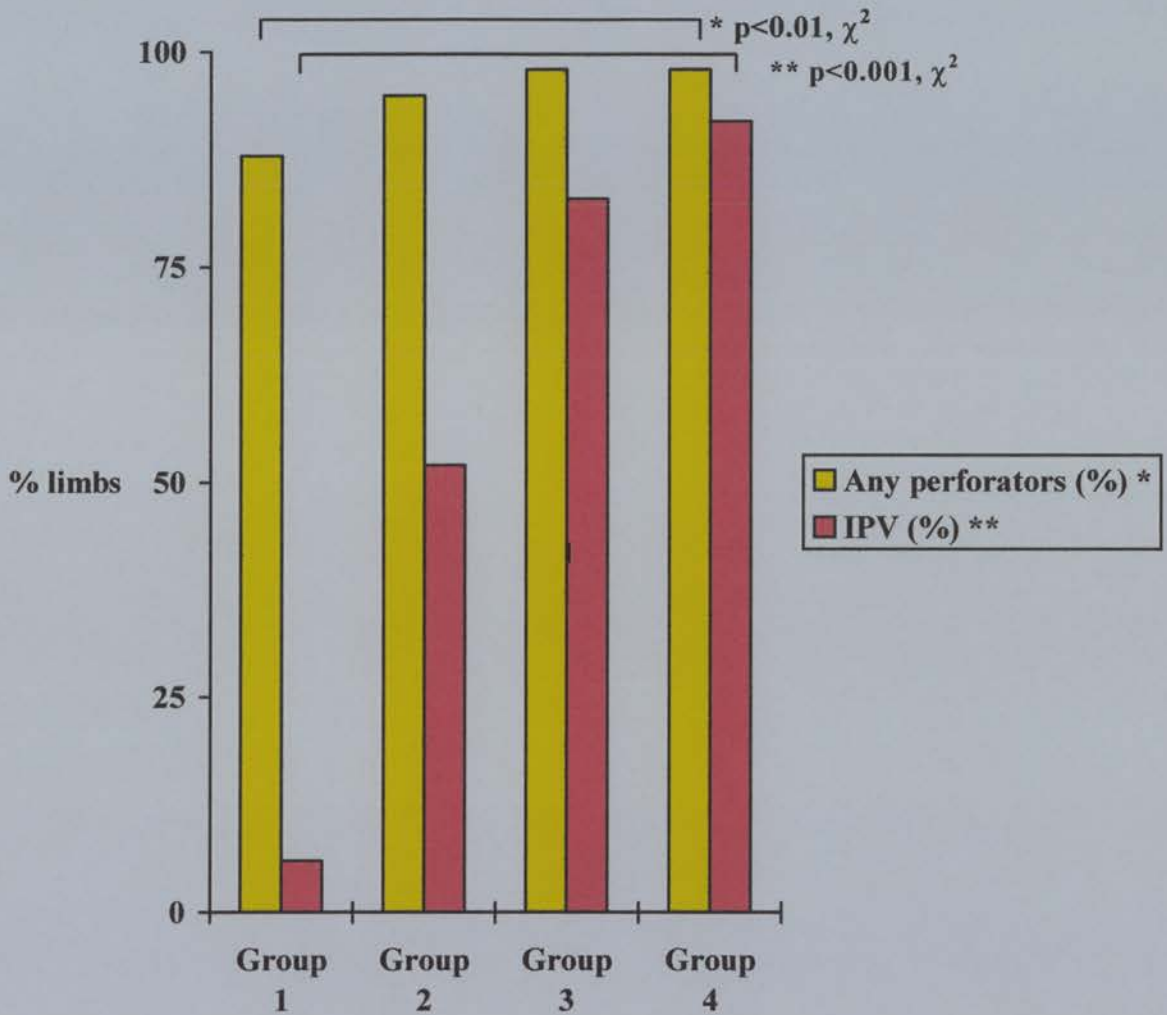
Deteriorating clinical status was associated with a small, but significant increase in the proportion of limbs in which medial calf perforating veins were detected (Table 3.3, Figure 3.2). More importantly, there was also a highly significant increase in the proportion of limbs in which IPV could be demonstrated. In Group 1 limbs (normal controls), only 3 (5%) of the 65 perforators imaged were IPV, compared with 193 (77%) of the 252 perforators visualised in the Group 4 limbs.

Table 3.3. The association between the number medial calf perforating veins imaged, flow characteristics and clinical status.

Perforator flow	Group 1 n (%)	Group2 n (%)	Group3 n (%)	Group 4 n (%)	p-value
Any flow	44 (88%)	90 (95%)	57 (98%)	106 (98%)	<0.01*
Only inward flow	41 (82%)	41 (43%)	9 (15%)	9 (8%)	<0.01*
outward and/or bidirectional flow	3 (6%)	49 (52%)	48 (83%)	97 (90%)	<0.001*

* χ^2 test

Figure 3.2. Relationship between the total number of medial calf perforators imaged (yellow), the number of IPV (red) and clinical group.



Both the total number of perforators (Figure 3.3) and the number of IPV (Figure 3.4) per limb increased significantly with deteriorating clinical status (Table 3.4).

Table 3.4. The median (IQR) number of medial calf perforators and IPV imaged per limb with clinical grade.

	Group 1 n (IQR)	Group 2 n (IQR)	Group 3 n (IQR)	Group 4 n (IQR)	p-value
All perforators	1(1-2)	2(1-3)	2(1-3)	2(2-3)	<0.001†
IPV only	0(0-0)	1(0-2)	1(1-2)	2(1-2)	<0.001†

IQR, inter-quartile range; IPV, incompetent perforating veins; † Kruskal-Wallis one-way analysis of variance; ns, not significant

Figure 3.3 Percentage of limbs demonstrating each number of medial calf perforators within each clinical grade (p<0.001, Kruskal-Wallis).

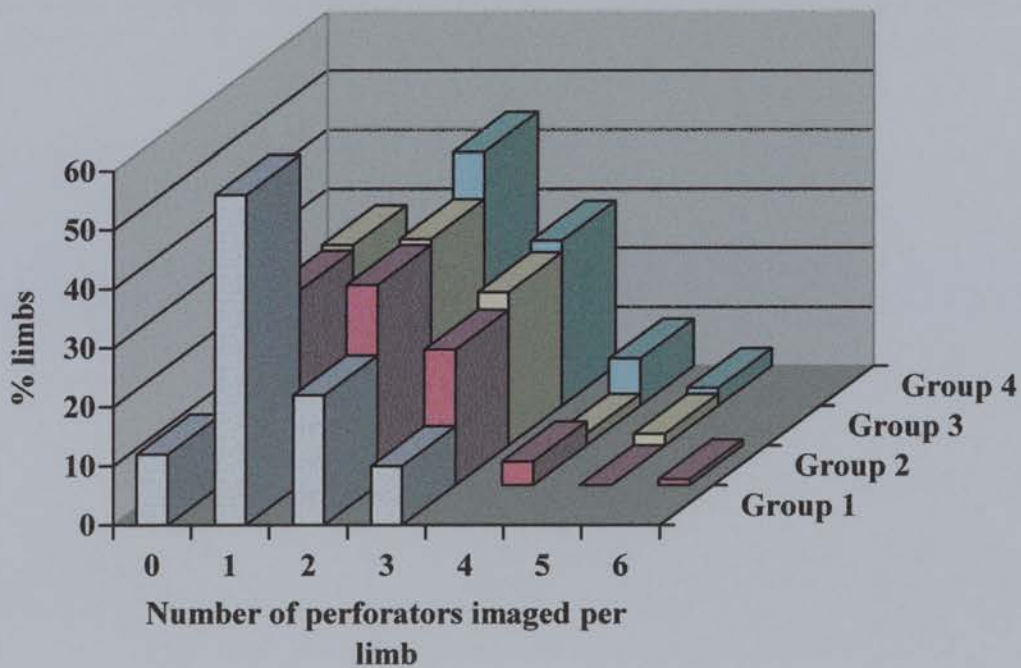
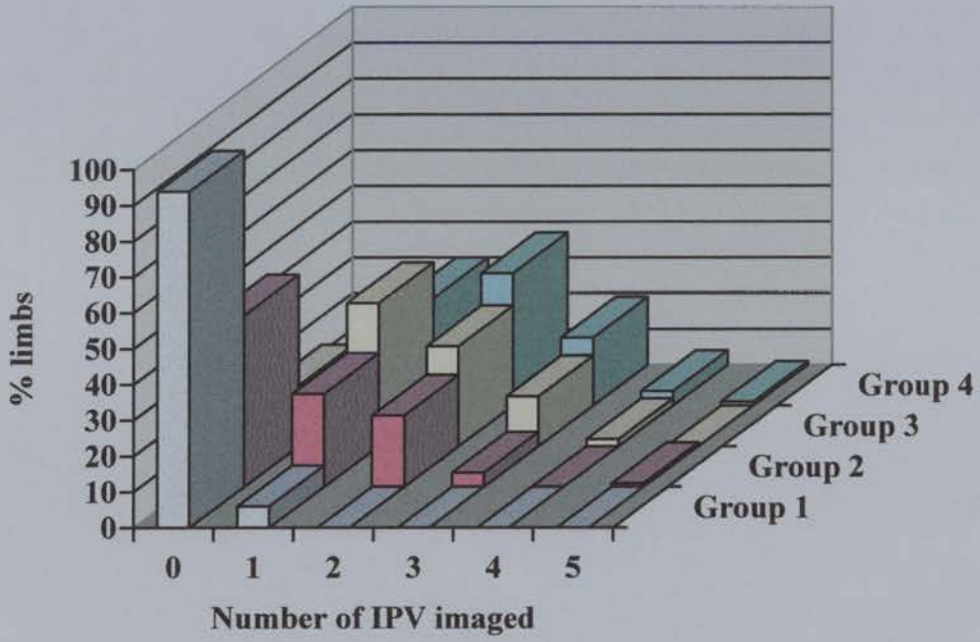


Figure 3.4 Percentage of limbs demonstrating each number of IPV within each clinical grade ($p < 0.0001$, Kruskal-Wallis).



3.5 The relationship between maximum perforating vein diameters and clinical grade

The median maximum perforator diameter rose significantly with deteriorating clinical grade (Table 3.5). In the group 1 subjects, those with no main-stem venous disease, perforators of 1 or 2mm diameter predominated. However, in the group of limbs with an ulcer history the majority of perforators were greater than 4mm in diameter (Figure 3.4).

Figure 3.5 The relationship between clinical grade and maximum perforator diameters. The percentage of perforators at each diameter is shown for the four clinical groups ($p < 0.0001$, Kruskal-Wallis one-way analysis of variance).

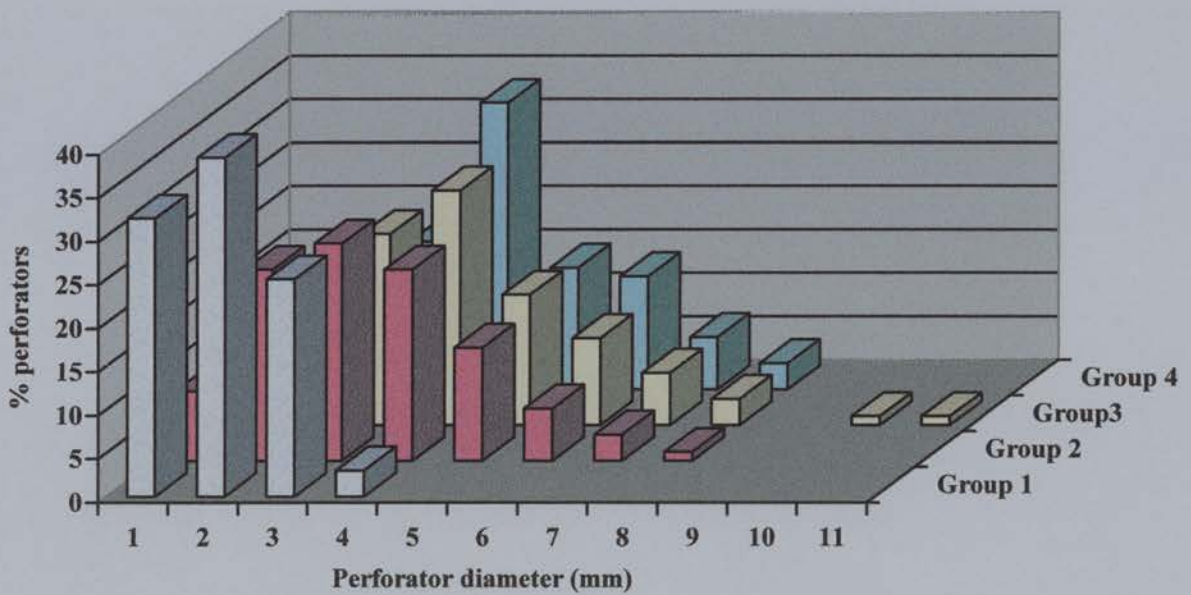


Table 3.5. Median maximum diameters of medial calf perforating veins with clinical grade.

	Group 1	Group 2	Group 3	Group 4	p-value
Median diameter (mm) of perforator (IQR)	2(1-3)	3(2-4)	4(3-5)	4(3-5)	<0.001†

IQR, inter-quartile range; † Kruskal-Wallis one-way analysis of variance.

3.6 The relationship between perforator physiology and maximum diameter

The diameters of IPV were significantly greater (median 4, range 1-11mm) than competent perforators (median 2, range 1-6mm; $p < 0.0001$, Mann-Whitney U), with most competent perforators (83%) being less than 4mm, and most IPV (81%) being 4mm or greater in maximum diameter (Table 3.6). As a result there was a significant increase in the median maximum perforator diameter with deteriorating clinical grade.

Table 3.6. The relationship between maximum observed perforator diameter and the flow patterns of medial calf perforators.

Diameter	Inward flow only (n)	Outward flow only (n)	Bidirectional flow (n)
1mm	37	2	-
2mm	92	4	8
3mm	63	4	56
4mm	29	4	118
5mm	5	2	66
6mm	3	1	49
7mm	-	-	28
8mm	-	1	11
9mm	-	-	-
10mm	-	-	1
11mm	-	-	1

$p < 0.0001$, χ^2 test for a contingency table.

3.7 Chapter summary

- (1) Deteriorating clinical grade is associated with a significant increase in the prevalence of IPV.
- (2) Deteriorating clinical grade is associated with a significant increase in the number of detectable perforators.
- (3) Deteriorating clinical grade is associated with a significant increase in the number and proportion of IPV per limb.
- (4) Deteriorating clinical grade is associated with a significant increase in the maximum diameter of perforators insonated.
- (5) Isolated IPV are rare, both in normal limbs and as the sole abnormality in limbs demonstrating signs of chronic venous insufficiency.

Chapter 4

The association between maximum perforator diameter, number, and competence and the gender and age of subjects and the distribution of main stem venous disease

4.1 Background and Aims

Data from the previous chapter established an association between clinical manifestation of venous disease and abnormalities of calf perforating veins. In particular, a strong association was demonstrated between deteriorating clinical status and increasing number, maximum diameter and likelihood of demonstrating bidirectional flow through medial calf perforating veins.

The present analysis addresses three further issues: the effect of patient age and gender on perforator competence; the relationship between the distribution of main stem venous disease (superficial system reflux, deep system reflux and obstruction) and perforator anatomy and physiology; and the identification of sites of reflux in the deep and superficial veins particularly associated with IPV.

4.2 Patients and Methods

The limbs studied comprised 50 limbs with no clinical or duplex evidence of venous disease in the deep or superficial venous systems (CEAP clinical group 0); 95 limbs exhibiting varicose veins, but no skin changes (CEAP 2/3); 55 limbs that were affected by lipodermatosclerosis, but with no history of venous ulceration (CEAP 4); and 107 limbs that had a history of venous ulceration, active or healed (CEAP 5/6).

The subjects and patients were examined clinically and by means of colour-flow duplex scanning as described in chapter 2.

Data were entered into a computer for analysis using SPSS for windows version 10 and SAS. The chi-squared test was used to examine differences in nominal variables across both CEAP grade and presence/absence of IPV. Students t-test was used to examine differences in mean age between IPV categories. PROC GENMOD of SAS was used to calculate the odds ratios (95% confidence intervals) of the risk of IPV for various patterns of disease. The odds ratios were then adjusted for age and gender. These analyses were performed by Dr. AJ Lee.

4.3 Results

The population studied comprised 307 limbs from 230 subjects. The demographic characteristics of the subjects and patients and CEAP grades of the limbs are given in Table 4.1. There were 168 (55%) limbs from females and 140 (45%) from males. The ages ranged from 19 to 87 years with a median of 58.

Table 4.1 Demographic features and CEAP clinical grades of patients and subjects.

<i>CEAP Clinical Grade</i>	<i>0</i>	<i>2/3</i>	<i>4</i>	<i>5/6</i>	<i>P value</i>
	<i>Group 1</i>	<i>Group 2</i>	<i>Group 3</i>	<i>Group 4</i>	
Subjects (n)	28	71	44	87	
Male:female	14:14	24:47	24:20	41:46	NS
Limbs (n)	50	95	55	107	
Median age in years	49.5	54	58	64.5	<0.01
(range)	(23 to 81)	(19 to 87)	(39 to 76)	(29 to 87)	

Analysis was χ^2 test or Kruskal-Wallis test. NS, not significant.

