

Current Best Practice in the Management of Varicose Veins

Mark Steven Whiteley 

The Whiteley Clinic, Guildford, GU2 7RF, UK

Correspondence: Mark Steven Whiteley, The Whiteley Clinic, 1 Stirling House, Stirling Road, Guildford, GU2 7RF, UK, Tel +44 330 058 1850, Email mark@thewhiteleyclinic.co.uk

Abstract: This article outlines the current best practice in the management of varicose veins. “Varicose veins” traditionally means bulging veins, usually seen on the legs, when standing. It is now a general term used to describe these bulging veins, and also underlying incompetent veins that reflux and cause the surface varicose veins. Importantly, “varicose veins” is often used for superficial venous reflux even in the absence of visible bulging veins. These can be simply called “hidden varicose veins”. Varicose veins usually deteriorate, progressing to discomfort, swollen ankles, skin damage, leg ulcers, superficial venous thrombosis and venous bleeds. Patients with varicose veins and symptoms or signs have a significant advantage in having treatment over conservative treatment with compression stockings or venotropic drugs. Small varicose veins or telangiectasia without symptoms or signs can be treated for cosmetic reasons. However, most have underlying venous reflux from saphenous, perforator or local “feeding veins” and so investigation with venous duplex should be mandatory before treatment. Best practice for investigating leg varicose veins is venous duplex ultrasound in the erect position, performed by a specialist trained in ultrasonography optimally not the doctor who performs the treatment. Pelvic vein reflux is best investigated with transvaginal duplex ultrasound (TVS), performed using the Holdstock-Harrison protocol. In men or women unable to have TVS, venography or cross-sectional imaging is needed. Best practice for treating truncal vein incompetence is endovenous thermal ablation. Increasing evidence suggests that significant incompetent perforating veins should be found and treated by thermal ablation using the transluminal occlusion of perforator (TRLOP) approach, and that incompetent pelvic veins refluxing into symptomatic varicose veins in the genital region or leg should be treated by coil embolisation. Bulging varicosities should be treated by phlebectomy at the time of truncal vein ablation. Monitoring and reporting outcomes is essential for doctors and patients; hence, participation in a venous registry should probably be mandatory.

Keywords: varicose veins, best practice, review, endovenous, treatment, management

Introduction

The understanding of what is called “varicose veins” has changed dramatically over the last 20 years. Traditionally, varicose veins have been thought of as bulging veins seen on the lower legs, and sometimes upper legs, when standing. Also, it is still widely believed that varicose veins are “only cosmetic”, and treatment depends on the wishes of the patient.¹

However, since the advent of colour flow duplex ultrasonography in the 1980s,² followed by the advent of endovenous surgery for the treatment of incompetent truncal veins in the 1990s,^{3,4} our understanding of venous reflux and its association with varicose veins has become much clearer.

Some of the major changes in our understanding are:

- All doctors know that patients with truncal saphenous vein reflux can develop bulging varicose veins visible on the surface. However, there are a significant number of patients with the same underlying pathophysiology who do not develop visible bulging varicose veins^{5,6} – called “hidden varicose veins” in 2011.⁷

- Varicose veins are not just a cosmetic problem. Most deteriorate with time, leading progressively to discomfort, swollen ankles, skin damage at the ankles, venous leg ulcers (VLU), superficial venous thrombosis (SVT – commonly called “thrombophlebitis”) and/or bleeding varicose veins.⁸
- Varicose veins are not only a problem of leg veins but can arise in part, or totally, from pelvic vein reflux (PVR) or “pelvic congestion syndrome” (PCS).⁹
- Varicose veins, and especially recurrence, are associated with incompetent perforating veins (IPV) in the legs.¹⁰
- Varicose veins are not predominantly a female problem, nor specifically related to pregnancy.^{11,12}
- The valves in the veins do not start to fail in the groin due to pressure from above and proceed in a descending pattern. Valve failure and venous reflux is an ascending problem starting from below.^{13,14}
- Stripping varicose veins out surgically does not permanently remove veins, as most grow back but without valves, during the healing process, causing the same problem to recur.^{15,16}

Although both health-care professionals and the public are aware of endovenous surgery, particularly with the profusion of websites and adverts on the internet for minimally invasive treatments for varicose veins, few are aware of the major changes in the understanding of varicose veins and their management.

Indeed, many doctors who perform endovenous surgery have merely replaced stripping with an endovenous procedure, without realising that the whole approach to the management of varicose veins has changed, and our understanding of the underlying pathophysiology has improved significantly. Hence, merely swapping stripping for endovenous treatment is unlikely to result in optimal results in the long term. To attain such optimal results, a full understanding of the underlying pathophysiology is needed, and targeted treatments need to be used based on current research.

This article will now highlight some of the major changes that are current in the management of varicose veins, to help doctors as well as other interested parties understand the current best practices.

Definition of Varicose Veins

At the time of writing this article, the Cambridge dictionary definition of “varicose vein” is:

“a swollen and often painful vein, especially in the legs:

- Pregnant women often get varicose veins.”¹⁷

This definition illustrates one of the major problems when discussing varicose veins. Most doctors and virtually all the public define medical conditions by what they observe. For example, a stroke patient with weakening of the right face, right hand and right leg and with speech affected is said to have had a “right sided stroke”. This originates from the ancient assumption that the person had been struck down on the right side by some deity.

However, we now know that such a patient with right-sided signs has had a left-sided cerebrovascular accident. Hence, we have an ongoing conflict between the names that have arisen due to clinical observations, and the new names given for the underlying pathophysiology.

We see the same in the venous world, as evidenced by the definition of “varicose vein”.¹⁷ Varicose veins are still defined by clinical observation – swollen veins especially in the legs. However, as stated before, we now know that only a proportion of people with significant superficial venous reflux show dilated veins visible on the surface. The others have pathological superficial venous reflux that can be determined on venous duplex ultrasound, but do not show the bulging veins that would give the clinical diagnosis of “varicose veins”, even if they have deteriorated clinically.¹⁸

This venous reflux without visible varicose veins follows the same deterioration as truncal vein reflux associated with visible varices. As it cannot be called “varicose veins”, it has been called “chronic venous incompetence” (CVI), “superficial venous incompetence” (SVI), “superficial venous reflux” (SVR) or a host of other names.

In 2009, I introduced the term “hidden varicose veins” to try and make this condition more understandable and published it in 2011.⁷ An internet search for “hidden varicose veins” has shown an increasing adoption of this term, helping patients understand that not all varicose vein problems show visible bulging veins.

For the rest of this article, I will use the term “varicose veins” to mean both varicose veins and “hidden varicose veins” unless otherwise indicated. I do this merely to make the text more readable, but it is important for the reader to understand that the use of the term varicose veins might also mean pathological venous reflux without visible bulging veins.

Causes of Varicose Veins

It is probably sensible to address the causes of varicose veins at this point in the article, so that we can define exactly what we are discussing, and so that we can exclude some clinically visible “varicose veins” that have a different underlying pathophysiology.

Considering the venous system in the legs, it is traditional to think of deep veins that are within the muscle, and superficial veins that are outside of the deep fascia that surrounds muscle. The superficial veins connect to the deep veins by perforating through the deep fascia and hence through the muscle. There are two major connections that perforate this fascia, the saphenofemoral junction (SFJ) where the great saphenous vein (GSV) joins the femoral vein in the groin, and the saphenopopliteal junction (SPJ) where the small saphenous vein (SSV) joins the popliteal vein usually behind the knee, although the level can be variable.