The distribution of main stem venous disease across the population is given in Table 4.2.

There was no association between the proportion of limbs demonstrating IPV and gender (Table 4.3). However, the limbs demonstrating IPV belonged to patients who were significantly older than those not demonstrating IPV ($p < 0.001$). This reflects the age differences across CEAP clinical grades as shown on Table 1,

rather than a true association between increasing age and increasing frequency of IPV. Worsening clinical CEAP grade was significantly associated with an increasing proportion of IPV (Table 4.4).

Table 4.2 The distribution of venous disease (reflux and obstruction) among the 308 limbs.

Site of reflux	n	%
No reflux	50	16.2
LSV	205	66.6
SSV	89	28.9
Any superficial reflux	242	78.6
Any deep reflux	106	34.4
Superficial reflux alone	152	49.4
Deep reflux alone	16	5.2
Both superficial and deep reflux	90	29.2
Deep system obstruction	11	3.6

LSV, long saphenous vein; SSV, short saphenous vein.

Table 4.3 The association between gender and age and the presence of IPV.

	No IPV (n=112)	IPV (n=196)	p value
Male	46.4 (52)	44.9 (88)	
Female	53.6 (60)	55.1 (108)	0.795
Age (years)	52.7 (1.62)	60.5 (0.94)	0.0001

Values are n (%) or mean (standard error). Analysis using the chi-squared test or the t-test.

Table 4.4 The relationship between CEAP grade and the presence of IPV

	No IPV (n=112)	IPV (n=196)	p value
CEAP grade 0	42 (47)	1.5 (3)	0.001 (χ^2 test)
CEAP grade 2/3	39.3 (44)	25 (49)	
CEAP grade 4	8.9 (10)	24 (47)	
CEAP Grade 5/6	9.8 (11)	49.5 (97)	

VV's, varicose veins; LDS, lipodermatosclerosis. Values are % (n) and analysis by chi-squared test.

In the absence of main stem venous reflux, incompetent perforators were rarely observed (3 limbs, 2%). However, a significantly higher number of subjects with superficial system reflux alone, deep system reflux alone and mixed superficial and deep disease demonstrated IPV (Table 4.5). A similar pattern was observed when analysis was repeated for the presence of any deep disease or any superficial disease on a limb regardless of the presence of disease in another anatomical site.

Table 4.5. The association between patterns of venous disease and the presence of IPV.

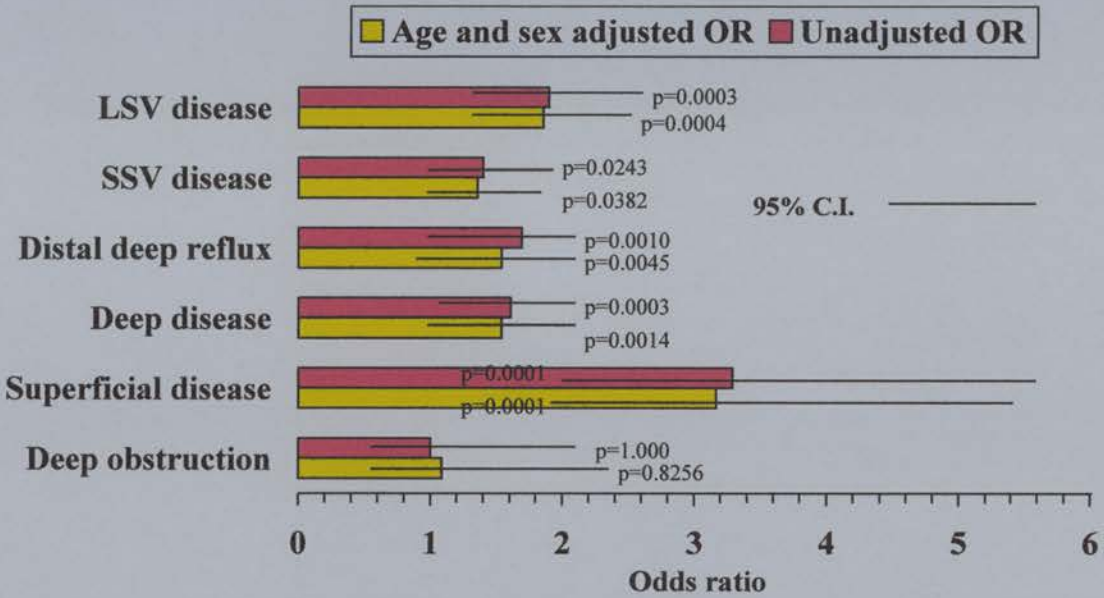
	No IPV (n=112)	IPV (n=196)	p value
No reflux	42 (47)	1.5 (3)	0.001
Superficial reflux only	45.5 (51)	51.5 (101)	
Deep reflux only	3.6 (4)	6.1 (12)	
Superficial and deep reflux	8.9 (10)	40.8 (80)	
Any deep disease	12.5 (14)	46.9 (92)	0.001
Any superficial disease	54.5 (61)	92.4 (181)	0.001
Deep obstruction	3.6 (4)	3.6 (7)	1.0
LSV disease	44.6 (50)	79.1 (155)	0.001
SSV disease	16.1 (18)	36.2 (71)	0.001
Deep distal reflux	12.5 (14)	42.9 (84)	0.001

LSV, long saphenous vein; SSV, short saphenous vein. Distal reflux is defined as that observed in the popliteal vein or below. Values are % (n) and analysis using the chi-squared test.

From analyses so far, it is clear that the presence of venous reflux disease, in many patterns, is associated with the presence of IPV on a limb (putting aside the issue of clinical grade). Odds ratios for the risk of IPV, within various patterns of venous disease were calculated with and without adjustment for age and sex (Figure 1). Superficial reflux appears to have the greatest association with IPV (adjusted odds ratio 3.17, 95% confidence interval 1.87 to 5.40). Deep system

obstruction was not associated with an increased risk of IPV (adjusted odds ratio 1.09, 95% confidence interval 0.51 to 2.33).

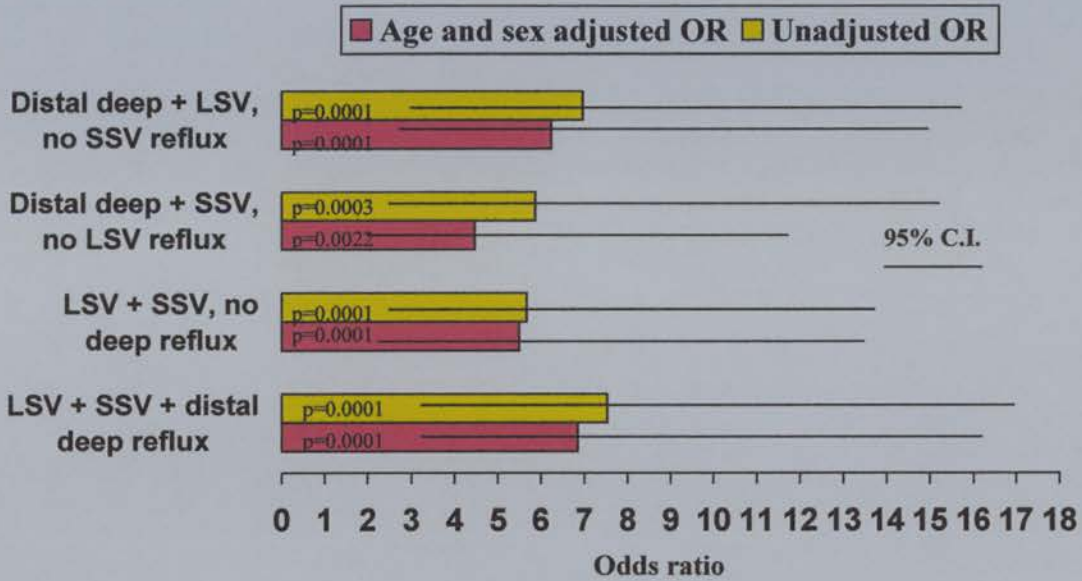
Figure 4.1. Odds ratios for the presence of IPV in association with various patterns of venous disease. Base group is no venous reflux or obstruction.



LSV, long saphenous vein; SSV, short saphenous vein, CI, confidence intervals.

Further odds ratios were calculated for the presence of IPV within various combinations of venous disease. There were 31 limbs with deep distal reflux (27 of these with IPV) and LSV disease, but no SSV disease; 15 limbs (11 with IPV) with deep distal reflux and SSV disease, but no LSV disease; 24 limbs (17 with IPV) with LSV and SSV disease, but no deep distal disease; 35 limbs (33 with IPV) with deep distal reflux disease and LSV and SSV disease. There were 56 limbs with no deep distal reflux, no LSV and no SSV reflux, and the risk of IPV in each of the four combinations was compared to this group (Figure 2).

Figure 4.2. Odds ratios (95% confidence interval) for the presence of IPV in association with various combinations of venous disease. Base group: no venous reflux or obstruction.



LSV, long saphenous vein; SSV, short saphenous vein; CI, confidence intervals; OR, odds ratio.

After adjustment for age and sex, the risk of IPV was highest among the group with SSV, LSV and deep distal disease (odds ratio 6.85, 95% confidence interval 2.97 to 15.83). The risk of IPV was lowest among those with deep distal disease and SSV disease, but no LSV disease (odds ratio 4.47, 95% confidence interval 1.71 to 11.67). However, all of the odds ratios were highly statistically significant ($p < 0.001$).

4.4 Chapter summary

- (1) IPV are most likely to be found associated with correctable superficial venous reflux disease.
- (2) The odds ratios (OR) for the presence of IPV on a limb were greater for superficial reflux, either long or short saphenous veins (either together or separately) than for deep venous reflux.
- (3) The odds ratio analysis was calculated for those limbs in which the deep system showed reflux in the popliteal venous segment and distally. The values were similar to those for either long saphenous or short saphenous reflux in isolation.
- (4) The OR values for limbs with deep system obstruction were approximately unity. In other words, the presence of IPV was similar to the base group that comprised limbs with no clinical or duplex ultrasound evidence of venous disease.
- (5) Calculations were performed for the combinations of venous reflux disease across the long and short saphenous and distal deep venous systems. Due to the small numbers in each subgroup, the 95% confidence intervals were found to be wide and, although all ORs were statistically significant, no particular combination seemed more likely to be associated with IPV than any other.
- (6) Similar OR calculations were not attempted for differential CEAP grades since the numbers in each group were so small the analysis would be meaningless.

Chapter 5

The effects of venous surgery on perforator anatomy and physiology

5.1 Background

In the first chapter, reference was made to potential alterations to perforator anatomy and physiology resulting from surgery to the saphenous system alone (Campbell and West 1995). The present chapter addresses the important issue of (1) reversibility of pathological perforator function and (2) the dependency of perforator incompetence on deep and superficial venous system reflux.

5.2 Summary of patients and methods

This chapter deals with the effects of varicose vein surgery on the saphenous system on the medial calf perforating veins. The subjects were patients admitted to the Edinburgh Vascular Unit for elective varicose vein surgery between May 1996 and December 1996. All patients, by definition, had varicose veins considered amenable to venous surgery.

The patients underwent duplex scanning prior to venous surgery and then a median of 14 (range 6 to 26) weeks post-operatively. As previously outlined, the patients' deep, superficial and perforator systems were examined. The actual surgery performed was left to the discretion of the operating surgeon. Routine practice was flush ligation at the sapheno-femoral junction, individual ligation of

groin tributaries, stripping of the long saphenous vein to a point just below the knee and multiple stab avulsions at sites marked pre-operatively. Short saphenous veins were flush ligated, but not stripped.

5.3 Results

Sixty-two limbs from 47 patients (18 male, 29 female) were examined. The subjects were of median age 58 (range 35-77) years. In 47 limbs there were varicose veins only, with no skin changes; five limbs demonstrated lipodermatosclerosis with no history of ulceration; and ten limbs had a history of venous ulceration. Sixteen (26%) of the sapheno-femoral junctions had previously been explored. The distribution of the pre-operative main stem venous reflux is shown on Table 4.1.

Table 5.1. Sites of pathological venous reflux.

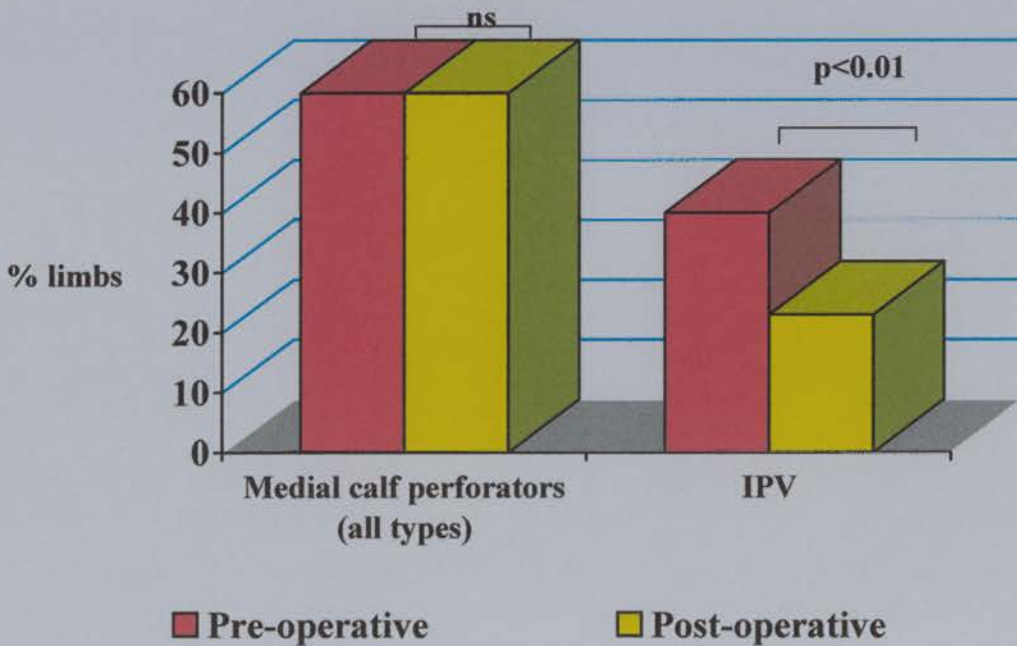
Site of reflux	Pre-operative n (%)	Post-operative n (%)
Long saphenous vein*	55 (89)	4 (6)
Short saphenous vein	12 (19)	3 (5)
Superficial femoral vein	8 (13)	7 (11)
Popliteal vein	6 (10)	6 (10)
Posterior tibial vein	6 (10)	6 (10)
Superficial reflux only	49 (79)	5 (8)
Deep reflux only	-	14 (23)
Deep and superficial reflux	13 (21)	2 (3)

* reflux in the above knee segment

Fifty-two patients underwent high saphenous ligation and stripping of the long saphenous vein (LSV) to the knee level. A further two patients underwent stripping of the LSV from a point lower than the groin, the groin not being re-explored in these two cases. Ten patients underwent ligation of the short saphenous vein in the popliteal fossa.

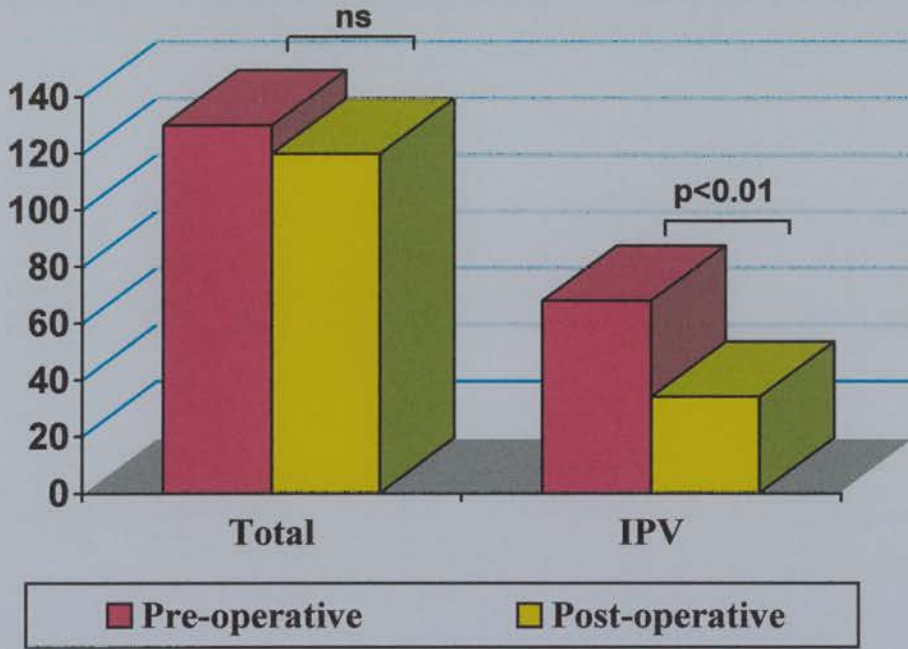
Pre-operatively, medial calf perforating veins, competent or otherwise, could be imaged in 60 limbs. This number was unchanged post-operatively. Forty limbs demonstrated incompetent calf perforating veins (IPV) pre-operatively, compared with 23 post-operatively ($p < 0.01$, χ^2 test) (Fig 5.1).

Figure 5.1. The effect of main stem venous reflux present post-operatively on the proportion of limbs demonstrating IPV (statistical test- χ^2 test).



A total of 130 perforators were seen pre-operatively. This had fallen to 120 post-operatively, but this change was not statistically significant. The total number of IPV in the series fell from 68 to 34 ($p < 0.01$, χ^2 test) (Fig 5.2).

Figure 5.2. The effect of main-stem venous reflux present post-operatively on the total numbers of medial calf perforators and IPV (statistical test- χ^2 test).

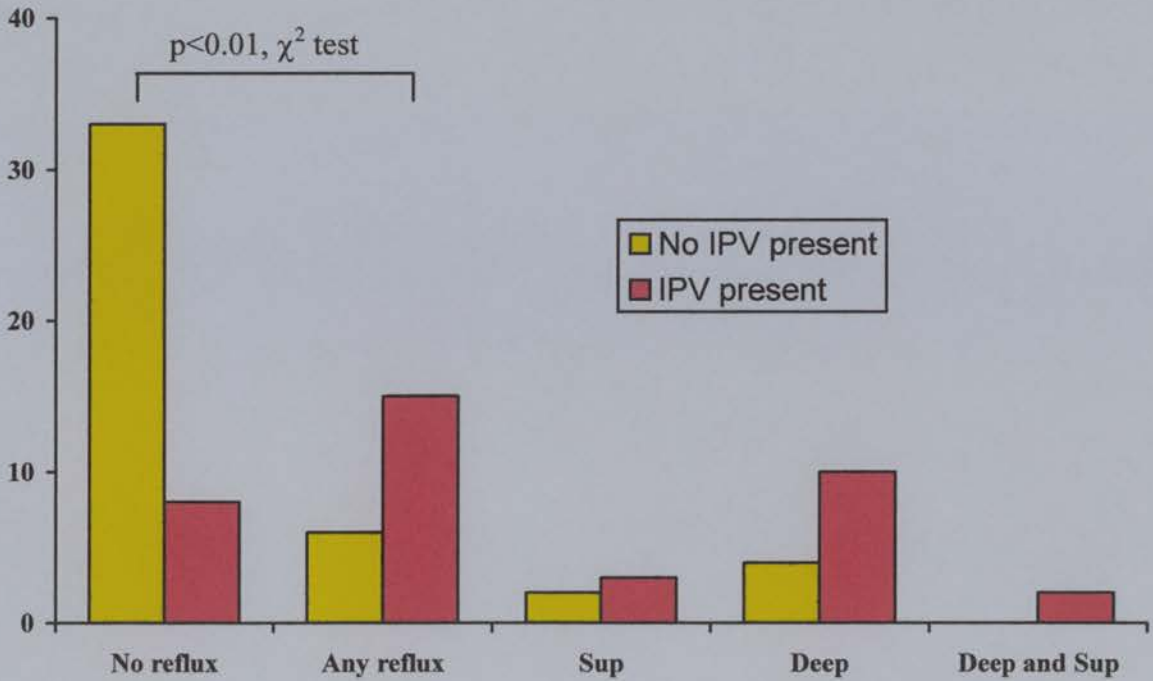


IPV, incompetent perforating vein; Sup, superficial system reflux; Deep, deep system reflux.

The effects of the remaining venous disease

Exploring this further, of the 41 limbs in which there was no main stem venous reflux present after saphenous surgery, only eight (20%) demonstrated IPV. This is compared with 15 (71%) of the 21 limbs in which there remained main-stem reflux (in either the deep, superficial or both systems) post-operatively ($p < 0.01$, χ^2 test). The distribution of IPV and post-operative venous reflux is illustrated on Figure 5.3.

Figure 5.3. The effect of reflux present post-operatively on the proportion of limbs demonstrating IPV.



IPV, incompetent perforating vein; Sup, superficial system reflux; Deep, deep system reflux.

Furthermore, of the 47 limbs in which there was no clinical evidence of lipodermatosclerosis or ulceration, 14 (30%) demonstrated post-operative evidence of remaining IPV. However, nine of the 15 limbs (60%) with the skin complications of CVI still had IPV post-operatively ($p < 0.05$, χ^2 test).

The median maximum diameter of all calf perforating veins fell significantly from 4mm (range 1-11) pre-operatively to 3mm (range 1-8) post-operatively ($p < 0.01$, Mann-Whitney U).

5.4 Chapter Summary

- (1) Surgical treatment of superficial venous reflux disease resulted in a small, non-significant reduction in the number of perforators imaged.
- (2) Surgical treatment of superficial venous reflux disease resulted in a significant reduction in the number of incompetent calf perforating veins.
- (3) Residual main-stem venous reflux was associated with the persistent presence of incompetent calf perforating veins.
- (4) Eradication of main-stem venous reflux, even in limbs with a normal deep system, does not always result in total eradication of IPV.

Chapter 6

Complications and Early Outcomes of Perforator Surgery

6.1 Background and aims

The published outcomes of Linton's and Cockett's procedures show a great deal of variation with respect to reported complication rates as well as ulcer healing and recurrence rates (Chapter 1, p 65, Table 1.4). Professor Ruckley had been performing Linton's procedure in Edinburgh until 1992 and had been performing SEPS from 1993 to 1997. Therefore, it was possible to examine the case notes for complications and immediate outcomes for comparison purposes.

As well as the change in operative technology between the two groups, namely SEPS, it is important to consider other possible differences between these two, non-randomised cohorts. The imaging performed pre-operatively would have been different. Most of the patient in the open procedure group would not have had duplex scanning, but would have been investigated by phlebography. The discharge policy is likely to have changed over the period under review, as part of a general move towards earlier discharge of surgical patients. Furthermore, as the open procedure was recognised to be a major addition to simple varicose vein surgery, the patients may have had a longer and more protracted ulcer history than the SEPS group.

6.2 Subfascial endoscopic perforator surgery is associated with significantly less morbidity and shorter hospital stay than open operation (Linton's Procedure)

Patients and Methods

The medical records of patients undergoing Linton's procedure and SEPS under the care of Professor Ruckley were reviewed. The patients were identified through the Lothian Surgical Audit (LSA) database and records retrieved. The records of all the patients identified by the LSA search were retrieved. The patients were divided into two groups, those who underwent an open, Linton's procedure, acting as a historical control group, and those who underwent SEPS. The Linton's group of patients underwent surgery between January 1978 and July 1992 and the SEPS group between September 1993 and July 1996.

A further prospective study of patients undergoing SEPS from August 1996 onwards was also performed. These patients were operated under the care of Professor Ruckley and Mr Bradbury. They were investigated by duplex ultrasonography before and after surgery. These limbs also formed the cohort for validation of duplex technique described in chapter 2.

The case notes of 61 patients who had interruption of calf perforating veins for lipodermatosclerosis or ulceration were reviewed. Thirty-one patients (22 male, nine female), median age 55 (range 23-82) years underwent 37 Linton's

procedures between January 1978 and July 1992. Thirty patients (13 male, 17 female) of median age 57.5 (range 37-83) years under went SEPS (30 procedures) between September 1993 and July 1996.

Results

There were no significant differences with respect to age or indication for surgery between the SEPS and the Linton's patients. However, significantly more patients had the long saphenous vein stripped in the SEPS group (Table 5.1).

Table 6.1 Indication for perforator interruption and concomitant procedures.

	Linton's procedure (n=37)	SEPS (n=30)
Indication for procedure		
Lipodermatosclerosis	5	5
Open ulceration	12	8
Healed ulceration	20	17
Concomitant procedures		
Perforator ligation alone	5	1
High saphenous ligation alone	13	2*
High saphenous ligation and stripping	17	26*
Short saphenous ligation	5	8
Skin grafting	4	2

SEPS, subfascial endoscopic perforator surgery. *p<0.01 versus Linton's procedure (χ^2 test).

(three), infection (four) and flap necrosis (two)) were the major cause of delayed discharge after Linton's procedure. Other complications are shown in Table 6.2.

Table 6.2 Post-operative complications

Complication	Linton's procedure (n=37)	SEPS (n=30)
None	21	22
Saphenous nerve injury	0	2
Deep venous thrombosis	1	1
Groin wound complications	3	3
Readmission	5	5
Calf wound complications	9	0*

SEPS, subfascial endoscopic perforator surgery. *p<0.01 versus Linton's procedure (χ^2 test).

The presence of open ulceration at the time of surgery was not associated with a significantly prolonged post-operative stay in either group. For the SEPS group the median stay was 2 (range 1-49) *versus* 3 (range 1-15) days and in the Linton's group 10 (range 3-30) *versus* 9 (range 5-21) days for the open and healed ulcer groups respectively.

One patient in each group was readmitted for radiologically proven proximal deep venous thrombosis requiring anti-coagulation.

6.3 Chapter summary

- (1) The demographic features, indications and concomitant procedures are similar for the two groups of patients.
- (2) SEPS is associated with fewer documented complications than the open procedure.
- (3) SEPS is associated with a shorter duration of post-operative stay in hospital than the Linton's procedure patients.

Chapter 7

Discussion and conclusions

7.1 Introduction

Proving a cause or even a role for a potential aetiological factor within given a disease process can be difficult. Koch laid down three postulates to determine whether an infective agent was responsible for a given disease: the bacterium must be present in every case of the disease; the bacterium must be isolated from the host and grown in culture; the specific disease must be reproduced when a pure strain of the culture is inoculated into a susceptible host and the bacterium must be recoverable from the experimental host. These postulates have caused problems within the world of microbiology, not least with respect to new infective disease processes such as Creutzfeldt-Jacob disease. However, the principles provide a framework within which it is possible to explore the role of a given aetiological factor in a given disease.

The evidence regarding the aetiology of venous ulceration is, by Koch's rigorous standards, far from complete. As stated at the end of chapter one, there exists no evidence, in the form of a randomised controlled trial, that venous surgery of any kind alters the natural history of ulcer disease. There is, however, evidence of association between various forms and combinations of venous disease and ulceration. Labropoulos' work, in particular, illustrates a strong association between an increasing proportion of the venous system exhibiting reflux disease

and deteriorating clinical status (Labropoulos 1996). It is accepted that venous ulceration occurs when venous disease causes the failure of the calf pump mechanism beyond a certain point. This point of failure has been defined in haemodynamic terms using AVP and APG (Nicolaidis 1993).

In a standing patient, the venous pressure at the foot is determined by the height of the column of blood from the right atrium to the point of measurement. The differences between healthy and diseased limbs occur with the effects of exercise, measured as a higher ambulatory venous pressure and a faster return to the resting pressure on cessation of exercise (Nicolaidis 1993). The question therefore remains: what is the precise role of perforator incompetence in this impairment of the calf pump mechanism?

7.2 Association

The principal findings of Chapter 3 are that, in patients with CVI, deteriorating clinical status is associated with an increase in the prevalence of IPV, an increase in the number of IPV insonated per limb and an increase in the maximum diameter of the duplex detectable calf perforators. Advancing clinical disease was also associated with a significant increase in superficial, particularly short saphenous, and deep, particularly distal, venous reflux. These data support the work of others, and confirm that the vast majority of IPV exist in association with superficial and/or deep venous reflux (Labropoulos 1996). It would appear therefore that isolated perforator incompetence is rare. The strongest association between IPV and venous reflux disease at another site, as calculated by odds ratios, was with long saphenous vein reflux. However, all venous disease, alone or in combination was associated with an increased odds ratio of IPV being present with perhaps, surprisingly, the exception of deep obstruction.

In Chapter 3 the changes in the anatomical distribution of venous disease associated with deteriorating clinical grade were demonstrated. Some consideration must be given to the sample selection. Subjects were either normal controls or patients attending the Vascular Surgical unit in Edinburgh. Therefore, there was no random component to the selection. Subjects were only categorised as “normal” if there was no history of venous disease, symptoms or intervention, and if no main stem venous disease was detected on duplex scanning. Consideration must therefore be given to the possibility that this group represents an atypical population with respect to venous disease. In particular, the CEAP

Grade 1 limbs are not represented. These are subjects with hyphen webs, reticular veins or telangectasiae. Similarly, those attending with symptomatic venous disease may represent a skewed population. Some people with obvious varicose veins have little or nothing in the way of symptoms. Patients attending clinics may complain of symptoms for a variety of reasons. The anatomical distribution for each individual patient was sufficient to cause complaints, whether cosmetic or physical. This series therefore has excluded those with main stem venous reflux or obstruction that are symptom free or have symptoms that are minor enough that they are not referred to hospital. These may represent a sizable and interesting population.

Despite these qualifications, it is possible to draw a number of conclusions. Long saphenous vein reflux is the commonest form of symptomatic venous abnormality presenting to hospital clinicians. Excluding the possible contribution of calf perforating veins, long saphenous incompetence alone, which is present in the region of 50% of most published series, can be associated with the full range of symptoms from minimal cosmetic considerations to chronic ulceration. This form of venous incompetence is also the most amenable to surgical correction. All the other anatomical patterns of venous incompetence are less common, but also carry the potential for the same spectrum of symptoms. The question can then be posed: which additional factors lead to deterioration in the clinical situation to the point of ulceration?

In the series of subjects and patients presented in this and other works, deteriorating clinical status is associated with a statistically significant increase in the frequency of venous reflux in all the anatomical distributions, except long saphenous reflux. This variable remains constant (Labropoulos 1996, Lees, 1993). LSV reflux is the most common form of venous reflux associated with varicose veins alone, but with deterioration in clinical status, LSV reflux assumes a smaller proportion of the burden of reflux disease in the population. In other words additional factors are implicated that appear to take the form of reflux at additional sites, including the calf perforating veins.

In our studies, the percentage of limbs in which perforators of any type could be imaged increased with deteriorating clinical status. This increase was small but statistically significant (Figure 3.1). The number of limbs in which incompetent perforators could be imaged increased dramatically (Figure 3.1). Deteriorating clinical grade was also associated with a small, but statistically significant, increase in the median (total) number of medial calf perforators imaged per limb (Table 3.2, Figure 3.2). More importantly perhaps, there was a highly significant rise in the median number of incompetent calf perforators per limb that could be demonstrated (Figure 3.3). Thus the absolute number and the proportion of IPV per limb can be seen to have increased. "Normal" limbs do have perforators present that can be imaged (present in 88% of subjects), but these are small vessels of predominately 1-2mm diameter. Furthermore, these vessels rarely demonstrate bidirectional flow. Of 65 perforating veins detected in 50 normal limbs, only 3 (6%) were abnormal, that is, manifesting bi-directional flow.

It is interesting that the total number of perforators rose with clinical disease severity. This is likely to have represented an increase in the diameter of perforators making them visible on duplex, rather than an increase in the actual number. The minimum diameter detectable by the Ultramark 9 machine is approximately 1mm. Alternatively, the increased number of vessels imaged could represent a proliferation of venous channels crossing the subfascial space. However, this would imply a neovascularisation process occurring across an anatomical boundary, which seems less likely.

The median diameters of vessels increased with deteriorating clinical status (Figure 3.4). IPV have a median diameter of 4 (range 1-11) mm compared with the 2 (range 1-6) mm median diameter of competent vessels. The number and proportion of these larger incompetent vessels increased with deteriorating disease category. The greater the vessel diameter, the lower the resistance to blood flow. The present study has shown that there are between one and four such low resistance vessels, each with a median diameter of 4mm, on the medial aspect of the calf in the typical limb affected by CVI and/or venous ulceration.

Vessels of less than 4mm in diameter are unlikely to be incompetent. In this study only 28 % demonstrated outward or bidirectional flow on testing (Table 3.3). However, vessels of diameter 4mm or greater are unlikely to be competent. A mere twelve percent of these larger vessels were competent.

The causal relationship is unclear. Do perforators that are dilated as a consequence of a chronically raised AVP then become incompetent, or do initially incompetent vessels become more dilated? A similar chicken and egg situation exists regarding the total limb disease and IPV. Do IPV contribute causally to the deteriorating clinical status, or are they simply another manifestation or secondary effect of a deteriorating situation analogous to thread veins on the skin?

There appeared to be a preponderance of elderly patients in the more severe disease groups (Table 3.1). Analysis was therefore performed to identify the effects of possible age and gender bias. Although there were no identifiable areas of bias, a correction for age was introduced for calculating odds ratios.

Regardless of age or sex of the subject, in this population the majority of those with long saphenous, short saphenous or distal segment deep venous reflux had IPV (Table 3.4). Of the entire population of 308 limbs examined, 112 did not demonstrate IPV. Forty-two percent of this group comprised those with no other venous disease (Table 3.5). However, a further 45.5% of those without IPV were subjects with superficial system reflux only. In other words superficial system reflux can often be present without IPV being manifest.

If we consider the data in tables 3.5 and 3.6 another way, it is clear that in the majority of limbs with venous reflux disease at any main stem site and in any given combination have IPV. Furthermore, an increase in the number of anatomical sites in which reflux occurs appears to correlate to an increase in the

proportion of limbs with IPV: 66% of limbs with superficial reflux and 75% of limbs with deep reflux have IPV compared with 89% of those with a combination of deep and superficial venous reflux disease. Therefore odds ratios (OR) were calculated to identify the risk of IPV from the various combinations of venous disease.