Valves in the deep and superficial veins ensure that blood only flows upwards towards the heart, or inwards from superficial to deep veins, from where it is then pumped upwards to the heart. When the valves fail in the great saphenous vein and/or the small saphenous vein, venous reflux occurs leading to varicose veins. Most doctors and nurses should recognise this pattern. However, a depressingly large number of doctors think that this is the end of the story with regards superficial venous reflux in varicose veins, and so they only investigate and treat these two truncal veins.

This very simplistic pattern misses out some very important points.

The first is that the superficial venous system is divided into two components. The first component is the truncal veins, the great and small saphenous veins, that sit in their own fascial compartments.¹⁹ These saphenous compartments lie deep to the superficial fat. When the saphenous veins become incompetent, it is very rare for them to dilate enough to be visible on the surface.

In addition, the anterior accessory saphenous vein is commonly involved in varicose veins,²⁰ and the posterior accessory saphenous vein can be involved, although much less commonly. Both accessory saphenous veins also sit deep to the superficial fascia in the upper thigh.

The second component is the network of veins that lie in the subcutaneous fat. When dilated due to venous reflux, they may become visible bulging veins depending on their size and depth. However, this does mean that there are three systems of veins in the legs:²¹

- Network 1 (N1) – Deep veins that lie in anatomical compartment 1 (AC1) which is the muscle of the leg deep to the deep investing fascia.
- Network 2 (N2) – Saphenous or truncal veins that lie in anatomical compartment 2 (AC2) which is the saphenous fascia.
- Network 3 (N3) – Superficial veins that lie in anatomical compartment 3 (AC3) which is the subcutaneous fat.

In addition, there are approximately 150 perforating veins in each leg²² that connect N2 or N3 veins directly to the N1 veins, running from the superficial AC2 or AC3 and perforating the deep investing fascia, draining into the N1 veins. When competent, these perforating veins drain from superficial to deep. However, when incompetent, they allow blood to reflux from the deep N1 veins into the superficial compartments. In IPVs, bi-directional flow or solely outward flow can be identified by duplex ultrasound.²³

It is surprising that doctors who understand reflux through the SFJ and SPJ from deep to superficial veins results in pathological venous reflux, usually regard reflux through other unnamed perforators in the leg from deep to superficial as inconsequential. Indeed, some doctors have tried to argue in the past that treatment of the truncal vein reflux will cause the IPVs to become competent again²⁴ when this has proven to be untrue.²⁵ It is probably because IPVs are difficult to diagnose and treat that most doctors try to ignore them.

However, there is evidence that the failure to treat IPVVs in patients with varicose veins is associated with recurrence in the future.^{10,26,27} Since the advent of the transluminal occlusion of perforator (TRLOP) technique in 2000,²⁸ percutaneous treatment of these veins has now become an ambulatory procedure.

Finally, it has become apparent that incompetence in the pelvic veins (gonadal veins and internal iliac veins) can cause pelvic venous reflux (PVR) and pelvic varicose veins.²⁹ This is generally termed “pelvic congestion syndrome” (PCS) although the recent UIP consensus document has called for this to be renamed “pelvic venous disorders” (PeVD).³⁰ Research from our own unit shows that this is a common cause of leg varicose veins, with 1 in 6 women presenting with leg varicose veins having a major contribution from PVR,³¹ and 1 in 30 men having the same.³²

Furthermore, we have published data showing that in a quarter of all cases and a third of women who had not had a hysterectomy, recurrent varicose veins are associated with the failure to treat PVR.³³

Varicose veins around the labia, vagina, perineum, scrotum, perianal area and buttocks without any extension onto the abdomen or flanks, are common signs of PVR. Although obstruction in the pelvic veins occasionally presents with these signs, reflux is much more common. These can usually be treated with the new techniques used for PVR, and therefore should be investigated and treated as outlined in the sections below.

Although haemorrhoids³⁴ in both sexes and scrotal varicoceles in men³⁵ are often thought to be gastrointestinal and urological problems, respectively, they are varicosities of the pelvic venous system. With the increasing interest of pelvic veins by phlebologists and venous surgeons, they should probably come under the management of those specialising in phlebology and venous surgery.

Hence, symptomatic varicose veins arise from a combination of valve failure causing venous reflux in any combination of truncal saphenous veins, perforating veins and pelvic veins. There are so many combinations that we must now understand there is no such thing as “typical varicose veins”.

Before the advent of venous duplex ultrasound, it was often thought that a history of deep-vein thrombosis (DVT) meant that there would be damage in the deep veins with scarring and deep vein incompetence (DVI) and any visible varicose veins were bypasses around deep vein problems. Hence, many doctors would not consider surgery on patients with varicose veins and a history of DVT, for fear of making the situation worse. Most of these patients were told that they would be in compression stockings for life.

However, it has now become clear that patients with a history of a single DVT that has been cleared quickly with anticoagulation can resolve without any deep vein scarring nor incompetence.³⁶ As such, all patients with leg varicose veins should undergo full investigation of their superficial and deep veins and should not be excluded from varicose vein surgery on the history of DVT alone.

If patients have varicose veins in the legs and a swollen leg, and a history of a very severe DVT or even multiple DVTs, then they may well have chronic obstruction and/or incompetence of the deep veins in the leg and iliac veins in the pelvis. This is called post thrombotic syndrome (PTS)³⁷ and such patients should not be offered varicose vein surgery unless they have been fully assessed by a venous specialist and it has been deemed to be in the patient’s best interest. This is a very specialist area and not for further discussion in this general article.

Varicose veins across the pubic region or up the flanks signify an obstruction in the iliac veins or inferior vena cava. Some of these patients are suitable for stenting of the obstruction. However, once again this is a very specialised area and should not be addressed by someone treating varicose veins who is not conversant with the latest advances in the treatment of deep venous problems. Therefore, apart from saying that such patients are difficult management problems, we will not discuss them further.

Finally, there are some specialised venous conditions such as Klippel-Trenaunay syndrome and other congenital venous abnormalities that can present to the doctor treating varicose veins. They should be recognised as being different from normal varicose veins and should only be treated by those specialising in such conditions.

Who Gets Varicose Veins?

As with all progressive conditions, the prevalence of varicose veins increases with age.³⁸ Venous reflux can be found in adolescents, although frank varicosities are uncommon.³⁹ The author has treated patients down to the age of 12 with severe truncal reflux and varicosities.

Although early reports claimed that varicose veins predominantly affect women, it is becoming clearer that most of these studies had a selection bias, reporting on those who presented for treatment rather than prevalence in the general population. As women are more health conscious than men, and more likely to seek medical advice, it is not surprising that it was always thought that women suffered from varicose veins more commonly than men.

In addition, it is commonly thought that pregnancy caused varicose veins, although this has now been disproven. Veins do dilate during pregnancy, but contract back down to their pre-pregnancy state after delivery.¹¹ No new reflux develops in veins that were competent pre-pregnancy⁴⁰ and the number of pregnancies has no effect on the prevalence of GSV reflux.⁴¹ However, this does not seem to be the case for pelvic venous reflux, which does seem to become more prevalent with pregnancy and increasing numbers of pregnancies.⁴²

Also supporting this is the Edinburgh vein study that showed that the prevalence of varicose veins in men and women at any particular age was broadly similar.^{12,38}

Clinical Course of Leaving Varicose Veins Untreated

It is depressing that despite all the evidence that has been accumulating over the last decade, and even the publishing of national guidelines in the UK,⁴³ America⁴⁴ and Europe,⁴⁵ so many doctors, nurses and patients consider varicose veins to be a benign and cosmetic condition that does not have significant health implications.