The single disease entity with the highest OR for IPV was long saphenous disease (Figure 4.1). Patients with LSV reflux were twice as likely to have IPV as the subjects without. Patients with any superficial reflux at all, either LSV or SSV, were three times more likely to have IPV. Combinations of venous disease demonstrated an additive effect. Patients with a “full house” of reflux in the long and short saphenous systems as well as the distal deep system (popliteal and calf veins) had a greater than four fold increase in risk for IPV (Figure 4.2). These risk values will be discussed further in the context of the effect of venous system surgery.

It is surprising to note that deep venous obstruction does not carry any increase in the likelihood of IPV in contrast to deep venous reflux that does. However, the total number of patients with deep venous obstruction was small (10 limbs). Nonetheless, this calls into question the Cockett model for the pathological development of IPV. This aspect will be discussed later.

7.3 Normal values

With a sample size of only fifty normal limbs, it is difficult to draw too many firm conclusions regarding normal perforator anatomy and physiology. This is further confused by the data from the Edinburgh Vein Study, despite the fact that this study did not investigate perforators (Evans 1999). The unexpectedly high prevalence of reflux in the deep and superficial systems in an otherwise “normal” population calls into question what constitutes a normal venous tree. Nonetheless a few rules can be formed from the data presented thus far.

(i) In the absence of main stem venous reflux, whether deep or superficial, incompetent perforating veins are rare. Only three limbs in the normal control group demonstrated IPV. The maximum diameter of these vessels was 3mm. The majority (88%) of these normal limbs however, did have perforators large enough to be detected by duplex.

(ii) In the presence of main stem venous reflux, incompetent perforators are likely to be found on a limb. As stated above, with deteriorating clinical status, the proportion of limbs with IPV increases. Limbs with “simple” varicose veins carry a 52% chance of having IPV.

(iii) It is normal to find perforators when duplex scanning normal limbs and these will number a median value of one medial calf perforator per limb. As indicated above, the median number of perforators identified increases with deteriorating clinical status to a maximum value of a median of two per limb (inter-quartile

range 2-3). This number has been confirmed operatively (Chapter 2) and by others (Pierik 1998, Labropoulos 1996). Assuming that new vessels do not grow across the fascia and that the increase in the number of perforators indicates an increase in the number detectable, it can be said that there are a median of two significant medial calf perforators per limb (interquartile range 2-3).

(iv) Vessels demonstrating outward flow only were observed in all clinical groups by the Middlesex group (Sarin 1992). The significance of these vessels is unclear. The diameters of these vessels are similar to those of the perforators that only exhibit inward flow (Table 3.6). Perhaps the presence of these vessels is physiological as proposed by Coleridge Smith (Shami 1993). Alternatively, as they are at the smaller end of the spectrum of diameters, the inward flow phase may have been missed on the duplex examination. The inward flow may have been below the detection threshold.

There are clinical messages that can be drawn from these findings. To search for the presence of IPV once other main stem reflux has been detected is only of value in specific clinical situations. There is a 52% chance that they will be seen in the presence of simple varicose veins, but as will be discussed below, there may be no need to intercept them surgically. If the limb demonstrates lipodermatosclerosis or there is a history of ulceration, IPV will almost certainly be present. The indication for imaging them would only be as for purposes of scientific study or as a prerequisite for perforator surgery.

7.4 Effects of surgery

Campbell and West's presentation to the Union International de Phlebologie meeting in 1995 has yet to be published in a peer reviewed journal, although it does appear in abstract form in the published proceedings of that conference (Campbell and West 1996). However, the data are very interesting and therefore the case for repeating the study compelling. The impression from the abstract is that the observations regarding IPV were a secondary finding in a study aimed primarily at auditing varicose vein surgery and the completeness of procedures. No stratification for concomitant deep venous disease was reported. We therefore designed a study with the specific intention of confirming the findings of Campbell and West. We wished to identify the factors determining which IPV responded to surgery performed on the superficial venous system with particular reference to the presence or absence of deep system reflux.

Surgery did not completely eradicate main stem venous disease from the subject population (Table 5.1). In twenty-one limbs main stem venous reflux was present postoperatively. In five limbs this was in the superficial venous system, in 14 limbs this was in the deep system and in two limbs there was mixed deep and superficial system reflux.

The number of limbs in which perforators were identified did not alter following operation. Similarly, there was only a marginal and statistically non-significant fall in the total number of perforators of any type seen (Figures 5.1 & 5.2). However, the number of limbs demonstrating IPV and the total number of IPV

seen post-operatively did fall significantly. It is therefore reasonable to conclude that surgery, even when not specifically targeted at perforators, has an impact on perforator physiology.

The next questions arising are firstly, which perforating vessels in particular are not corrected by superficial surgery alone, and secondly, what is the mechanism for this change in perforator function?

Figure 5.3 demonstrates the effect of persisting main stem reflux on the possible presence of IPV on a limb. Twenty percent of limbs still demonstrated IPV at follow-up, even after the total eradication of main stem venous reflux. By contrast in limbs in which main stem reflux remained, regardless of whether this reflux was in the superficial or deep systems, or both, 71% of limbs demonstrated persistent IPV. The limbs most likely to fall into the latter category were unfortunately those with the most advanced forms of the skin complications of CVI.

Further discussion of the potential mechanisms of change in perforator physiology and anatomy will be given below.

7.5 Classification of perforator disease

Based upon the above findings, a classification for perforating vessels can be proposed. This classification may have some clinical merit and will certainly have a bearing on the possible outcome of any trials of perforator surgery.

Type I IPV: Occur in the presence of superficial (saphenous) reflux and the majority will correct physiologically with adequate superficial venous surgery.

Type II IPV: Occur in the presence of deep venous reflux. These are not corrected by superficial venous surgery.

Type III IPV: Occur in the presence of mixed superficial and deep venous reflux. These are not corrected by superficial venous surgery

Type IV IPV: Occur in the absence of other main stem disease. These vessels appear to be very rare.

Type V IPV: These vessels occur in the presence of deep venous obstruction and may in fact represent collateral channels by-passing the occluded segment. Venous surgery on such limbs must be considered hazardous and interruption of any venous channel may make the clinical state worse.

7.6 Mechanisms of perforator competence and incompetence

The anatomical findings outlined in Chapter 1 suggest the possibility of a more complex mechanism of perforator competence than the simple bicuspid valve of the main venous channels. In the absence of a clear anatomical competence mechanism, a physiological competence can be postulated. Analogous to the arrangement at the gastro-oesophageal junction, several factors seem to come together to produce competence of perforators. At rest, in the erect patient, with the ankle in the neutral position, the channels between the deep and superficial systems are open, however the column of blood, which will ultimately reach the right atrium, slowly builds up on either side of the fascia and the pressure gradient required to induce flow is absent. On plantar flexion of the ankle joint, several component act together. The muscle contracts, shortening in the process, and compresses the perforator crossing the subfascial space. The fascia is moved proximally, relative to the bone, by the moving muscle and in so doing both stretches the perforator and draws it across the fascia, kinking the vessel.

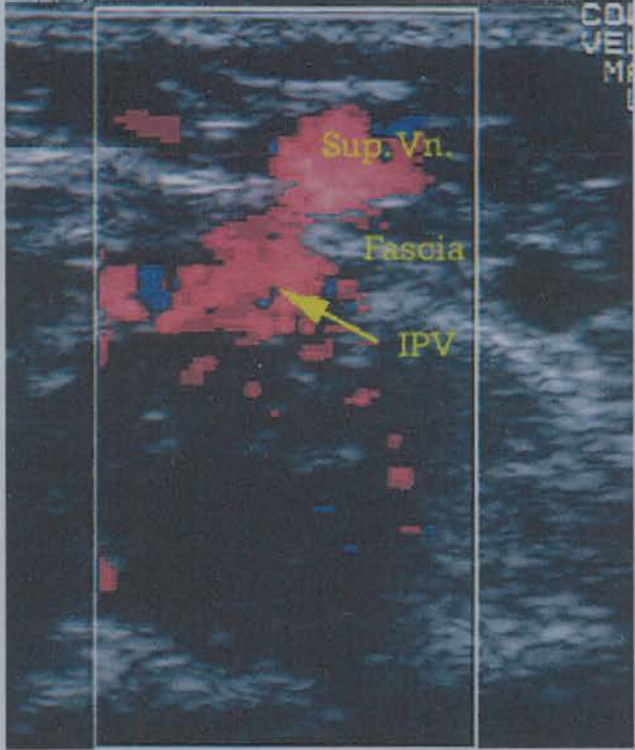
This hypothesis does not, however, explain the observations of the present work that are based upon flow induced in a limb in which there is no active movement of the ankle joint and in which the flow is induced by a squeeze to the sole of the foot. The fact that both competence and incompetence can be detected by this method suggests that another, passive factor is involved. Perhaps this is the role of the venous valves, such as they are. Another possible explanation is that the pressures generated by the foot squeeze are sub-physiological and do not truly test the perforating vessel system. In the same way that dye can infiltrate down a

resting recumbent leg during descending phlebography, perhaps this unnatural test of the perforator system does not allow the perforator competence mechanism to come into play.

How perforators become incompetent is also open to speculation and debate. Cockett's model of valvular damage secondary to thrombus can be questioned. Furthermore, work from the Middlesex Hospital has indicated that a proportion of calf perforators can be induced to exhibit bidirectional flow in healthy limbs if the compression is applied proximal to the vessel (Sarin 1992). Coleridge Smith made the observation that incompetent calf perforating veins have a waist, being pinched by the unyielding fascia, but dilated on either side. This observation is supported by the present work (Fig 7.1). This dilatation may be enough to separate the venous valve cusps rendering the calf perforating vein incompetent. If the pressure for the dilation originated as a column of blood coming down a refluxing main stem venous channel, the situation may indeed be a reversible one, accounting for the post-operative findings of Chapter 5.

Considering an alternative explanation, a high-pressure column of blood may also be sufficient to overwhelm the postulated non-valvular competence mechanism. Similarly, this situation would correct with surgery to the refluxing segment.

Figure 7.1 The incompetent perforating vein (IPV) can be seen crossing the fascia and connecting with the superficial vein (Sup. Vn.). Note the pinched appearance to the vein as it crosses the fascia.



7.7 Safety of SEPS

The SEPS procedure has been performed for almost fifteen years now, using a variety of instruments and techniques. As yet the number of adverse events reported in the published series appears to be acceptably low (Gloviczki 1997, Wittens 1995). Whiteley et al reported one serious adverse event. Posterior tibial nerve damage resulted from SEPS and this case report sounds a cautionary note (Whitely 1997).

The results of the retrospective comparison of SEPS and Linton's procedure must be interpreted in the light of changing hospital discharge policies over the last twenty years. Similarly, the comparison between the rates of complication and concomitant procedures is made with caution in non-randomised groups. Nonetheless, the greater number and severity of complications in the Linton's group remains the most significant factor in the prolonged post-operative stay after this procedure.

The data presented in this series (Chapter 6) illustrate the high complication rates experienced by many centres and why many surgeons abandoned open calf perforator interruption long before SEPS became widely available. By contrast the data in Chapter 6 demonstrate the SEPS procedure itself is associated with little morbidity over and above that which might reasonably be expected for varicose vein surgery performed on patients in this age group. In many cases SEPS can be performed as a day case procedure.

Many of the problems encountered in the prospectively audited data reflect the learning curve experienced by the surgeons. Further experience with the technique and the equipment ironed out problems associated with equipment failure and opening up the subfascial space. Division of the septum that divides the deep and superficial posterior compartments space as described by Wittens group (Pierik 1997), makes more perforators accessible.

It would appear therefore, that cost and operative time are the major negative aspects of SEPS. The importance of establishing clear clinical pathophysiological indications for the procedure grows if SEPS is not to be used inappropriately and thus become devalued.

7.8 The role of calf perforating veins in CVI

The question therefore remains, what if any is the role of calf perforating veins in the development of CVI? Is the clinical time and expense of SEPS justified?

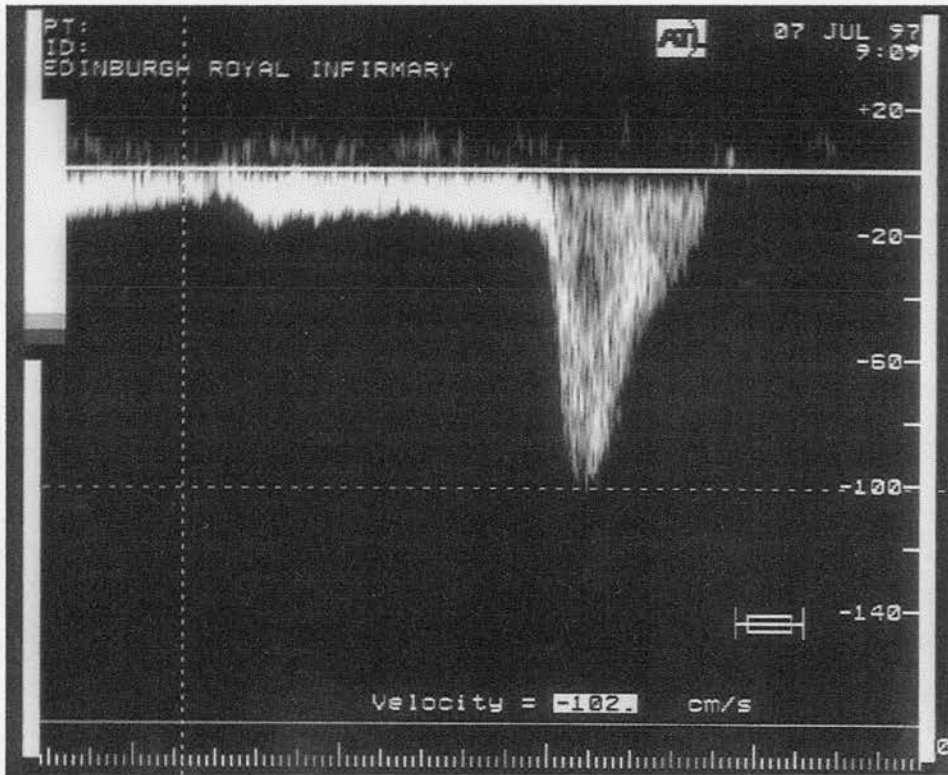
The evidence of an association between IPV and the skin changes of CVI is overwhelming. The earlier work of Labropoulos has been re-examined and refined to the point where confident predictions regarding the number, size and competence of IPV can be made. Furthermore, IPV represent a reversible (putative) aetiological factor. This very reversibility may explain the long-term benefits of saphenous surgery alone (Darke 1992). This reversibility creates enormous difficulties when attempting to separate the effects of the various components of venous disease.

The haemodynamic evidence remains equivocal. No investigators have been able to demonstrate haemodynamic benefits of perforator surgery. The most ambitious project by Akesson et al failed to demonstrate any haemodynamic improvement following staged surgery (Akesson 1990). Zukowski et al demonstrated the presence of a group of perforators that have a potential for compromising the venous haemodynamics of a limb (Zukowski 1991). Hard evidence is not yet forthcoming. Part of the problem is that having demonstrated a strong association between IPV and main stem venous disease to the point where it is clear that IPV are seen to exist in isolation only rarely it is virtually impossible to separate the effects of these co-existing pathologies on the pathogenesis of lipodermatosclerosis and ulceration.

I have been able, on rare occasions only, to image and obtain a Doppler trace from an IPV in a dynamic situation. The ankle joint was worked up and down against resistance. It is clear that large quantities of blood can be expelled (Figure 7.2). In the illustrated example shows blood expelled at a velocity of over 100cm per second through a vessel of 5mm diameter. (The more proximal vessels in the deep system were blocked so the background flow is also outwards.)

The question is therefore raised, “does this represent a significant proportion of the “failure” of the calf muscle pump?” If three or four of these vessels are present does the combined loss of pump performance in venous systole result in failure, or are these volumes trivial in the face of massive popliteal or saphenous system reflux? Complex computer-generated models would be required to calculate flow through various diameters of vessel. Cross-sectional areas could be calculated and the contribution of IPV assessed and compared with that of the other sites of reflux.

Figure 7.2 Outward flow through an incompetent IPV during rest, followed by forced plantar flexion of the foot. Note the maximum outward flow of 102 cm/s. This IPV was acting as a collateral round an obstructed deep segment.



There are two possible mechanisms for a contribution by IPV to the development of the skin changes of CVI. Firstly, the vessels directly transmit high-pressure pulses of blood to the skin capillaries, causing the trauma necessary to initiate white cell activation and the subsequent damage. The distribution of skin changes in relation to the anatomical location of IPV may support this view. However, this mechanism would be more tenable if the aphorism of an incompetent perforator feeding every ulcer had been proven. The second mechanism would be

as a component in the failure of the calf pump mechanism, analogous to mitral regurgitation in cardiac failure. The latter seems the more likely mechanism.

Confining the discussion to those avenues explored already, conclusions can be drawn.

(1) Quantities of blood of undetermined haemodynamic significance do flow through IPV. Vessels with diameters wide enough to be used for arterial grafting carry blood out of the deep vessels of the calf into the superficial system at high velocity.

(2) These vessels are firmly placed at or proximal to the sites of venous ulceration.

(3) The competence of perforators is dependent in a reversible manner on the venous disease in the main stem vessels.

(4) IPV may contribute to chronic venous insufficiency by compromising the calf pump mechanism, adding to volume overload of the leg.

(5) In the presence of main stem venous disease entirely correctable by surgery SEPS is unjustified. In the presence of non-correctable, non-occlusive venous disease there may be a role for SEPS however these patients also carry the poorest prognosis for recurrent venous ulceration.

7.9 Future studies

As indicated above the haemodynamic effects of IPV could be calculated by comparing the total volume refluxing with that coming through the IPV in simulated ambulation. This could be achieved by calculating the area under the curve of a Doppler flow trace, taken together with knowing the cross-sectional area of the vessel being insonated.

The major missing link in the present work, as with so many others, is the relationship between duplex ultrasonographic findings and the pathological and clinical endpoint of tissue destruction. The trigger for white cell activation remains far from clear with very little to suggest the initiating sequence. From a scientific point of view, this is the most obvious area of interest.

Finally, to truly find the clinical role of IPV in CVI, there must be a randomised controlled trial of SEPS. SEPS and saphenous surgery must be compared with saphenous surgery alone. The endpoints of such a trial would be healing times and recurrence rates. A trial would require stratification of patients according to concomitant venous disease. The patients with deep vessel occlusion would almost certainly require exclusion as the notion of causing greater harm cannot be avoided. Patients with superficial disease only with their incompetent perforators may not show any differences, in terms of ulcer healing or recurrence rates, to a control group and accordingly this group must be separated from the others as the whole study may then return a negative result. The group of most interest, and the

patients most likely, if any, to benefit from SEPS, are those with deep vessel reflux, with or without superficial reflux.

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Appendix

Presentations and published papers resulting from the present work

Presentations

(1) **Stuart WP**, Adam DJ, Allan PL, AW Bradbury, Ruckley CV. What is the relationship between abnormal calf perforators, venous function and clinical status?

Presented at the *Annual Meeting of the Royal Society of Medicine Venous Forum*. Manchester, 11 Oct 1996.

Abstract published: *Phlebology*, 1996; 11: 169-170.

(2) **Stuart WP**, Adam DJ, Harnaryan P, Bradbury AW, Ruckley CV. Subfascial Endoscopic Perforator Surgery (SEPS) is associated with significantly less morbidity and shorter hospital stay than open operation (Linton's procedure).

Presented at *Association of Surgeons of Great Britain and Ireland Annual Meeting, Bournemouth*, 10 April 1997.

Abstract published: *Br J Surg*, 1997; 84 (Suppl 1): 19.

(3) **Stuart WP**, Adam DJ, Allan PL, Bradbury AW, Ruckley CV. Chronic venous insufficiency (CVI) is associated with increasing diameter and number of "incompetent" calf perforating veins permitting bi-directional flow.

Presented at *Association of Surgeons of Great Britain and Ireland Annual Meeting, Bournemouth*. April 1997 (poster).

(4) **Stuart WP**, Adam DJ, Allan PL, Bradbury AW, Ruckley CV. Calf perforating veins; the relationship between number, size and flow and the haemodynamic and clinical severity of chronic venous insufficiency.

Presented at the *American Society of Vascular Surgeons Annual Meeting*, Boston, June 1997 (poster).

(5) **Stuart WP**, Adam DJ, Allan PL, Bradbury AW, Ruckley CV. Calf perforating veins; the relationship between number, size and flow and the haemodynamic and clinical severity of chronic venous insufficiency.

Presented at the *International Society for Cardiovascular Surgery 23rd World Congress*, London, 25 Sept 1997.

Abstract published: *Cardiovascular Surgery* 1997; 5 (Suppl 1):99.

(6) **Stuart WP**, Bradbury AW, Adam DJ, Allan PL, Ruckley CV. The relationship between clinical grade of venous disease and calf perforating vein physiology.

Presented at the *Vascular Surgical Society of Great Britain and Ireland AGM*, London, 27th November 1997. (BJS Prize session).

(7) **Stuart WP**, Bradbury AW, Adam DJ, Allan PL, Ruckley CV. Saphenous surgery does not correct perforator incompetence in the presence of persisting superficial or deep venous reflux.

Presented at the annual meeting of the *American Venous Forum*, Orlando, Florida, 19th February, 1998.

(8) **Stuart WP**, Bradbury AW, Adam DJ, Allan PL, Ruckley CV. The relationship between the number, competence and diameter of calf perforating veins and the clinical status in patients with lower limb venous disease.

Presented at the *Union Internationale De Phlebologie European Congress*, Bremen. 1 October 1999

(9) **Stuart WP**, Lee AJ, Allan PL, Ruckley CV, Bradbury AW. Incompetent calf perforating veins are most strongly associated with superficial venous reflux and may not therefore require specific surgical intervention

Presented at the 13th Annual Meeting of the *American Venous Forum*, Fort Meyers, Florida, 25th February, 2001.

Published Papers

(1) **Stuart WP**, Adam DJ, AW Bradbury, Ruckley CV. Subfascial Endoscopic Perforator Surgery (SEPS) is associated with significantly less morbidity and shorter hospital stay than open operation (Linton's procedure).

British Journal of Surgery 1997; 84: 1364-1365.

(2) **Stuart WP**, Adam DJ, Allan PL, Ruckley CV, Bradbury AW. Saphenous surgery does not correct perforator incompetence in the presence of persisting superficial or deep venous reflux.

Journal of Vascular Surgery 1998; 28: 834-8.

(3) **Stuart WP**, Adam DJ, Allan PL, Ruckley CV, Bradbury AW. The relationship between the number, competence and diameter of calf perforating veins and the clinical status in patients with lower limb venous disease.

Journal of Vascular Surgery 2000; 32: 138-43.

(4) **Stuart WP**, Lee AJ, Allan PL, Ruckley CV, Bradbury AW. Most incompetent calf perforating veins are found in association with superficial venous reflux.

Journal of Vascular Surgery 2001; 34: 774-9.

Subfascial endoscopic perforator surgery is associated with significantly less morbidity and shorter hospital stay than open operation (Linton's procedure)

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Background Subfascial endoscopic perforator surgery (SEPS) is the minimally invasive alternative to the open (Linton's) procedure. This new technique may allow perforating vein interruption with fewer complications and a shorter postoperative hospital stay.

Methods This study was a case note review of 67 procedures: 30 SEPS and 37 Linton's.

Results There were no significant differences between the two groups in age, sex and indication for surgery. SEPS was associated with a significantly reduced postoperative stay in hospital (median 2 (range 1-49) days) compared with the Linton's procedure (median 9 (range 3-36) days) ($P < 0.01$). Nine patients who had Linton's procedure suffered a calf wound complication compared with none who had SEPS. The presence of an open ulcer at the time of surgery did not prolong the duration of stay in either group, nor did it increase the incidence of calf wound complications.

Conclusion In patients undergoing calf perforator interruption for chronic venous insufficiency, SEPS is associated with significantly less morbidity and a shorter hospital stay than Linton's procedure. SEPS can be performed safely at the same time as skin grafting and in the presence of an open ulcer without any increase in wound complications.

In 1938, Linton¹ described subfascial dissection and ligation of the perforating veins of the calf. Despite a number of modifications by Cockett (describing an extrafascial approach), Rob, Dodd and DePalma, the popularity of open perforator surgery waned because of the high incidence of complications and recurrent ulceration², together with an increasing use of sclerotherapy³.

The advent of subfascial endoscopic perforator surgery (SEPS)⁴ has rekindled the debate over the possible benefits of perforator interruption in the management of chronic venous insufficiency⁵. SEPS is a minimally invasive alternative to Linton's open procedure and may be associated with fewer complications and a shorter postoperative hospital stay. The aim of the present study was to examine the morbidity associated with SEPS and to compare it with that experienced in a historical series of patients undergoing Linton's procedure.

Patients and methods

The case notes of 61 patients who had interruption of calf perforating veins for lipodermatosclerosis and/or ulceration have been reviewed.

Thirty-one patients (22 men, nine women) of median age 55 (range 23-82) years underwent 37 Linton's procedures between January 1978 and July 1992. Thirty patients (13 men, 17 women) of median age 57.5 (range 37-83) years underwent SEPS (30 procedures) between September 1993 and July 1996.

Results

There were no significant differences with respect to age, sex or indication for surgery between the SEPS and Linton's patients. However, significantly more patients

had the long saphenous vein stripped in the SEPS group (Table 1).

Patients who underwent SEPS had a shorter postoperative stay in hospital (median 2 (range 1-49) days) compared with those who had Linton's procedure (median 9 (range 3-36) days) ($P < 0.01$, Mann-Whitney *U* test) (Fig. 1). The patient in the SEPS group with a postoperative stay of 49 days had an open ulcer at the time of surgery and discharge was delayed because of failed skin grafting, not because of a complication of SEPS.

Nine patients in the Linton's group suffered a calf wound complication compared with none after SEPS. Calf wound complications (delayed wound healing (three), infection (four) and flap necrosis (two)) were the major

Table 1 Indication for perforator interruption and concomitant procedures

	Linton's procedure (n = 37)	SEPS (n = 30)
Indication for procedure		
Lipodermatosclerosis	5	5
Open ulceration	12	8
Healed ulceration	20	17
Concomitant procedure		
Perforator ligation alone	5	1
High saphenous ligation only	13	2*
High saphenous ligation and stripping	17	26*
Short saphenous ligation	5	8
Skin grafting	4	2

SEPS, subfascial endoscopic perforator surgery. * $P < 0.01$ versus Linton's procedure (χ^2 test)

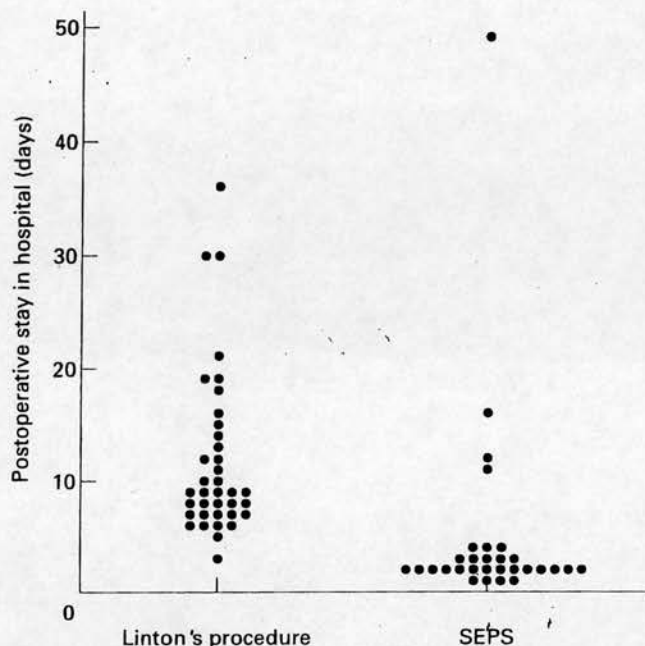


Fig. 1 Comparison of postoperative stay in hospital after Linton's procedure and subfascial endoscopic perforator surgery (SEPS)

Table 2 Postoperative complications

Complication	Linton's procedure (n = 37)	SEPS (n = 30)
None	21	22
Saphenous nerve injury	0	2
Deep vein thrombosis	1	1
Groin wound complications	3	3
Readmission	5	5
Calf wound complications	9	0*

SEPS, subfascial endoscopic perforator surgery. * $P < 0.01$ versus Linton's procedure (χ^2 test)

cause of delayed discharge after Linton's operation. Other complications are shown in Table 2.

The presence of open ulceration at the time of surgery was not associated with a significantly prolonged postoperative stay in either group. For the SEPS group the median stay was 2 (range 1-49) versus 3 (range 1-15) days and in the Linton's group 10 (range 3-30) versus 9 (range 5-21) days for the open and healed ulcer groups respectively.

One patient in each group was readmitted for radio- logically proven proximal deep venous thrombosis requiring anticoagulation.

Discussion

Although there is considerable controversy over whether interruption of calf perforating veins confers any additional benefit over standard saphenous surgery in patients with chronic venous insufficiency, SEPS is increasingly practised in both Europe and North America. The attraction of this minimally invasive technique is that calf perforating veins can be ligated and divided through a single 10-mm skin incision, placed in normal skin in the upper calf².

The patient discharge policy has changed on this unit in the past 20 years, as it has throughout the UK, with a shift towards shorter hospital stay. The present data regarding duration of stay in hospital must, therefore, be interpreted in this light. Similarly, it was with caution that tests of statistical significance were used to compare both the number of concomitant procedures and complication rates between two non-randomized groups. The greater number and severity of complications in the Linton's group remains, however, the most significant factor in the prolonged postoperative stay after this procedure.

The advent of duplex ultrasonographic imaging and a better understanding of the causes and sites of varicose vein recurrence led to the increase in long saphenous vein stripping in the SEPS group. It is recognized that this may also improve the long-term outcome after SEPS.

The long-term results of the open Linton's operation performed for venous ulceration in this unit have been described previously⁶. The present study confirms the high rate of calf wound complications and, in keeping with many centres, Linton's procedure was abandoned when SEPS became available. SEPS is associated with little or no morbidity over and above what might reasonably be expected from concomitant saphenous vein surgery. SEPS is also associated with a significantly shorter hospital stay and may even be performed as a day-case procedure. These data show why in patients undergoing calf perforating vein interruption for chronic venous insufficiency, SEPS is now the procedure of choice.

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Saphenous surgery does not correct perforator incompetence in the presence of deep venous reflux

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Purpose: To determine which patients require subfascial endoscopic perforator surgery (SEPS) in addition to saphenous surgery to correct pathologic outward flow within incompetent medial calf perforating veins (IPVs).

Methods: Sixty-two limbs of 47 patients undergoing sapheno-femoral ligation, stripping of the long saphenous vein in the thigh, and multiple phlebectomies ($n = 51$), sapheno-popliteal ligation and multiple phlebectomies ($n = 10$), or both ($n = 1$) were examined with color flow duplex ultrasound scan, immediately before and a median of 14 weeks (range, 6 to 26 weeks) after the operations. Indications for surgery were varicose veins ($n = 47$, Clinical, Etiologic, Anatomic, Pathophysiologic grades $C_{2\&3}$), skin changes ($n = 5$, C_4), and ulceration ($n = 10$, C_5).

Results: Surgery resulted in a significant reduction in the total number of limbs in which IPVs were imaged (40/62 or 65% preoperatively vs 23/62 or 37% postoperatively, $P < .01$, χ^2 test), a significant reduction in the proportion of perforators imaged that were incompetent (68/130 or 52% preoperatively vs 34/120 or 28% postoperatively, $P < .01$, χ^2 test), and a reduction in median IPV diameter (4 mm, with a range of 1 to 11 mm preoperatively, vs 3, with a range of 1 to 8 mm postoperatively, $P < .01$, Mann-Whitney U test). IPVs remained in 8 of 41 (20%) limbs in which main stem reflux was abolished, compared with 15 of 21 (72%) limbs in which superficial or deep reflux remained ($P < .01$, χ^2 test).

Conclusion: Eradication of main stem saphenous reflux corrects IPV reflux in most cases in which reflux is confined to the superficial system. However, in patients with superficial reflux that persists postoperatively, or when there is coexistent deep venous reflux, saphenous surgery alone fails to correct IPVs reflux. In these circumstances, the only way of reliably correcting pathologic outward flow in medial calf perforating veins is to perform SEPS. (*J Vasc Surg* 1998;28:834-8.)

A variety of surgical procedures designed to interrupt incompetent medial calf perforating veins (IPVs) have been described and advocated for the management of chronic venous insufficiency (CVI).¹⁻⁴ However, it is now widely agreed that open perforator ligation (Linton's procedure) is associated with an unacceptable level of morbidity, and, there-

fore, the procedure has largely been abandoned. The advent of subfascial endoscopic perforator surgery (SEPS)^{5,6} has rekindled the debate about the role of perforators in the pathogenesis of CVI and reawakened interest in their surgical interruption.⁷ Although the feasibility, safety, and early efficacy of SEPS has been confirmed by reports from both Europe⁸ and North America,⁹ and the significant advantages SEPS has over Linton's procedure have been clearly demonstrated,¹⁰ the indications for this operation remain controversial.^{11,12} Uncontrolled data support the contention that, in the presence of isolated superficial venous reflux, saphenous surgery comprising sapheno-femoral ligation, stripping of the long saphenous vein in the thigh, and multiple phlebectomies or sapheno-popliteal ligation and multiple phlebectomies, as indicated, promotes healing and

From the University Department of Surgery, Royal Infirmary. Presented at the Tenth Annual Meeting of the American Venous Forum, Lake Buena Vista, Fla, Feb 18-21, 1998.

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reduces recurrence of chronic venous ulceration.^{13,14} However, most patients with venous ulceration have deep venous reflux, either in isolation or in combination with superficial reflux, together with more dilated medial calf perforating veins permitting outward pathological flow.¹⁵ In these circumstances, the beneficial effects of saphenous surgery alone are less certain. Although several authors have advocated and reported low recurrence rates after perforator ligation and saphenous surgery,^{16,17} others have suggested that saphenous surgery alone will correct IPV reflux, rendering direct perforator interruption unnecessary.¹⁸ Our aim, therefore, was to determine which patients, if any, require SEPS in addition to standard saphenous surgery to correct pathologic flow within medial calf perforating veins.