A review of epidemiological studies following patients with varicose veins who did not have treatment shows a gradual deterioration of approximately 4.3% of patients per year.⁸ Deterioration was defined by the clinical stages of the CEAP grade, C2 – varicose veins, C3 – swollen ankles, C4 – skin damage (venous eczema or hemosiderin) and C6 (venous leg ulcers). As C5 is a healed venous ulcer, it was not part of this progression.

A randomised controlled trial called the REACTIV trial confirmed that patients randomised to best medical treatment (graduated compression stockings) had a worse quality-of-life after two years than patients who were randomised to treatment of their varicose veins.⁴⁶ It is interesting to note that this trial was based on stripping of the varicose veins, and it is highly likely that if it were to be treated using modern ambulatory endovenous techniques, the crossover in advantage in terms of quality-of-life would be noted much sooner.

Therefore, there is now a very good evidence that if patients with varicose veins are not treated, a significant proportion will end up with reduced quality-of-life and a progressive deterioration towards fasciocutaneous damage, leg ulceration as well as superficial venous thrombosis and the risk of bleeding varicose veins.

Who Should Be Investigated and Treated?

In July 2013, the National Institute for Health and Clinical Excellence (NICE) in the UK published clinical guidelines CG 168 which recommended which patients should be investigated and treated.⁴³

“These state that:

- Patients with bleeding varicose veins should be referred immediately.
- Patients with varicose veins or suspected hidden varicose veins and any of the following, should be referred to a vascular service for investigation and treatment:

- Varicose veins (primary or recurrent) with symptoms (defined as “pain, aching, discomfort, swelling, heaviness and itching”)
- Eczema or pigmentation of the lower leg
- Superficial vein thrombosis
- A venous leg ulcer
- A healed venous leg ulcer”

This gives very clear guidelines as to who should be investigated and treated for medical indications. These patients are being investigated and treated not only to treat the current problem, but because robust scientific evidence shows that there is a medical advantage to prevent further deterioration and reduction in quality of life.

However, it must also be remembered that some patients want to have varicose veins or leg telangiectasia (often called “thread veins” or “spider veins”) treated for purely cosmetic reasons. If these patients do not fit into any of the above categories, in other words, they have no symptoms or signs of lower leg venous disease apart from visible varicose veins or telangiectasia, then they can be investigated and treated provided the doctor treating them is aware that they are providing a cosmetic service, rather than treating a medical condition.

When a patient is being investigated and treated for a cosmetic condition, it is essential that doctors consent patients adequately, as they are treating the present aesthetic concern, and not offering medical advantage to the patient. Patients must be aware of this, as any adverse outcome is likely to cause concern. Also, such treatments are unlikely to be covered by medical insurance.

Because of this, doctors and nurses must be up to date with the research showing the very strong link between telangiectasia and underlying venous reflux from saphenous veins, IPV and incompetent local veins that “feed” the telangiectasia.^{47–49} In view of the literature that has been published, treatment of leg telangiectasia without a preoperative assessment with duplex ultrasound looking for underlying reflux is probably indefensible.

Investigations

Since the 1990s, the standard investigation for varicose veins and venous reflux in the legs is colour flow venous duplex ultrasonography (VDU).^{43,50,51} This ultrasound combines grey scale imaging with dynamic Doppler colour flow to image flow in the veins, and gated Doppler to measure waveforms and velocities if needed.

For VDU examinations, patients are examined standing with their weight on the contralateral leg to that being examined, or lying at an angle,⁵² as gravity is required for passive (diastolic) venous reflux.⁷ Flow up the veins is usually stimulated by manual calf compression (MCC), and Doppler ultrasound is used to observe the blood flow. As the calf compression is relaxed, any passive reflux is seen.⁵² Active or systolic reflux is noted by blood flowing the wrong way through a vein during the compression phase.⁷

There are several modifications of MCC where researchers have suggested replacing MCC with standardised compression pumps,⁵³ standing on tiptoes⁵⁴ or stimulating leg muscle contraction by pushing the patient, in order to obtain a more physiological response.⁵⁵ GSV diameter has been shown to correlate with haemodynamic impairment, but this is when measured in the erect non-weight bearing position.⁵⁶ Hence, VDU for the assessment of varicose veins should never be performed in the supine position.

More controversially is the question “who should perform the venous duplex ultrasound?” Although many doctors like to perform their own VDU, there are several good reasons as to why I believe they should not.

Firstly, it is well recognised that in any practical endeavour, the more hours spent performing a procedure, the more expert a person becomes.^{57–59} Hence as VDU is operator dependent, it is logical that someone who is trained to perform VDU examinations in a course lasting several years, who has passed exams in the understanding of the physics and pathophysiology behind the technique, and who performs examinations day in day out without any other distractions is likely to get optimal results.

A doctor who might have a good understanding of pathophysiology but has not had the same teaching experience in performing VDU, and who only does it for part of the day as they have other things to do such as operating, injecting, and consulting, is unlikely to attain the same results as someone trained solely in this investigation.

In some territories or practices, doctors specialise in venous treatments alone and can become very adept at VDU. However, even if this is the case, there is another significant reason why they should not perform VDU on the patients that they subsequently treat.

Secondly, VDU reports or images are very subjective. The person performing the scan builds up a picture of the pattern of reflux as they interrogate each vein or section of vein in turn, performing the appropriate manoeuvres. Unlike magnetic resonance imaging (MRI), computerised tomography (CT) or other static images, it is almost impossible to record an examination for others to get a full understanding at a later date. As the veins that are diagnosed on VDU as incompetent are ablated, it is quite possible that an erroneous diagnosis of reflux will be destroyed by this treatment, destroying all evidence of the diagnosis. There has already been a case in the UK where a doctor was struck off the medical register for over-diagnosing venous reflux.⁶⁰ This allows inflation of fees for performing unnecessary treatments.

As such, it is much better to employ the “four eyes” principle⁶¹ (also called the “two-man” or “two-person” rule) where one fully qualified and trained professional performs the investigation, and then a second person acts upon it. Although not explicitly outlined in the NICE CG168 guidelines, these guidelines do point out that investigations and treatment should be performed by a “team” of professionals rather than an individual.⁴³

For leg veins, N1, N2 and N3 as well as perforator veins, VDU is usually the only investigation that is required. If there is any suspicion of an outflow obstruction either in the deep veins of the legs or iliac veins, then doctors might wish to investigate further with venography,⁶² magnetic resonance venography (MRV),⁶³ CT with contrast,⁶⁴ intravascular ultrasound (IVUS)⁶⁵ or my preferred option air-plethysmography (APG)^{66,67} which gives a functional report of the presence of outflow obstruction. The concern with static images that show partial obstruction is that the question of hemodynamic significance is not answered. APG gives a functional view as to whether there is any obstruction, and if any is identified, imaging can be used subsequently to identify where it is.

Turning now to PVR, the gold standard investigation has been shown to be the transvaginal venous duplex ultrasound scan (TVDUS) using the Holdstock-Harrison protocol.⁶⁸ The patient is placed in a 45° head up position, allowing passive reflux by gravity following a “Kegel squeeze”, where the patient is asked to contract their pelvic muscles and then relax.⁶⁹ This is the stimulating contraction that is the equivalent of the MCC in leg VDU examinations.

In addition to this, transabdominal ultrasound can also be used to identify nutcracker syndrome (left renal vein compression by the superior mesenteric artery onto the aorta) and pseudo-nutcracker syndrome, by tipping the patient head down and seeing if the renal vein dilates with gravity.⁶⁹

In males who have pelvic venous reflux causing leg varicose veins,³² and females who cannot or will not have TVDUS, we then have to resort to transabdominal venous duplex ultrasound.⁷⁰ If this is not diagnostic, or the anatomy looks abnormal, then venography,⁷¹ CT⁶⁴ or MRV⁷² can be used to try and ascertain where the problem is.

These cross-sectional imaging methods do not show venous reflux in real time and rely upon dilatation of the vessels in the supine position, which has been shown to be a poor marker for reflux.⁷³ In addition, diagnosis by venography assumes that contrast injected under pressure behaves the same as normal venous blood and that all veins that are relevant are opacified. Therefore, there is no gold standard test for PVR in patients who are unable to undergo TVDUS using the Holdstock-Harrison protocol.

Treatments

Graduated compression stockings are not a treatment for varicose veins.⁴³ Wearing graduated compression stockings may reduce venous reflux whilst they are being worn, but as soon as they are removed, the reflux resumes. Therefore, there is no case for them, nor any other form of compression, to be recommended as a treatment for varicose veins, unless a patient is unable or unwilling to have curative intervention. Moreover, there is no logic in any requirement to wear them for a period of time before treatment, to see if there is any improvement in symptoms or signs. Such a strategy only delays investigation and treatment. It is for this delay alone that funders of healthcare often insist on a trial of compression before approving treatment. The only time that compression is an appropriate treatment for varicose veins is if they are secondary to PTS and/or DVI in which case the condition being treated is not the varicose veins and hence is beyond the scope of this article.

In many areas of the world, doctors prescribe venotropic medications for varicose veins (such as micro-purified flavonoid fraction or MPFF). Research has shown that such drugs can reduce symptoms and swelling due to CVI.^{74–77} Indeed, it has even been suggested that some venotropic drugs might prevent the changes in the vein wall caused by venous stasis.⁷⁸ However, at the current time, it must be understood that venotropic drugs only treat some of the symptoms and signs of varicose veins and do not treat the underlying venous reflux. Hence, just like compression, they provide temporary relief when being used, but do not have any curative role.

As varicose veins are now curable with endovenous surgery, venotropic drugs are only needed in patients who are unable or unwilling to have curative treatment. As endovenous surgery can now be performed as an ambulatory technique under local anaesthesia, there are few (if any) patients with varicose veins who are not able to have treatment. As before, this excludes patients presenting with varicose veins that turn out to be secondary to other problems such as

PTS or DVI. As such venotropic drugs do not fall within “current best practice in the management of varicose veins” and so will not be discussed further.

It is internationally recognised that the first-line treatment of incompetent N2 truncal veins associated with varicose veins or symptoms or signs of venous disease is endovenous thermal ablation (EVTA).^{43–45} This is usually performed by endovenous laser ablation (EVLA) or radiofrequency ablation (RFA), although there are other forms of EVTA such as steam vein sclerosis (SVS)^{79,80} and endovenous microwave ablation (EMWA).⁸¹

There are many different forms of EVLA and RFA. In the most basic forms, EVLA fibres can be bared-tipped,⁴ jacket-tipped (to reduce vein wall contact),⁸² tulip-tipped (to prevent all vein wall contact),⁸³ or radial (to direct the laser energy laterally directly into the vein wall)⁸² - with the advent of a single ring or double ring radial fibre⁸⁴ available. RFA devices can be monopolar⁸⁵ or bipolar⁸⁶ which pass electric current through the vein wall at radiofrequency rates to cause heating, or segmental where a coil of metal at the end of the device is heated by radiofrequency current and heat is passed into the vein wall by simple conduction.⁸⁷ A new modification of this is a device that has a variable length of coil that can be used depending on how much vein needs to be treated.⁸⁸

Provided that the optimal amount of energy (which is measured as the Linear Endovenous Energy Density of “LEED”)^{89,90} is given over the optimal time,⁹¹ EVTA should produce transmural death of the vein wall with permanent fibrosis and atrophy of the treated vein segment.⁹² Inadequate treatment with EVTA results in damage to the endothelium and intima only⁸² which initially appears to give successful closure due to thrombus formation within the vein, only to re-open subsequently as the media and adventitia act as a living “vein skeleton”⁹³ allowing recanalization.

The second-line treatment for incompetent N2 truncal veins is ultrasound guided foam sclerotherapy (UGFS).^{43–45} Although some doctors advocate this as the optimal treatment for truncal vein incompetence due to simplicity in terms of equipment and administration, and reduced cost compared to EVTA devices,⁹⁴ both laboratory-based models of sclerotherapy in veins with thick walls⁹⁵ and clinical studies have shown an inferior long-term occlusion of incompetent truncal veins compared to EVTA.⁹⁶

UGFS is more successful if given by catheter rather than injected up the vein from a single point,⁹⁷ and with tumescence injected around the vein, increasing the sclerosant dwell time.⁹⁸ However, this reduces the simplicity of the procedure and makes the process similar to EVTA – but with inferior results. On the positive side, in small diameter⁹⁹ and thin-walled veins such as small varicosities and reticular veins,¹⁰⁰ neovascular tissue,¹⁰¹ strip tract revascularisation¹⁶ and primary avalvular venous anomalies (PAVA) tissue,¹⁰² UGFS is currently the optimal treatment. Phlebectomy is inappropriate in most of these veins and they are too small and superficial for EVTA.

Open surgery, high ligation usually accompanied by stripping, is only the third line recommended treatment after EVTA or UGFS for incompetent N2 truncal veins.^{43–45} This is appropriate due to the pain and discomfort of the procedure, and the proven revascularisation of the strip tract with 23% of people showing some strip tract revascularisation within one year¹⁵ and over 80% in 5–8 years.¹⁶ There has been a flurry of randomised controlled studies suggesting that open surgery has similar outcomes as EVTA, leading some surgeons to use these results to continue the practice of open surgery.^{103–106}

However, these randomised trials do not note the presence of IPVs nor treat them, nor look for the presence of PVR nor treat it. Also, they do not note the presence of PAVA tissue nor strip tract revascularisation. Interestingly, although UGFS has much lower rates of GSV occlusion than open surgery or EVTA in these studies, it does not have a correspondingly lower improvement of quality of life nor incidence of recurrent varicose veins.

As such, the actual conclusion of these randomised trials should probably be that treatment of truncal vein reflux alone without looking for, nor treating, other sources of reflux such as IPVs and PVR, results in incomplete and hence inadequate treatment. Also, the clinical effects of having varicosities and the associated venous stasis are probably underestimated by doctors who concentrate on reflux alone. Hence, UGFS, which spreads widely into varicosities as well as trunks, may achieve better clinical outcomes in terms of quality of life, and even recurrence, than treatments that focus solely on the incompetent GSV.