PATIENTS AND METHODS

The series comprised 47 patients (18 male, 29 female; median age, 58 years; range, 35 to 77 years; 62 limbs) who underwent sapheno-femoral ligation, stripping of the long saphenous vein in the thigh, and multiple phlebectomies ($n = 51$), sapheno-popliteal ligation and multiple phlebectomies ($n = 10$), or both ($n = 1$). The indications for surgery were varicose veins ($n = 47$, Clinical, Etiologic, Anatomic, Pathophysiologic [CEAP] clinical classes 2 and 3), skin changes ($n = 5$, CEAP clinical class 4), and ulceration ($n = 10$, CEAP clinical class 5). Three patients had clearly documented histories of deep venous thrombosis (DVT; CEAP etiologic class E_s). The remaining 10 patients with deep venous reflux may have suffered either a subclinical or unrecognized episode of DVT, or alternatively represent cases of primary deep venous valvular insufficiency (CEAP etiologic class E_p). The presence of venous reflux in the deep and superficial systems and in medial calf perforating veins was determined by means of color flow duplex ultrasonography using a 4 MHz linear array transducer (Ultramark 9, Advanced Technology Laboratories, Bothell, Wash). Examinations were performed immediately before surgery and a median of 14 weeks (range, 6 to 26 weeks) postoperatively. Reflux was considered to be pathologic if it exceeded 0.5 seconds. Main stem deep reflux, superficial reflux, or both was elicited with the patient in the erect position after induction of cephalad venous flow by means of a calf squeeze. Medial calf perforating veins were examined with the patient seated and with the legs dependent, hanging freely. A medial calf perforating vein was defined as a vessel lying between the medial subcutaneous border of the tibia and the posterior midline of the calf that was clearly seen to be crossing

the deep fascia.⁸ The maximum diameter of each perforator was measured. Flow through the perforator was induced by squeezing and then releasing the foot, and flow was recorded using the color flow and the spectral Doppler functions. A vessel was determined to be incompetent if any outward flow was observed with either method.

Long saphenous surgery comprised flush ligation of the sapheno-femoral junction, stripping of saphenous vein to immediately below the knee, and multiple phlebectomies. Short saphenous surgery comprised flush sapheno-popliteal ligation and multiple phlebectomies. When performing phlebectomies, the surgeon was instructed to avoid avulsing varices in the immediate vicinity of the medial calf perforating veins, which had been localized and marked preoperatively.

RESULTS

The pattern of preoperative deep and superficial main stem venous reflux is shown in Table I. Medial calf perforating veins, competent or incompetent, were imaged in 60 limbs both preoperatively and postoperatively. In 2 limbs, medial calf perforating veins were not imaged either before or after surgery. Surgery was associated with a small reduction in the total number of perforators, competent or incompetent, imaged (preoperatively, $n = 130$ vs postoperatively, $n = 120$); a significant reduction in the total number of limbs in which incompetent perforators were imaged (40/62 or 65% preoperatively vs 23/62 or 37% postoperatively, $P < .01$, χ^2 test); a significant reduction in the proportion of perforators imaged that were incompetent (68/130 or 52% preoperatively vs 34/120 or 28% postoperatively, $P < .01$, χ^2 test); and a reduction in median diameter (4 mm, with a range of 1 to 11 mm preoperatively, vs 3 mm, with a range of 1 to 8 mm postoperatively, $P < .01$, Mann-Whitney U test) of all perforators imaged.

IPVs were detected postoperatively in only 8 of 41 (20%) limbs in which main stem venous reflux was abolished by means of surgery and deep venous reflux was absent. By comparison, IPVs were imaged in 15 of 21 limbs (72%) in which deep venous reflux was present or surgery failed to completely eradicate main stem superficial reflux ($P < .01$, χ^2 test). IPVs were imaged in 14 of 47 limbs (30%) operated on for uncomplicated varicose veins (CEAP clinical class 2 and 3), compared with 9 of 15 limbs (60%) operated on for LDS (CEAP clinical class 4) or healed ulceration (CEAP clinical class 5; $P < .05$, χ^2 test). The relationship between the postoperative distribution of main stem venous reflux and the presence of

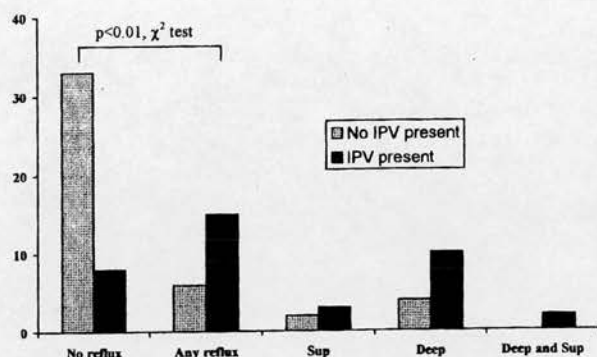


Fig 1. The effect of postoperative reflux on the proportion of limbs demonstrating IPVs. *IPV*, Incompetent perforating vein; *Sup*, superficial system reflux; *Deep*, deep system reflux. Deep reflux numbers exclude common femoral vein reflux.

IPVs is shown in Fig 1. All 6 patients in whom posterior tibial vein reflux was demonstrated also had IPVs postoperatively, as did the 3 patients with clear histories of DVT.

DISCUSSION

In patients undergoing saphenous surgery in the presence of an apparently healthy deep venous system, complete eradication of main stem superficial reflux leads to correction of pathological outward flow in medial calf perforating veins in most (33 of 41), but not all, cases.

In those cases in which outward flow was abolished by means of surgery, one might hypothesize that medial calf perforating veins have been rendered incompetent preoperatively because of (reversible) dilatation caused by excessive filling of the deep venous system from the refluxing saphenous system during calf muscle pump diastole. Eradication of superficial venous reflux allows perforating veins to return to their normal diameter and regain competence. That superficial venous reflux may overload the deep venous system leading to "secondary" deep venous reflux is supported by 2 previous studies showing that surgical eradication of superficial venous reflux can correct reflux in the femoral vein, presumably because of removal of thigh perforators at the time of superficial venous stripping.^{19,20} We observed a similar effect of superficial surgery on femoral vein and calf perforating vein incompetence, but not on popliteal or tibial vein incompetence, possibly because in this study calf perforating veins were purposely left undisturbed.

An alternative explanation of the changes in IPV

Table I. Sites of pathologic venous reflux

Site of reflux	Preoperative n (%)	Postoperative n (%)
Long saphenous vein	55 (89)	4 (6)
Short saphenous vein	12 (19)	3 (5)
Common femoral vein	36 (58)	26 (58)
Superficial femoral vein	8 (13)	7 (11)
Popliteal vein	6 (10)	6 (10)
Posterior tibial vein	6 (10)	6 (10)
Superficial reflux only	49 (79)	5 (8)
*Deep reflux only	—	14 (23)
*Deep and superficial reflux	13 (21)	2 (3)

*Excluding common femoral vein reflux.

competence is that medial calf perforating veins were simply disrupted during the performance of multiple calf phlebectomies. Although perforators were localized and marked preoperatively and the surgeon was requested to refrain from performing phlebectomies in their immediate vicinity, one cannot exclude the possibility that perforating veins were interrupted. Thus, the total number of perforators imaged fell from 130 preoperatively to 120 postoperatively. A third possible explanation is that, although the great majority of perforators clearly remained in situ despite calf phlebectomies, the outflow from the perforators was decreased or obstructed.

In 8 patients, surgical eradication of superficial main stem reflux did not abolish outward flow in medial calf perforating veins, despite the presence of apparently healthy deep venous systems. In these cases, one might speculate that, despite saphenofemoral disconnection, stripping of the long saphenous vein in the thigh, and multiple phlebectomies, a sufficient degree of reflux remains in one or more tributaries to maintain perforator incompetence. Alternatively, these patients may have had a degree of posterior tibial vein reflux that was not apparent on duplex scanning, or the dilatation of the perforators had been so long-standing that, despite removal of saphenous reflux, they could not regain competence.

Therefore, in the absence of deep venous reflux, eradication of main stem superficial reflux by means of standard saphenous surgery will normalize 80% of medial calf IPVs. These data may explain why previous authors have reported excellent long-term ulcer healing after saphenous surgery alone in patients with ulceration and isolated superficial venous reflux.^{13,14} At the present time, it is not possible to identify preoperatively the 20% of patients who may benefit from SEPS because their IPVs will not be corrected by saphenous surgery.

Previous work from our unit and other units has demonstrated that most patients with venous ulceration have deep reflux, with or without superficial reflux, and more incompetent medial calf perforators when compared with patients with uncomplicated varicose veins.^{15,21,22} The present study clearly indicates that, in such patients, saphenous surgery alone fails to correct outward perforator flow in the great majority of cases. This is perhaps to be expected, because removal of superficial varices will not affect the transmission of high pressure venous blood from the calf muscle pump to the microcirculation of the skin of the gaiter area (the so-called "blow-out" syndrome).²³ The only means of interrupting this pathway is by performing direct perforator interruption, preferably by means of SEPS.

These and previous data have led the Edinburgh group to develop a perforator classification based on the distribution of venous reflux associated with the IPVs and the type of venous surgery required to correct pathological outward perforator flow:

Type I IPVs: fed by a refluxing saphenous vein (long and/or short) in the presence of a normal deep system. In most (80%) of these cases, saphenous surgery alone will correct outward perforator flow.

Type II IPVs: found in association with isolated deep venous reflux. That is, there is no significant saphenous reflux. In these circumstances, IPVs may require direct surgical interruption.

Type III IPVs: found in association with mixed superficial and deep venous reflux. In these circumstances, saphenous surgery alone is inadequate, and on the basis of present data, SEPS appears to be required to correct outward flow.

Type IV IPVs: act as part of a collateral circulation bypassing an occluded deep venous system. Such IPVs must be clearly identified, because perforator interruption, with or without saphenous extirpation, could be detrimental to the patient.

Type V IPVs: occur in the apparent absence of other venous reflux or obstruction. In our experience, these constitute a small group.

Based on the Edinburgh classification, the incidence of the 5 types of IPV in this population were: type I IPV, 47 limbs (76%); type II IPV, 0 limbs; type III IPV, 13 limbs (21%). Type IV IPV were not encountered in this study. However, most patients in the present series were operated on for uncomplicated varicose veins, and among a population of ulcer patients, one might expect types II and III to predominate, thus making the numbers of patients who might benefit from SEPS considerably higher.

Widely disparate results have been reported after

perforator surgery, leading to continued controversy about the appropriateness of perforator ligation in the management of different grades of venous disease. This may, in large part, be caused by differences in case mix and selection between series. For example, we would not expect patients with type I IPVs to gain any additional hemodynamic or clinical benefit from perforator ligation performed in addition to standard saphenous surgery in most cases. Furthermore, perforator ligation in patients with type IV IPVs may be detrimental. In contrast, saphenous surgery alone may not lead to ulcer healing in the presence of type III IPVs. These factors should be taken into account when selecting patients for SEPS and when designing trials to demonstrate the efficacy of SEPS in the management of CVI.

However, these patients represent a different population from those in whom SEPS is performed. We reserve SEPS for those patients with signs of lipodermatosclerosis and ulceration. Type IV and type V IPV are not represented in this population. Isolated (type V) IPVs are rare, and we feel that SEPS is not indicated in patients with significant deep vessel obstruction or stenosis. Superficial venous surgery may also be detrimental to limb hemodynamics, as indicated by tourniquet testing. We now routinely perform SEPS and superficial vein surgery during the same operation.

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The relationship between the number, competence, and diameter of medial calf perforating veins and the clinical status in healthy subjects and patients with lower-limb venous disease

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Purpose: The role of medial calf perforating veins in the pathogenesis of the skin changes of chronic venous insufficiency (CVI) remains controversial. This study examined the relationship between abnormal medial calf perforating vein structure and function and the clinical severity of CVI.

Methods: Duplex ultrasound was used as a means of determining the number, flow characteristics, and diameter of medial calf perforating veins, and the presence of deep and superficial main stem reflux or occlusion in 50 limbs with no clinical or duplex evidence of venous disease (clinical, etiological, anatomical, and pathological grade [CEAP] 0), 95 limbs with varicose veins only (CEAP 2/3), 58 limbs affected by lipodermatosclerosis but not ulcer (CEAP 4), and 108 limbs affected by healed or open venous ulcer (CEAP 5/6).

Results: The proportion of limbs in which any perforating veins and incompetent perforating veins (IPVs) were demonstrated increased significantly with deteriorating clinical status (CEAP 0, 88% and 6%; CEAP 2/3, 95% and 52%; CEAP 4, 98% and 83%; and CEAP 5/6, 98% and 90%, respectively). The total number of perforators, the total number of IPVs, and the median diameters of perforators increased with deteriorating grade (CEAP 0 median diameter, 2 mm [interquartile range, 1 to 3 mm]; CEAP 2/3 median diameter, 3 mm [interquartile range, 2 to 4 mm]; CEAP 4 median diameter, 4 mm [interquartile range, 3 to 5 mm]; and CEAP 5/6 median diameter, 4 mm [interquartile range, 3 to 5 mm]).

Conclusion: The deteriorating CEAP grade of CVI is associated with an increase in the number and diameter of medial calf perforating veins, particularly those permitting bidirectional flow. (*J Vasc Surg* 2000;32:138-43.)

Uncontrolled data suggest that the eradication of superficial venous reflux in patients with normal deep veins augments the healing and reduces the recurrence of chronic venous ulceration.¹⁻³

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Competition of interest: nil.

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However, the benefits of venous surgery in patients with deep venous disease are much less certain, and, in particular, the value of interrupting incompetent perforating veins (IPVs) on the medial aspect of the calf in an attempt to protect the skin of the gaiter area from excessively high deep venous pressures remains unproved.⁴⁻⁶ Because of the high incidence of wound-related complications, open perforator ligation (Linton's and Cockett's procedures) has largely been abandoned, despite some evidence that the operation might be beneficial in patients with popliteal vein reflux who have a poor prognosis.⁷ More recently, interest in perforator surgery has been reawakened by the ability to locate precisely medial calf perforators with color-flow duplex ultrasound scanning

Table I. Demographic characteristics of subjects in relation to clinical, etiological, anatomical, and pathological (CEAP) grade

CEAP clinical grade	0	2/3	4	5/6	P value
Subjects/patients	28	71	46	87	
Men:women ratio	14:14	24:47	24:22	41:46	NS*
Limbs	50	95	58	108	
Median age in years (range)	49.5 (23 to 81)	54 (19 to 77)	58 (39 to 76)	64.5 (29 to 87)	< .01†

* χ^2 test.

†Kruskal-Wallis one-way analysis of variance.

NS, Not significant.

Table II. The relationship between duplex findings and clinical, etiological, anatomical, and pathological (CEAP) grade

CEAP	0	2/3	4	5/6	P value
LSV reflux, n (%)	-	82 (86%)	42 (72%)	74 (68%)	NS
SSV reflux, n (%)	-	18 (19%)	19 (33%)	39 (36%)	.046*
SFV reflux, n (%)	-	13 (14%)	11 (19%)	34 (31%)	.014*
PopV reflux, n (%)	-	14 (15%)	18 (31%)	53 (49%)	.002*
PTV reflux, n (%)	-	3 (3%)	12 (21%)	44 (41%)	< .001*
Deep occlusion, n (%)	-	-	-	11 (10%)	
Number (%) of limbs with perforators demonstrating					
Any flow	44 (88%)	90 (95%)	57 (98%)	106 (98%)	< .01*
Only inward flow	41 (82%)	41 (43%)	9 (15%)	9 (8%)	
Outward or bidirectional flow	3 (6%)	49 (52%)	48 (83%)	97 (90%)	< .001*
Median number (IQR) of perforators per limb					
All perforators	1 (1 to 2)	2 (1 to 3)	2 (1 to 3)	2 (2 to 3)	< .001†
IPV only	0	1 (0 to 2)	1 (1 to 2)	2 (1 to 2)	< .001†
Median diameter of perforators (mm)					
All perforators	2 (1 to 3)	3 (2 to 4)	4 (3 to 5)	4 (3 to 5)	< .001†

* χ^2 test.

†Kruskal-Wallis one-way analysis of variance.

LSV, Long saphenous vein; SSV, short saphenous vein; SFV, superficial femoral vein; PopV, popliteal vein; PTV, posterior tibial vein; IQR, interquartile range; IPV, incompetent perforating veins; NS, not significant.

and by the advent of subfascial endoscopic perforator surgery (SEPS).^{8,9} Combining these techniques means that reliable perforator ligation can now be performed with the same level of morbidity that would be expected after standard saphenous vein surgery in this group of patients.¹⁰ This study examined the relationship between the number, flow characteristics, and diameter of medial calf perforating veins and the clinical severity of chronic venous insufficiency (CVI) according to clinical, etiological, anatomical, and pathological (CEAP) grade.