We can get a feel for the relative contributions of truncal reflux and venous stasis when we find that VLUs secondary to superficial venous disease can be effectively treated either by ablation of the venous reflux¹⁰⁷ or alternatively UGFS directly into the veins surrounding the ulcer.¹⁰⁸

As noted previously, many doctors ignore IPVs as part of the pattern of venous reflux. Before 1985 there was no treatment available apart from open ligation. However, in 1985, Hauer invented the sub fascial endoscopic perforating vein (SEPS) procedure to clip the veins sub-fascially using an endoscope introduced into the below knee sub-fascial compartment.¹⁰⁹ However, SEPS still requires a 2–3 cm incision, usually a general anaesthetic with quite a lot of post-operative discomfort from manipulation of the muscle, and restriction of treatment of perforators to the medial aspect of the lower leg. In 2000, we invented the TRLOP procedure, which we presented nationally and internationally.¹¹⁰

Under ultrasound control, the IPV was cannulated, and a device passed into the perforator to ablate it. Initially, we used radiofrequency and have subsequently used endovenous laser. TRLOP was “reinvented” in 2007 as the “perforator ablation procedure” (PAPS)¹¹¹ although there is no difference at all between the techniques.¹¹² Other workers have modified this further by injecting cyanoacrylate glue.¹¹³ The TRLOP method can be used with any of these methods to produce local ablation of an IPV, even if the vein is short.

Some doctors advocate closing IPVs with UGFS.^{114,115} As UGFS flows through the local veins and does not stay where it was injected, UGFS treatment of IPVs is likely to result in inadequate ablation of the perforator (too little foam), or an increased risk of a DVT in veins local to the treatment area (too much foam). As such, although this has been described, UGFS treatment of IPVs should only be performed with the knowledge of the risks of doing so, and if TRLOP is not possible.

In the treatment of PVR, treatments are generally performed by an interventional radiological approach.⁹ A jugular approach is ideal as the veins to be treated are in a relatively straight line from the right internal jugular vein,¹¹⁶ although some prefer a transfemoral approach. Our research has shown that although the gonadal veins can be involved, in over 95% of cases at least one internal iliac vein or its tributaries are a major cause of the problem.⁶⁸ Therefore, ablation of the internal iliac veins and their tributaries is often essential in addition to, or instead of, treating the gonadal veins.

Once the target veins have been cannulated under x-ray control, the most widely used treatments are embolic coils¹¹⁶ or embolic plugs.¹¹⁷ Many workers inject foam sclerotherapy first into the pelvic varicosities, followed by coils or plugs into the main truncal part of the vein. Other workers have advocated using a balloon to isolate the incompetent pelvic vein and then inject foam sclerotherapy distally.¹¹⁸ However, unless an embolic device is used proximal to the foam sclerotherapy, this approach is unlikely to give good long-term results due to the size of vein and thickness of the vein wall.⁹⁵

In patients complaining of vulval or leg varicose veins arising from PVR, and with no pelvic symptoms of PCS, some doctors advocate that only the pelvic escape points need treatment. There are between four and seven escape points described where PVR can exit the bony pelvis and join with veins in the genital region or in the legs.^{119,120} The idea of this approach is to treat the causes of the external pelvic varicosities in the genital region and varicose veins in the legs without having to treat asymptomatic pelvic veins within the pelvis.

There are some advantages to this approach in terms of simplicity and cost. However, treatment of the exit points is fiddly, often requiring open surgery and therefore incisions that can get infected and are painful. Endovenous techniques to close these exit points have not been well described nor reported.

Returning to the treatment of incompetent N2 truncal veins, there has been a move towards non-thermal catheter-based treatments of incompetent truncal veins. One of these is UGFS that has been discussed above, although foam sclerotherapy is not generally delivered via a catheter.

Currently, the major non-thermal catheter-based techniques that are widely used are the mechanochemical ablation devices (MOCA)^{121,122} and cyanoacrylate glue (CAG).^{123,124} In most specialised vein clinics, patients are treated by an ambulatory approach, only using local or tumescent anaesthesia and without any sedation, regional blocks nor general anaesthesia. This approach allows patients to walk in, have treatment and then return home fully mobile with minimal risk of complications such as DVT. This is achieved as the patient does not need to starve pre-operatively and so can remain hydrated, and does not lie still without muscle movement, as they would under general anaesthesia.

A further advantage of a non-thermal endovenous technique is the avoidance of any thermal damage to nearby skin or nerves, which is particularly useful in the below knee GSV and the distal SSV which are closely related to the saphenous and sural nerves, respectively.¹²⁵

In this environment, the most painful part of the EVTA procedures has been shown to be the tumescent anaesthesia.¹²⁶ Therefore, any procedure that can take away the need for tumescent anaesthesia will have an advantage for the patient, provided that they are as effective as the EVTA procedures.

Currently, the MOCA and CAG procedures have not had a major impact in the venous world and are generally restricted to certain enthusiasts or studies. There are two main devices currently available for MOCA.^{121,122} Both of these work on the principle of mechanical damage to the vein wall to enhance the effect of sclerotherapy.^{127–129} In other words, trying to ensure that the chemical ablation from the sclerosant becomes transmural. However, neither device is designed for treating IPVs and so is restricted to incompetent N2 truncal veins. One is simpler and less expensive than the other, but both need to be proven to be cost-effective as compared to EVTA for them to become major competitors to the well-established endovenous thermal techniques.

With CAG, a catheter is passed up the vein to be treated under ultrasound control and is withdrawn following a set pattern of lengths and time, with injections of CAG at set points. The exact pattern of withdrawal and injections depends on which of the CAG devices and formulations is being used. CAG ablation is quick as no tumescence is needed. A further advantage of CAG over MOCA is that it can be used directly down a needle into an IPV, using a TRLOP technique.^{113,130} However, the leading CAG product is currently expensive compared to EVTA and there have been several reports of inflammation, sometimes very severe, as well as extension into the deep veins.^{131–134} As with MOCA, good proof of cost effectiveness is required for CAG ablation to become a major competitor to EVTA.

There are some other techniques to treat varicose veins that are promoted by enthusiasts. Among these, there are at least two different designs of injecting foam sclerotherapy into an incompetent N2 truncal vein whilst using low power EVLA simultaneously.^{135–137} The enthusiasts claim that the combination of endovenous laser, at a much lower power than would normally be used for EVTA, along with the foam sclerotherapy has a synergistic effect causing ablation but without pain. In this way, they are trying to avoid tumescent anaesthesia. There are also certain clips for veins¹³⁸ and balloon occlusion devices allowing foam sclerotherapy to be injected to increase the dwell time.¹³⁹ All of these require more proof to show if they have a role in the future.

Many doctors, particularly in southern Europe and the southern hemisphere, promote “haemodynamic surgery”. CHIVA¹⁴⁰ (the conservative and hemodynamic treatment of ambulatory venous insufficiency) is based upon the concept of ligating escape points where blood refluxes from N1 to N2 veins, or N2 to N3 veins, relying on perforators to drain blood back to the deep venous pump. This decompresses the superficial veins and allows all veins to drain, whether competent or not. Although great results are claimed,¹⁴¹ and the fact that the saphenous vein is spared, CHIVA has not gained wide acceptance in the northern hemisphere. Indeed, many doctors who regularly treat varicose veins are unaware of the haemodynamic approach.

A much simpler haemodynamic approach called ASVAL¹⁴² suggests that simple removal of varicosities by phlebectomies can make an incompetent great saphenous vein competent again by removing the distal reservoir. However, there are many cases where this approach is not appropriate and so it is not a technique that can be used in many patients.

Finally, the latest technique for treating incompetent N2 truncal veins and IPVs, is High Intensity Focused Ultrasound (HIFU). HIFU allows ultrasound energy to be focused from a curved transducer outside of the body and to be directed through the skin and subcutaneous fat, to ablate tissue at the focal point.¹⁴³ The first machine of its kind commercially available for treating varicose veins is called “Sonovein” and is made by Theraclion in France.

Some have questioned whether there is anything new in this technique, pointing out that the actual mechanism of ablation is still thermal.¹⁴⁴ However, unlike EVTA, the fact that HIFU is totally non-invasive is clearly an advantage, and as the extra-corporeal treatment is guided by ultrasound imaging, there is a real possibility that this whole treatment could be guided and performed by artificial intelligence in the future.¹⁴⁵ The prospect of a fully automated treatment for varicose veins is clearly a novel technology.

Treatment of N3 veins really depends upon their size, distribution and how they respond to the treatment of any underlying venous reflux. Large varicosities can be removed by phlebectomy either at the time of ablation of the N2 truncal veins or IPVs or can be left to see if they resolve by themselves with a delayed phlebectomy procedure reserved for those that need it.

The advantage of this approach is that some people end up not needing phlebectomies. However, the disadvantages are that some end up with pain and skin marking due to thrombosis in the varicosities, and those that need further treatment have to undergo a second procedure. The AVULS randomised trial concluded that performing the phlebectomies at the same time as truncal vein treatment resulted in better clinical outcomes, stopped the need for any second procedures and showed a better improvement in quality-of-life.¹⁴⁶

Some doctors have replaced phlebectomies with UGFS of the varicosities, either performed at the time of the initial ablation or as a delayed procedure. If veins are small and thin-walled,⁹⁹ then this is a good option. However, if veins are large, bulging and thick-walled, it is likely to increase the risk of superficial venous thrombosis with pain and inflammation, with the potential of skin marks in the medium to long term. As such, this should be avoided until randomised controlled trials have shown which patient groups might get an advantage for this approach, if any.

It is beyond the scope of this article to discuss treatment of reticular veins and telangiectasia.

Monitoring and Registry

With the large number of doctors and clinics treating varicose veins with very different standards of investigation and treatment, it is essential that results are reported so that practices that lead to poor results can be identified, and those that lead to optimal treatments can be propagated. It is impossible for all doctors to publish all their results and so the only way to effectively achieve this is through a venous registry.

The power of registries is that consenting patients can be added anonymously, with all their preoperative and operative data added. This enables patients to be stratified into different patterns of venous reflux, different severities of venous disease and the different approaches and techniques used in the treatment to be noted.

However, the importance of a registry is then to know what the outcome is. This is why the College of Phlebology Venous Registry¹⁴⁷ encrypts the patients' email (provided that they consent to this) and the patient gives annual feedback directly to the registry, completing a quality-of-life assessment form and answering questions as to any recurrence or need for further treatment. In this way, patients can be followed up in the long term without any bias from the treating doctor nor expense to the patient.

Such a registry allows doctors to benchmark their treatments against others, funders of healthcare to ensure acceptable outcomes, equipment manufacturers to monitor the outcomes from their devices and of course most importantly, gives patients the confidence that their doctors are having their results monitored.

Conclusion

The current best practice in the management of varicose veins is becoming clear, although we must always be aware of new developments and research to allow us to update this. Currently, both doctors and patients should be aware that "varicose veins" is a general term that encompasses the bulging veins seen on the legs and in the genital region on standing, usually caused by underlying venous reflux from incompetent veins. However, it also includes the same venous reflux causing the same symptoms and signs, with the one exclusion of visible bulging veins - the so-called "hidden varicose veins".

Doctors and patients should be aware that varicose veins deteriorate, with the general progression to worsening symptoms and signs including swollen ankles, skin damage, leg ulcers, superficial venous thrombosis and venous bleeds. There is good evidence that patients with varicose veins and any symptoms or signs will have a significant advantage in having them treated rather than wearing graduated compression stockings or not having formal treatment.

Patients who have small varicose veins or telangiectasia with no other symptoms or signs may request treatment for cosmetic reasons. If doctors or nurses agree to do this, they should understand the research showing underlying venous reflux and should get a VDU before treatment. Treatment of the underlying reflux should be performed first using the current best practice for the veins found to be incompetent, and then adequate consent should be obtained as to treatments used for the small varicose veins or telangiectasis and the expected outcomes.

The best practice for the investigation of leg varicose veins is VDU performed by a specialist trained in duplex ultrasonography and optimally not the doctor who then performs the treatment. VDU should be performed with the patient standing with their weight on the other leg, or in a similar position. The best investigation for PVR is the TVDUS

performed using the Holdstock-Harrison protocol. In men or in women for whom TVDUS is not possible, venography, CT with contrast or MRV will have to be used.

Best practice for treating truncal vein incompetence is EVTA. There is evidence accruing that IPVs associated with symptoms or signs of varicose veins should be treated by the TRLOP technique and thermal ablation. There is also evidence accruing that incompetent pelvic veins with venous reflux demonstrated into symptomatic varicose veins in the genital region or legs should be treated by coil embolisation or possibly plugs as an alternative, although direct treatment of the pelvic escape points might prove to be sufficient, if there are no pelvic symptoms.

Once the underlying reflux has been treated, best practice for treating any bulging varicosities of the legs is phlebectomy at the time of the truncal vein ablation.

Monitoring treatments and outcomes is essential for doctors to benchmark their work and for patients to have confidence in their treatment, and so active membership of a venous registry is encouraged and should probably be mandatory.

Disclosure

Mark Steven Whiteley reports being the founder of the College of Phlebology, during the conduct of the study and outside the submitted work. The author reports no other potential conflicts of interest for this work.