PATIENTS AND METHODS

Color-flow duplex ultrasound scanning (Ultramark 9, Advanced Technology Laboratories, Bothell, Wash; 4-MHz linear array transducer) was

performed on 311 limbs (in 232 subjects) as a means of determining the number, flow characteristics, and diameter of medial calf perforating veins and the presence of deep and superficial main stem venous reflux and occlusion. The clinical groups were 50 limbs that had no clinical or duplex evidence of venous disease in the deep or superficial venous systems (CEAP clinical group 0); 95 limbs that had varicose veins, but no skin changes (CEAP 2/3); 58 limbs that were affected by lipodermatosclerosis, with no history of ulceration (CEAP 4); and 108 limbs that had a history of venous ulceration, active or healed (CEAP 5/6).

The deep and superficial (saphenous) venous systems were examined with the patient almost upright, supported on a tilting examination table. Blood flow was induced by means of a calf squeeze-and-release

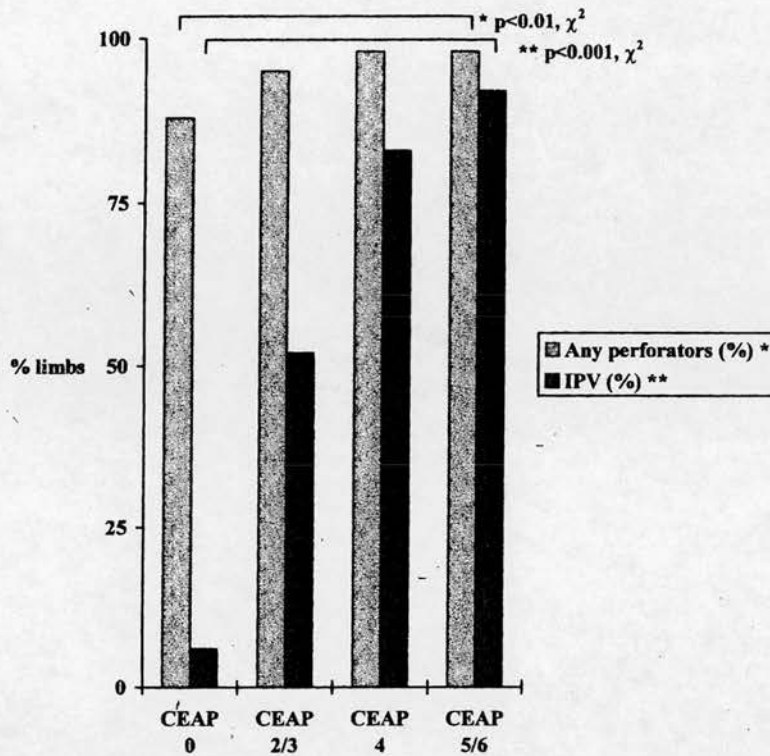


Fig 1. Relationship between medial calf perforators imaged and clinical, etiological, anatomical, and pathological (CEAP) grade.

maneuver. Pathological reflux was defined as reflux exceeding 0.5 seconds' duration.¹¹

Medial calf perforating veins were defined as vessels situated between the medial subcutaneous border of the tibia and the posterior midline of the calf, which were seen to cross the deep fascia and to connect the deep venous system (usually posterior tibial vein) with the superficial venous system. Medial calf perforators were sought with the subject seated on a couch with the legs dependent, hanging freely.

Each perforator was examined by the use of color-flow Doppler and, when possible, the spectral Doppler analysis functions of the machine. To our knowledge, no standard technique for the examination of perforators exists in the literature. A vessel was determined to be competent when it exhibited only inward flow and to be incompetent (IPV) when it was seen to allow deep to superficial (venous) flow, whether flow was unidirectional outward or bidirectional. The maximum diameter of the vessel (millimeter) was also recorded. The lower limit of resolution of the duplex scanner allowed detection of perforators as small as 1 mm in diameter.

Statistical analysis was performed by using the Statistical Package for Social Sciences (SPSS version

8.0; SPSS, UK). The χ^2 test was used as a means of examining the association between categorical variables. The Kruskal-Wallis one-way analysis of variance test was used as a means of examining whether the medians of the outcome variables were significantly different across CEAP grades. The Mann-Whitney *U* test was used as a means of examining the differences in perforator diameters between the competent and incompetent perforator groups. In all tests, a *P* value less than .05 was taken to be significant, and *P* values are quoted when appropriate.

RESULTS

The demographic features of the four groups of patients are summarized in Table I. The increase in age across the clinical groups reached statistical significance at the level of *P* < .01 (Kruskal-Wallis). The relationship among the number, flow characteristics, and diameter of medial calf perforating veins, superficial and deep main-stem venous reflux, and the severity of CVI are summarized in Table II.

Deteriorating clinical status was associated with a significant increase in the prevalence of short saphenous and deep venous reflux. In particular, a history of open or healed ulceration (CEAP 5/6) was

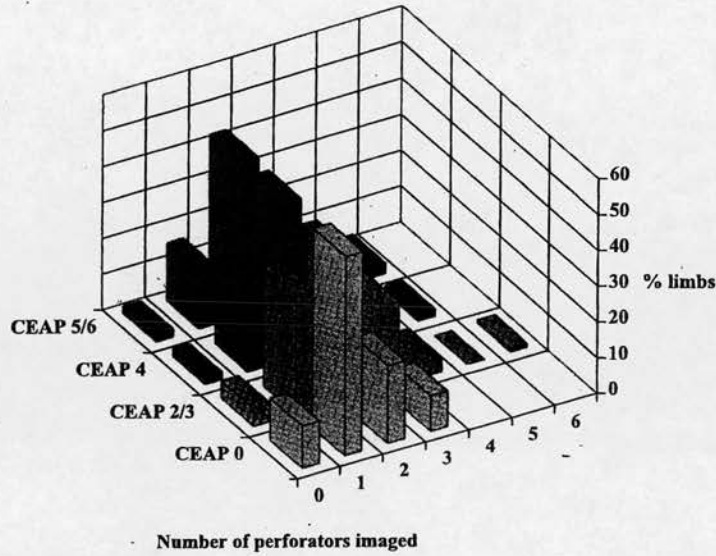


Fig 2. Number of medial calf perforators imaged per limb and clinical, etiological, anatomical, and pathological (CEAP) grade ($P < .001$, Kruskal-Wallis). Percentage of limbs showing each number of medial calf perforators ($P < .001$, Kruskal-Wallis).

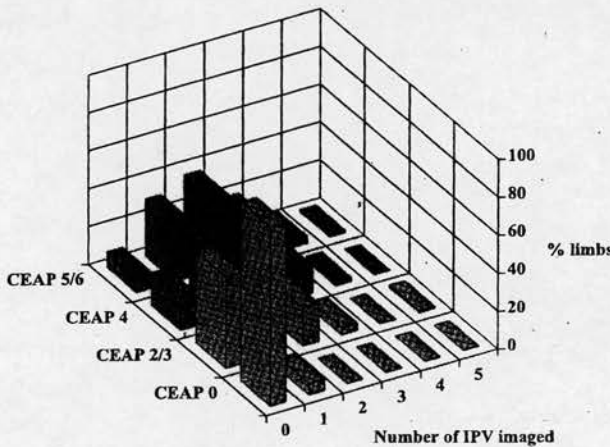


Fig 3. Number of incompetent perforating veins (IPVs) imaged and clinical, etiological, anatomical, and pathological (CEAP) grade. Percentage of limbs showing each number of incompetent perforating veins (IPVs; $P < .0001$, Kruskal-Wallis).

strongly associated with reflux in the popliteal and posterior tibial veins. Six patients had a history of deep venous thrombosis (DVT), proved by means of duplex ultrasound scanning or venography. However, it was suggested by means of duplex findings that a higher proportion of patients may have had undiagnosed DVT.

Table III. The relationship between maximum diameter and the flow patterns of medial calf perforators

Diameter (mm)	Inward flow only (n)	Outward flow only (n)	Bidirectional flow (n)
1	37	2	-
2	92	4	8
3	63	4	56
4	29	4	118
5	5	2	66
6	3	1	49
7	-	-	28
8	-	1	11
9	-	-	-
10	-	-	1
11	-	-	1

$P < .0001$, χ^2 test for 3×2 contingency table.

Deteriorating CEAP grade was associated with a small but significant increase in the proportion of limbs in which medial calf perforating veins were detected (Fig 1). More importantly, a highly significant increase also existed in the proportion of limbs in which IPV could be demonstrated. In CEAP 0 limbs, only three of the 65 perforators imaged (5%) were IPVs, compared with 193 of the 252 perforators visualized in the CEAP 5/6 limbs (77%). Both the total number of perforators (Fig 2) and the

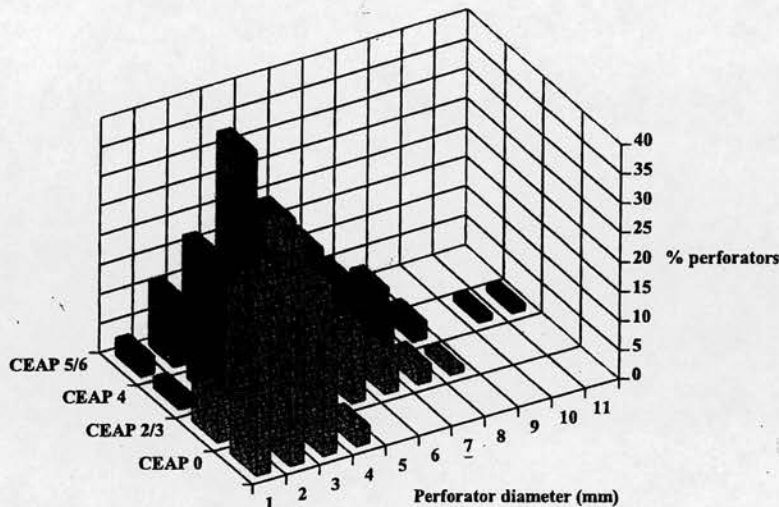


Fig 4. Clinical, etiological, anatomical, and pathological (CEAP) grade and perforator diameters. The percentage of perforators at each diameter is shown for the four clinical groups ($P < .0001$, Kruskal-Wallis one-way analysis of variance).

number of IPVs (Fig 3) per limb also increased significantly with deteriorating CEAP grade.

The diameter of IPVs was significantly greater (median, 4 mm; range, 1 to 11 mm) than competent perforators (median, 2 mm; range, 1 to 6 mm; $P < .0001$, Mann-Whitney U test), with most CPVs (83%) being smaller than 4 mm and most IPVs (81%) being 4 mm or greater in maximum diameter (Table III). As a result, the median perforator diameter increased significantly with deteriorating CEAP grade (Fig 4). Less than 10% of perforators 2 mm or smaller in maximum diameter were incompetent (Table III).

DISCUSSION

The principal findings of the present study are that, in patients with CVI, deteriorating CEAP grade is associated with an increase in the prevalence of IPVs, an increase in the number of IPVs per limb, and an increase in the maximum diameter of the duplex-detectable calf perforators insonated. Advanced disease (CEAP 5/6) was also associated with a significant increase in superficial, particularly short saphenous, and deep, particularly distal, venous reflux. These data support the work of other authors and confirm that most IPVs exist in association with superficial and/or deep venous reflux. Isolated perforator incompetence appears to be rare.^{12,13}

We previously examined the effect of superficial venous surgery on the flow characteristics and max-

imum diameters of medial calf perforating veins and used this as the basis for a classification of IPVs.¹⁴ In patients with isolated superficial venous reflux, eradication of that reflux allows most IPVs to regain competence.¹⁴ These so-called type I perforators may be rendered incompetent because of saphenous dilatation and reflux. Eradication of such reflux may allow perforators to return to a (near) normal diameter and regain competence. In contrast, IPVs in patients with mixed superficial and deep reflux (type III IPVs) are not rendered competent by means of superficial venous surgery alone, presumably because they are still being "fed" with refluxing blood from the deep venous system. In these circumstances, the only means of preventing the outward flow of blood through IPVs appears to be interrupting them surgically or surgically correcting the deep venous reflux or obstruction.

The crucial question facing surgeons is whether hemodynamic or clinical benefits can be accrued with perforator surgery, more than with standard saphenous surgery, in patients with advanced CVI. The present data strongly suggest that, with the deterioration of CEAP grade, there is an increased capacity for large volumes of blood to be expelled down a pressure gradient through markedly dilated low-resistance IPVs during calf systole. Furthermore, the current study has shown that there are between one and four such low-resistance vessels, each with a median diameter of 4 mm, in the typical limb affected by venous ulceration.

Although these proposed pathological mechanisms seem logical, and the ulcer-healing benefits claimed for perforator surgery seem plausible,^{15,16} the hemodynamic benefits of perforator surgery have yet to be satisfactorily demonstrated in a clinical situation.¹⁷ Our previous work has shown open perforator surgery to be associated with hemodynamic improvements in ejection fraction and refilling time on foot volumetry. However, most of these patients underwent concomitant saphenous surgery, and the hemodynamic benefits of surgery were much less impressive in those patients who had popliteal, in addition to superficial venous, reflux.⁷ To date, the only study that has used staged surgical intervention in an attempt to separate the hemodynamic effects of superficial (saphenous) and perforator surgery demonstrated no additional benefit from the latter.¹⁸ The clinical aspects, by using robust end points of ulcer healing and recurrence rates, have yet to be adequately addressed. This can only be achieved within the confines of a randomized controlled trial.

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Most incompetent calf perforating veins are found in association with superficial venous reflux

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Purpose: The indications for surgical perforator interruption remain undefined. Previous work has demonstrated an association between clinical status and the number of incompetent perforating veins (IPVs). Other studies have demonstrated that correction of IPV physiology results from abolition of saphenous system reflux. The purpose of this study was to identify which, if any, patterns of venous reflux and obstruction are particularly associated with IPV.

Patients and Methods: Two hundred thirty patients and subjects (103 men, 127 women, 308 limbs) with varying grades of venous disease were examined both clinically and with duplex ultrasound scan. The odds ratios (ORs) for the presence of IPVs were calculated for different anatomical distributions of main-stem venous reflux and obstruction. The base group are those with no main-stem venous disease.

Results: There were no significant associations between the proportions of limbs demonstrating IPVs and patient age or sex. The ORs for the presence of IPVs in association with other venous disease are as follows (age/sex adjusted): long saphenous vein reflux, OR = 1.86, range = 1.32-2.63; short saphenous vein reflux, OR = 1.36, range = 1.02-1.82; deep system venous reflux, OR = 1.61, range = 1.2-2.15; superficial system reflux, OR = 3.17, range = 1.87-5.4; and deep system obstruction, OR = 1.09, range = 0.51-2.33. The ORs for combinations of venous disorders were calculated. Combinations of disease produced higher odds for the presence of IPVs than those above, the highest being long saphenous vein, short saphenous vein, and deep reflux combined, OR = 6.85 (95% CI, 2.97-15.83; $P = .0001$).

Conclusions: Although the presence of IPVs is associated with venous ulceration, the highest ORs for the presence of IPVs were found in patients with superficial disease alone or in combination with deep reflux. Many of these may be corrected by saphenous surgery alone. (*J Vasc Surg* 2001;34:774-8.)

Subfascial endoscopic perforator surgery (SEPS) now has the status of being an established surgical technique with well-tested supporting technology.¹⁻⁶ The procedure has been shown to be safe and superior to open perforator ligation (Linton's⁷ or Cockett's⁸ procedure) in terms of complications and postoperative stay in hospital.⁶ However, the benefits of SEPS over and above those of saphenous surgery alone are yet to be demonstrated and so the clear indications for surgical interruption of incompetent medial calf perforating veins (IPVs) are as yet undefined.⁹⁻¹¹

Saphenous surgery alone has been demonstrated to correct perforator physiology in the absence of deliberate intervention aimed at these vessels in patients without deep system reflux.^{12,13} The median diameters of the medial calf perforating veins were also seen to decrease after saphenous

surgery. However, the total eradication of IPVs was dependent on the abolition of all main-stem venous reflux from both the superficial (saphenous) and deep venous systems.

Previously published data from this group have established a strong association between increasing number and diameter of IPVs and advanced clinical, anatomical, etiological, and pathological (CEAP) clinical grade.^{14,15} The present analysis addresses three further issues—the effect of patient age and sex on perforator competence, the relationship between the distribution of main-stem venous disease (superficial system reflux and deep system reflux and obstruction) and perforator anatomy and physiology, and the identification of sites of reflux in the deep and superficial veins particularly associated with IPV.

PATIENTS AND METHODS

The clinical groups were comprised of 50 limbs with no clinical or duplex scan evidence of venous disease in the deep or superficial venous systems (CEAP clinical group 0), 95 limbs exhibiting varicose veins but no skin changes (CEAP 2/3), 55 limbs that were affected by lipodermatosclerosis but with no history of venous ulceration (CEAP 4), and 108 limbs that had a history of venous ulceration, active or healed (CEAP 5/6).¹⁵ The subjects were recruited as volunteers who had no history or signs of venous disease (normal controls) and from patients attending the ward or outpatient department for treatment of venous disease.

All subjects were examined clinically and by means of color-flow duplex scanning (Ultramark 9 4-MHz linear array transducer, Advanced Technology Laboratories,

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Competition of interest: nil.