References

1. Amelia FM. Current concepts in the management of varicose veins. *Can J Surg.* 1986;29(1):21–23.
2. Vasdekis SN, Clarke GH, Nicolaides AN. Quantification of venous reflux by means of duplex scanning. *J Vasc Surg.* 1989;10(6):670–677. doi:10.1016/0741-5214(89)90011-6
3. Pichot O, Sessa C, Chandler JG, Nuta M, Perrin M. Role of duplex imaging in endovenous obliteration for primary venous insufficiency. *J Endovasc Ther.* 2000;7(6):451–459. doi:10.1177/15266028000700605
4. Navarro L, Min RJ, Boné C. Endovenous laser: a new minimally invasive method of treatment for varicose veins—preliminary observations using an 810 nm diode laser. *Dermatol Surg.* 2001;27(2):117–122. doi:10.1046/j.1524-4725.2001.00134.x
5. Chiesa R, Marone EM, Limoni C, Volontè M, Petrini O. Chronic venous disorders: correlation between visible signs, symptoms, and presence of functional disease. *J Vasc Surg.* 2007;46(2):322–330. doi:10.1016/j.jvs.2007.04.030
6. Chiesa R, Marone EM, Limoni C, Volontè M, Schaefer E, Petrini O. Chronic venous insufficiency in Italy: the 24-cities cohort study. *Eur J Vasc Endovasc Surg.* 2005;30(4):422–429. doi:10.1016/j.ejvs.2005.06.005
7. Whiteley MS. *Understanding Venous Reflux – The Cause of Varicose Veins and Venous Leg Ulcers.* Guildford, UK: Whiteley Publishing; 2011. ISBN: 978-1908586001.
8. Pannier F, Rabe E. Progression in venous pathology. *Phlebology.* 2015;30(1 Suppl):95–97. doi:10.1177/0268355514568847
9. Greiner M, Gilling-Smith GL. Leg varices originating from the pelvis: diagnosis and treatment. *Vascular.* 2007;15(2):70–78. doi:10.2310/6670.2006.00030
10. Rutherford EE, Kianifard B, Cook SJ, Holdstock JM, Whiteley MS. Incompetent perforating veins are associated with recurrent varicose veins. *Eur J Vasc Endovasc Surg.* 2001;21(5):458–460. PMID: 11352523. doi:10.1053/ejvs.2001.1347
11. Sparey C, Haddad N, Sissons G, Rosser S, de Cossart L. The effect of pregnancy on the lower-limb venous system of women with varicose veins. *Eur J Vasc Endovasc Surg.* 1999;18(4):294–299. doi:10.1053/ejvs.1999.0870
12. Robertson L, Lee AJ, Evans CJ, et al. Incidence of chronic venous disease in the Edinburgh Vein Study. *J Vasc Surg Venous Lymphat Disord.* 2013;Jan(1):59–67. doi:10.1016/j.jvsv.2012.05.006
13. Fassiadis N, Holdstock JM, Whiteley MS. The saphenofemoral valve: gate keeper turned into rear guard. *Phlebology.* 2002;17(1):29–31. doi:10.1177/026835550201700107
14. Labropoulos N, Giannoukas AD, Delis K, et al. Where does venous reflux start? *J Vasc Surg.* 1997;26(5):736–742. doi:10.1016/s0741-5214(97)70084-3
15. Munasinghe A, Smith C, Kianifard B, Price BA, Holdstock JM, Whiteley MS. Strip-track revascularization after stripping of the great saphenous vein. *Br J Surg.* 2007;94(7):840–843. doi:10.1002/bjs.5598
16. Ostler AE, Holdstock JM, Harrison CC, Price BA, Whiteley MS. Strip-track revascularization as a source of recurrent venous reflux following high saphenous tie and stripping: results at 5–8 years after surgery. *Phlebology.* 2015;30(8):569–572. doi:10.1177/0268355514535927
17. Varicose vein. Available from: <https://dictionary.cambridge.org/dictionary/english/varicose-vein>. Accessed October 31, 2021.
18. Lee AJ, Robertson LA, Boghossian SM, et al. Progression of varicose veins and chronic venous insufficiency in the general population in the Edinburgh Vein Study. *J Vasc Surg Venous Lymphat Disord.* 2015;3(1):18–26. doi:10.1016/j.jvsv.2014.09.008
19. Caggiati A. Fascial relationships of the long saphenous vein. *Circulation.* 1999;100(25):2547–2549. doi:10.1161/01.cir.100.25.2547
20. Schul MW, Schloerke B, Gomes GM. The refluxing anterior accessory saphenous vein demonstrates similar clinical severity when compared to the refluxing great saphenous vein. *Phlebology.* 2016;31(9):654–659. PMID: 26354286. doi:10.1177/0268355515604532
21. Franceschi C, Zamboni P. The unsolved puzzle of multiple sclerosis and venous function. *J Neurol, Neurosurg Psychiatry.* 2009. doi:10.1136/jnnp.2008.168179
22. Labropoulos N. Current views on the management of incompetent perforator veins. *Ann Phlebol.* 2020;18:1–3. doi:10.37923/phle.2020.18.1.1
23. Labropoulos N, Mansour MA, Kang SS, Gloviczki P, Baker WH. New insights into perforator vein incompetence. *Eur J Vasc Endovasc Surg.* 1999;18(3):228–234. PMID: 10479629. doi:10.1053/ejvs.1999.0812