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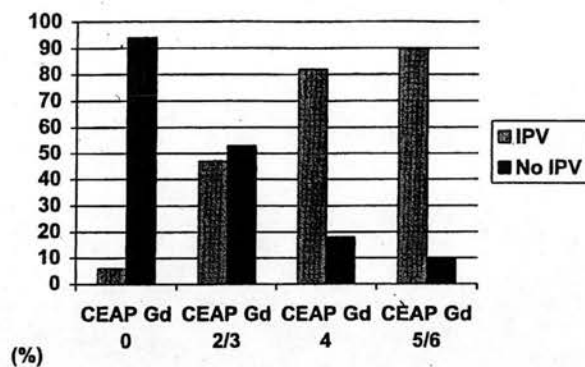


Fig 1. The relationship between CEAP grade and the presence of IPV. $P \leq .001$, χ^2 test. Gd, Grade.

Bothell, Wash). The method of duplex ultrasound scanning has previously been described.^{13,14}

The deep and superficial (saphenous) venous systems were examined with the patient almost upright, supported on a tilting examination table. Blood flow was induced by means of a calf squeeze-and-release maneuver. This is the standard technique in our institution. Pathologic reflux was defined as that exceeding 0.5 seconds in duration.¹⁶

Medial calf perforating veins were defined as vessels situated between the medial subcutaneous border of the tibia and the posterior midline of the calf and which were seen to cross the deep fascia and connect the deep (usually posterior tibial) with the superficial venous systems. Medial calf perforators were sought with the subject seated on a couch with the legs dependent, hanging freely.

Each perforator was examined using the color-flow Doppler scan and, where possible, the spectral Doppler analysis functions of the machine. A vessel was determined to be competent if it exhibited only inward flow and to be incompetent if it allowed deep to superficial (venous) flow, whether or not flow was unidirectional outward or bidirectional. The maximum diameter of the vessel was also recorded on the grayscale function rather than during color-flow analysis. The lower limit of resolution of the duplex scanner allowed detection of perforators down to 1 mm in diameter.

Data were entered into a computer for analysis using SPSS for Windows release 10.0 (SPSS, Inc, Chicago, Ill) and SAS (SAS Institute, Inc, Cary, NC). The χ^2 test was used to examine differences in nominal variables across both CEAP grade and presence or absence of IPV. Student *t* test was used to examine differences in mean age between IPV categories. PROC GENMOD of SAS was used to calculate the odds ratios (95% CIs) of the risk of IPVs for various patterns of disease. The odds ratios were then adjusted for age and sex.

RESULTS

The population studied included 308 limbs from 230 subjects. The demographic features and CEAP grades of

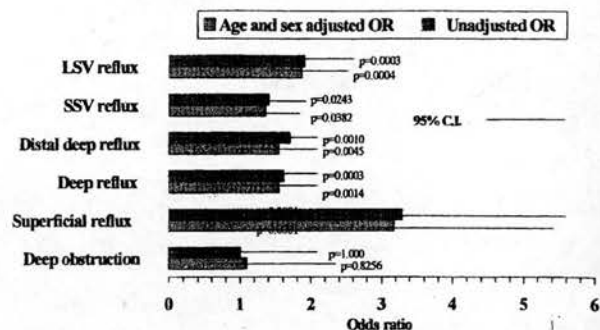


Fig 2. Odds ratios for the presence of IPV within various patterns of venous disease. Base group is no venous reflux or obstruction. OR, Odds ratio.

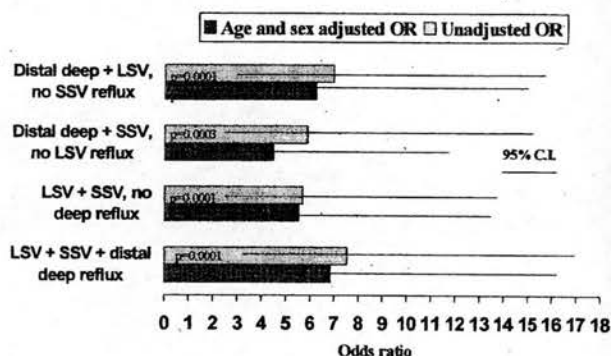


Fig 3. Odds ratios (95% CI) for the presence of IPV within various combinations of venous disease. Base group is no venous reflux or obstruction. OR, Odds ratio.

the subjects are given in Table I. There were 168 (55%) limbs from female subjects and 140 (45%) from male subjects. The age of the subjects ranged from 19 to 87 years with a median of 58 years. The distribution of main-stem venous disease across the population is given in Table II.

There was no association between the proportion of limbs demonstrating IPVs and gender (Table III). The limbs demonstrating IPVs belonged to patients who were significantly older than those not demonstrating IPVs ($P \leq .001$). However, this reflects the age differences across CEAP clinical grades, as shown on Table I, rather than a true association between increasing age and increasing frequency of IPVs. Worsening CEAP clinical grade was significantly associated with an increasing proportion of IPVs (Fig 1). Nonetheless, the data for further analyses are presented showing the calculations with and without the age/sex adjustments.

In the absence of main-stem venous reflux, incompetent perforators were rarely observed (3 limbs, 2%). However, a significantly higher proportion of subjects with superficial system reflux alone, deep system reflux alone, and mixed superficial and deep reflux demonstrated IPVs (Table IV). A similar pattern was observed when analysis was repeated for

Table I. Demographic features and CEAP clinical grades of patients and subjects

CEAP grade	0	2 or 3	4	5 or 6	P value
Subjects (n)	28	71	44	87	
Male:female ratio	14:14	24:47	24:20	41:46	NS
Limbs (n)	50	95	55	108	
Median age (y) (range)	49.5 (23-81)	54 (19-87)	58 (39-76)	64.5 (29-87)	≤.01

Analysis was χ^2 test or Kruskal-Wallis test. NS, Not significant.

Table II. Distribution of venous disease (reflux and obstruction) among the 308 limbs

Site of reflux	n	%
No reflux	50	16.2
LSV reflux	205	66.6
SSV reflux	89	28.9
Any superficial reflux	242	78.6
Any deep reflux	106	34.4
Superficial reflux alone	152	49.4
Deep reflux alone	16	5.2
Both superficial and deep reflux	90	29.2
Deep system obstruction	11	3.6

the presence of any deep disease or any superficial disease on a limb regardless of disease in another site.

Odds ratios for the risk of IPVs within various patterns of venous disease were calculated with and without adjustment for age and sex (Fig 2). Superficial reflux appears to have the greatest association with IPVs (adjusted odds ratio, 3.17; 95% CI, 1.87-5.40). Deep system obstruction was not associated with an increased risk of IPVs (adjusted odds ratio, 1.09; 95% CI, 0.51-2.33).

Further odds ratios were calculated for the risk of IPVs within various combinations of venous disease. There were 31 (27 of these with IPVs) limbs with deep distal reflux and long saphenous vein (LSV) disease but no short saphenous vein (SSV) disease, 15 limbs (11 with IPVs) with deep distal reflux and SSV disease but no LSV disease, 24 limbs (17 with IPVs) with LSV and SSV disease but no deep distal disease, and 35 limbs (33 with IPVs) with deep distal reflux disease and LSV and SSV disease. There were 56 limbs with no deep distal disease, no LSV reflux, and no SSV reflux, and the risk of IPVs in each of the four combinations was compared with this group (Fig 3). After adjustment for age and sex, the risk of IPVs was highest among the group with SSV, LSV, and deep distal disease (odds ratio, 6.85; 95% CI, 2.97-15.83). The risk of IPVs was lowest among those with deep distal disease and SSV disease but no LSV disease (odds ratio, 4.47; 95% CI, 1.71-11.67). However, all of the odds ratios were highly statistically significant ($P \leq .001$).

DISCUSSION

Definite proof of a contributory role for IPVs in the processes of lipodermatosclerosis and chronic venous

Table III. Association between sex and age and the presence of IPV*

Patient characteristic	No IPV (n = 112)	IPV (n = 196)	P value
Male	46.4 (52)	44.9 (88)	
Female	53.6 (60)	55.1 (108)	.795
Age (y)	52.7 (1.62)	60.5 (0.94)	.0001

*Values are percentage (n) or mean (standard error). Analysis used the χ^2 test or the *t* test.

ulceration has yet to be produced. Similarly, clear evidence of clinical benefits derived from SEPS is not yet forthcoming, although it would appear that SEPS continues to be performed.³ Fortunately, there is little to suggest that the procedure is detrimental to patients or that it delays ulcer healing.

The strongest link between IPVs and the skin changes of chronic venous insufficiency is associative. The median number of IPVs imaged per limb has been demonstrated to increase with deteriorating clinical status.^{14,17} The median diameter of medial calf perforating veins also rises with deteriorating clinical status. Evidence of a hemodynamic role for IPVs is less clear. The evidence is contradictory and inconsistent.^{9,18} Furthermore, there is strong evidence that the most important prognostic factor in terms of venous disease is the presence of popliteal vein reflux.¹⁹⁻²¹

Previous data published by our group have demonstrated that if main-stem venous reflux is eradicated, the majority of IPVs return to a caliber and functional state similar to "normal" values.¹³ The principal finding of the present work is a demonstration that IPVs are most likely to be found associated with correctable superficial venous reflux disease. The odds ratios for the presence of IPVs in a limb were greater for superficial reflux, in both LSVs and SSVs (either together or separately), than for deep venous reflux. This suggests that more IPVs are found in association with correctable, superficial main-stem venous disease.

The odds ratio analysis was calculated for those limbs in which the deep system showed reflux in the popliteal venous segment and distally. The values were similar to those for either long saphenous or short saphenous reflux in isolation. More surprisingly, the odds ratios for limbs with deep system obstruction were approximately unity. In other words, the presence of IPVs was similar to the base

Table IV. Association between patterns of venous disease and the presence of IPV

Site of reflux	No IPV (n = 112)	IPV (n = 196)	P value
No reflux	42 (47)	1.5 (3)	≤.001
Superficial reflux only	45.5 (51)	51.5 (101)	≤.001
Deep reflux only	3.6 (4)	6.1 (12)	≤.001
Superficial and deep reflux	8.9 (10)	40.8 (80)	≤.001
Any deep disease	12.5 (14)	46.9 (92)	≤.001
Any superficial disease	54.5 (61)	92.4 (181)	≤.001
Deep obstruction	3.6 (4)	3.6 (7)	1.0
LSV disease	44.6 (50)	79.1 (155)	≤.001
SSV disease	16.1 (18)	36.2 (71)	≤.001
Deep distal reflux*	12.5 (14)	42.9 (84)	≤.001

*Distal reflux is defined as that observed in the popliteal vein or below. Values are percentage (n) and analysis using the χ^2 test.

group that was comprised of limbs with no clinical or duplex ultrasound scan evidence of venous disease. These findings would suggest the possibility that calf perforator function is determined by the presence of reflux disease in the main-stem vessels and, in particular, the superficial main-stem vessels.

Calculations were performed for the combinations of venous reflux disease across the long saphenous, short saphenous, and deep distal venous systems. Because of the small numbers in each subgroup, the 95% CIs were found to be wide, and, although all odds ratios were statistically significant, no particular combination seemed more likely to be associated with IPV than any other.

Similar odds ratio calculations were not attempted for differential CEAP grades because the numbers in each group were so small that the analysis would be meaningless, and even if trends were present, the senior statistical author considered it inappropriate to present potentially misleading data.

In summary, IPV would appear to be most strongly associated with superficial (saphenous) system main-stem venous reflux. This finding may significantly influence the outcome of a randomized controlled trial of perforator surgery. If IPV are most commonly found in limbs with correctable venous disease, the trial may return a negative result. It is possible that the group of patients most likely to benefit from SEPS are those with deep venous incompetence and IPV regardless of the state of the superficial system. A randomized controlled trial would require stratification to take this into account to avoid a potential false-negative result. However, this may be problematic because studies have demonstrated that the long-term prognosis for recurrent ulceration is poorest in this population.^{19,20} The present work is an observational study, and it is therefore not appropriate to draw firm conclusions regarding the potential effects of surgical intervention for IPV from these data.

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DISCUSSION

Dr Peter Gloviczki (Rochester, Minn). Thank you very much, Dr Stuart. This was an excellent presentation. Professor Ruckley and his team in Edinburgh have had a long-term interest and expertise in the management of chronic venous disease, and I am sure that this paper will be another important contribution to the literature on this topic.

Based on duplex scan analysis of 380 limbs with venous disease of different severity, the authors concluded that, number one, incompetent perforating veins are associated most strongly with superficial venous reflux and that therefore, number two, incompetent perforating veins may not require specific surgical interventions. While I have some reservations and questions on both of these conclusions, let me point out again what I think is the most important finding of this paper. That is the high prevalence of incompetent perforating veins in patients with chronic venous disease and the correlation of the incompetent perforating veins with the severity of disease. If you remember Dr Stuart's slides, 90% of the patients with C5-6 disease have an incompetent perforating vein, while less than a half of the patients with C2 disease have incompetent perforators. So incompetent perforator veins are clearly associated with venous ulcers, and the question, of course, what we all search for an answer for, is whether these incompetent perforating veins have any hemodynamic significance and whether they really contribute to the inflammatory changes in these limbs.

I have three questions for Dr Stuart. The first concerns the main conclusion of the study which means that incompetent perforating veins are most frequently associated with superficial reflux. We found, and I presented some of the data yesterday, that in patients who are candidates for perforator interruptions, the incidence of deep vein reflux can be as high as 90%. In other large studies on patients who have ulcers, the incompetence of the deep system is at least 50%, so I am wondering if your conclusion that incompetent perforating veins are most frequently associated with superficial reflux is true in patients with C5 and C6 disease?

My second question deals with the second main conclusion, which is in the title of your paper, that incompetent perforating veins may not require specific interventions. You obviously refer to your previous paper, which found in a limited number of patients at an average of 6 months after surgery a lower rate of incompetent perforating veins after saphenous vein stripping when the patients did not have deep venous incompetence. We observe that the number of recurrent incompetent perforating veins increases with time. In our material, even patients who underwent SEPS had an increasing number of recurrent perforating veins, and this number increases beyond 6 months. I am wondering if your original paper has a conclusion that has merit and whether you have investigated those patients with a longer follow-up and maybe by now you have a larger number of patients.

The final question concerns the importance of perforating veins in deep venous occlusion. We find that deep venous occlusion is a predictor of incompetent perforating veins, but indeed your studies have not confirmed that so I wonder if you can explain that.

It looks to me that Professor Ruckley really created the school in Edinburgh, and I think, Professor, you can enjoy your retirement right now because you have a great team of workers who will continue your work. I enjoyed very much the presentation, and I thank the society for the privilege of discussing this paper.

Dr Stuart. Dr Gloviczki, thank you very much for your kind comments and also for your helpful questions. Dr Lee performed the analysis of these data and I asked her if she would do the same analysis for C5 and C6 grades only. She performed this analysis and told me that in fact the numbers had become too small. I asked her—for the figures anyway, and she said she was not going to give them to me because I am a surgeon and the figures were not of statistical significance but I would go ahead and present them anyway and call them a trend, so she was protecting me from standing up and presenting statistical lies. I cannot answer your question as to whether these analyses hold true when you move into the patients with grade 5 and grade 6 disease.

With regards to whether perforators recur, I think that is a very interesting question, and extended follow-up on patients that I originally examined would be very interesting, as would extended follow-up on the patients that Professor Burnand, who I see standing there, and Professor Bradbury have also presented. They demonstrated that people with popliteal venous reflux, in particular people with popliteal venous reflux secondary to DVT, had an appalling prognosis for recurrent ulceration. It would be interesting to get a hold of these patients, find out how many of these people had recurrent perforating veins, and whether this indicated that periodic revisitation of these patients for harvesting of further perforators would help the situation.

I accept his criticism regarding deep venous obstruction and I would also accept that this may in fact be a statistical error reflecting a small sample size. Thank you very much.

Dr Kevin Burnand (London, England). I have, like Dr O'Donnell, an extreme sense of I am sure *deja vu* because if you actually go back to the literature you will see that with rather less complex systems than duplex scanning we showed very similar results, that there are a lot of perforating veins that are associated with superficial reflux.

My real anxiety is your conclusion two, which is that because they are found in association with superficial reflux, it is unlikely that they need to be treated. If ever there is something calling out for a prospective study to be done, this is; you should randomize half to stripping alone in association with Peter Gloviczki, who it pains me to be in agreement with, and the other half with stripping plus perforator ligation. It is only in that way that we will really know, and you have to follow them up unfortunately for 5 years, but that is the study that you should be doing rather than drawing that conclusion in advance.

Dr Stuart. I accept that point. One of the differences between doctors and scientists is that scientists are quite prepared to discuss theoretical outcomes long before experiments are performed to demonstrate the outcome. I would argue that speculating theoretically as to what might happen is quite an interesting intellectual exercise and may in fact allow us to define which studies should be done more clearly, and I think this is a case in point. If we do not develop an appropriate stratification for a randomized controlled trial, we may end up throwing the baby out with the bath water. I strongly suspect that the patients who have long saphenous disease alone will have no benefit from SEPS, whereas patients with deep disease are the ones most likely to benefit, and, because of this, stratification will be critically important in a randomized controlled trial. I hope that answers your comment.