24. Campbell WA, West A. Duplex ultrasound audit of operative treatment of primary varicose veins. *Phlebology*. 1995;1(Suppl 1):407–409.
25. Kianifard B, Holdstock J, Allen C, Smith C, Price B, Whiteley MS. Randomized clinical trial of the effect of adding subfascial endoscopic perforator surgery to standard great saphenous vein stripping. *Br J Surg*. 2007;94(9):1075–1080. doi:10.1002/bjs.5945
26. Bissacco D, Castronovo EL, Romagnoli S, Domanin M. Recurrent varices after surgery: a clinical and color-Doppler ultrasound scan analysis. *Int Angiol*. 2018;37(2):176–180. doi:10.23736/S0392-9590.18.03939-1
27. Bush RG, Bush P, Flanagan J, et al. Factors associated with recurrence of varicose veins after thermal ablation: results of the recurrent veins after thermal ablation study. *ScientificWorldJournal*. 2014;2014:505843. doi:10.1155/2014/505843
28. Bacon JL, Dinneen AJ, Marsh P, Holdstock JM, Price BA, Whiteley MS. Five-year results of incompetent perforator vein closure using TRans-Luminal Occlusion of Perforator. *Phlebology*. 2009;24(2):74–78. PMID: 19299275. doi:10.1258/phleb.2008.008016
29. Gavrilov S, Moskalenko YP, Mishakina NY, Efremova OI, Kulikov VM, Grishenkova AS. Stratification of pelvic venous reflux in patients with pelvic varicose veins. *J Vasc Surg Venous Lymphat Disord*. 2021;9(6):1417–1424. doi:10.1016/j.jvsv.2021.04.019
30. Antignani PL, Lazarashvili Z, Monedero JL, et al. Diagnosis and treatment of pelvic congestion syndrome: UIP consensus document. *Int Angiol*. 2019;38(4):265–283. doi:10.23736/S0392-9590.19.04237-8
31. Marsh P, Holdstock J, Harrison C, Smith C, Price BA, Whiteley MS. Pelvic vein reflux in female patients with varicose veins: comparison of incidence between a specialist private vein clinic and the vascular department of a National Health Service District General Hospital. *Phlebology*. 2009;24(3):108–113. doi:10.1258/phleb.2008.008041
32. Dabbs EB, Dos Santos SJ, Shiangoli I, Holdstock JM, Beckett D, Whiteley MS. Pelvic venous reflux in males with varicose veins and recurrent varicose veins. *Phlebology*. 2018;33(6):382–387. doi:10.1177/0268355517728667
33. Whiteley AM, Taylor DC, Dos Santos SJ, Whiteley MS. Pelvic venous reflux is a major contributory cause of recurrent varicose veins in more than a quarter of women. *J Vasc Surg Venous Lymphat Disord*. 2014;2(4):411–415. doi:10.1016/j.jvsv.2014.05.005
34. Holdstock JM, Dos Santos SJ, Harrison CC, Price BA, Whiteley MS. Haemorrhoids are associated with internal iliac vein reflux in up to one-third of women presenting with varicose veins associated with pelvic vein reflux. *Phlebology*. 2015;30(2):133–139. doi:10.1177/0268355514531952
35. Yetkin E, Ozturk S, Cuglan B, Turhan H. Symptoms in Dilating Venous Disease. *Curr Cardiol Rev*. 2020;16(3):164–172. doi:10.2174/1573403X16666200312101245
36. Milne AA, Stonebridge PA, Bradbury AW, Ruckley CV. Venous function and clinical outcome following deep vein thrombosis. *Br J Surg*. 1994;81(6):847–849. doi:10.1002/bjs.1800810618
37. Waheed SM, Kudaravalli P, Hotwagner DT. Deep vein thrombosis. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2021. PMID: 29939530.
38. Evans CJ, Fowkes FG, Hajivassiliou CA, Harper DR, Ruckley CV. Epidemiology of varicose veins. A review. *Int Angiol*. 1994;13(3):263–270. PMID: 7822904.
39. Weindorf N, Schultz-Ehrenburg U. Le développement de la varicose chez les enfants et les adolescents [The development of varicose veins in children and adolescents]. *Phlebologie*. 1990;43(4):573–577. French. PMID: 2093907.
40. Sparey C, Sissons G, Haddad N, Rosser S, de Cossart L. Serial colour flow duplex scanning of the veins of the lower limb throughout pregnancy. *Br J Obstet Gynaecol*. 1999;106(6):557–562. doi:10.1111/j.1471-0528.1999.tb08324.x
41. Engelhorn CA, Cassou MF, Engelhorn AL, Salles-Cunha SX. Does the number of pregnancies affect patterns of great saphenous vein reflux in women with varicose veins? *Phlebology*. 2010;25(4):190–195. PMID: 20656957. doi:10.1258/phleb.2009.009057
42. Szary C, Wilczko J, Plucinska D, et al. The number of pregnancies and deliveries and their association with selected morphological and hemodynamic parameters of the pelvic and abdominal venous system. *J Clin Med*. 2021;10(4):736. doi:10.3390/jcm10040736
43. Varicose veins: diagnosis and management. Clinical guideline [CG168]; 2013. Available from: <https://www.nice.org.uk/guidance/cg168>. Accessed October 31, 2021.
44. Gloviczki P, Comerota AJ, Dalsing MC, et al. Society for Vascular Surgery; American Venous Forum. The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. *J Vasc Surg*. 2011;53(5Suppl):2S–48S. doi:10.1016/j.jvs.2011.01.079
45. Wittens C, Davies AH, Bækgaard N, et al. Editor’s choice - management of chronic venous disease: clinical practice guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg*. 2015;49(6):678–737. doi:10.1016/j.ejvs.2015.02.007
46. Michaels JA, Campbell WB, Brazier JE, et al. Randomised clinical trial, observational study and assessment of cost-effectiveness of the treatment of varicose veins (REACTIV trial). *Health Technol Assess*. 2006;10(13):1–196, iii–iv. doi:10.3310/hta10130
47. Ruckley CV, Evans CJ, Allan PL, Lee AJ, Fowkes FG. Telangiectasia in the Edinburgh Vein Study: epidemiology and association with trunk varices and symptoms. *Eur J Vasc Endovasc Surg*. 2008;36(6):719–724. doi:10.1016/j.ejvs.2008.08.012
48. Somjen GM, Ziegenbein R, Johnston AH, Royle JP. Anatomical examination of leg telangiectases with duplex scanning. *J Dermatol Surg Oncol*. 1993;19(10):940–945. doi:10.1111/j.1524-4725.1993.tb00982.x
49. Engelhorn CA, Engelhorn AL, Cassou MF, Salles-Cunha S. Patterns of saphenous venous reflux in women presenting with lower extremity telangiectasias. *Dermatol Surg*. 2007;33(3):282–288. PMID: 17338684. doi:10.1111/j.1524-4725.2007.33063.x
50. van der Heijden FH, Bruyninckx CM. Preoperative colour-coded duplex scanning in varicose veins of the lower extremity. *Eur J Surg*. 1993;159(6–7):329–333.
51. Khaira HS, Parnell A, Crowson MC. Colour flow duplex in the assessment of recurrent varicose veins. *Ann R Coll Surg Engl*. 1996;78(2):139–141.
52. Sarin S, Sommerville K, Farrah J, Scurr JH, Coleridge smith PD. Duplex ultrasonography for assessment of venous valvular function of the lower limb. *Br J Surg*. 1994;81(11):1591–1595. doi:10.1002/bjs.1800811108
53. Vettorello GF, Gasbarro V, Mascoli F, et al. La “deambulazione simulata” nella valutazione del sistema venoso con duplex. Correlazioni clinico-strumentali [“Simulated walking” in the duplex evaluation of the venous system. The clinical and instrumental correlations]. *Minerva Cardioangiologica*. 1994;42(12):559–567. Italian.
54. Habenicht M, Rabe E, Amsler F, Mendoza E. Toe elevation manoeuvre to assess venous reflux in comparison to manual calf compression and release. *Vasa*. 2016;45(4):299–304. Erratum in: *Vasa*. 2016 Nov;45(6):432. doi:10.1024/0301-1526/a000541

55. Franceschi C. Mesures et interprétation des flux veineux lors des manoeuvres de stimulation. Compressions manuelles et manoeuvre de Parana. Indice dynamique de reflux (IDR) et indice de Psatakis [Measures and interpretation of venous flow in stress tests. Manual compression and Parana manoeuvre. Dynamic reflux index and Pstakis index]. *J Mal Vasc.* 1997;22(2):91–95. French.
56. Navarro TP, Delis KT, Ribeiro AP. Clinical and hemodynamic significance of the greater saphenous vein diameter in chronic venous insufficiency. *Arch Surg.* 2002;137(11):1233–1237. doi:10.1001/archsurg.137.11.1233
57. Ericsson KA, Krampe RT, Tesch-Romer C. The role of deliberate practice in the acquisition of expert performance. *Psychol Rev.* 1993;100(3):363–406. doi:10.1037/0033-295X.100.3.363
58. Gladwell M. *Outliers (Book) Little.* USA: Brown and Company; 2008. ISBN: 978-0316017923.
59. Ericsson KA. Towards a science of the acquisition of expert performance in sports: clarifying the differences between deliberate practice and other types of practice. *J Sports Sci.* 2020;38(2):159–176. doi:10.1080/02640414.2019.1688618
60. Florian Johannes NETZER GMC reference no: 7086642. Available from: <https://www.gmc-uk.org/doctors/7086642>. Accessed November 19, 2021.
61. Four eyes principle. Collaboration in research and methodology for official statistics. Available from: https://ec.europa.eu/eurostat/cros/content/four-eyes-principle_en. Accessed November 19, 2021.
62. Bentley PG, Hill PL, de Haas HA, Mistry F, Kakkar VV. Radionuclide venography in the management of proximal venous occlusion. A comparison with X-ray contrast venography. *Br J Radiol.* 1979;52(616):289–301. doi:10.1259/0007-1285-52-616-289
63. Massenburg BB, Himel HN, Blue RC, Marin ML, Faries PL, Ting W. Magnetic resonance imaging in proximal venous outflow obstruction. *Ann Vasc Surg.* 2015;29(8):1619–1624. doi:10.1016/j.avsg.2015.06.083
64. Marston W, Fish D, Unger J, Keagy B. Incidence of and risk factors for iliofemoral venous obstruction in patients with active or healed venous leg ulcers. *J Vasc Surg.* 2011;53(5):1303–1308. doi:10.1016/j.jvs.2010.10.120
65. Gagne PJ, Tahara RW, Fastabend CP, et al. Venography versus intravascular ultrasound for diagnosing and treating iliofemoral vein obstruction. *J Vasc Surg Venous Lymphat Disord.* 2017;5(5):678–687. doi:10.1016/j.jvsv.2017.04.007
66. Lattimer CR, Doucet S, Geroulakos G, Kalodiki E. Validation of the novel venous drainage index with stepwise increases in thigh compression pressure in the quantification of venous obstruction. *J Vasc Surg Venous Lymphat Disord.* 2017;5(1):88–95. doi:10.1016/j.jvsv.2016.06.019
67. Lattimer CR, Mendoza E, Kalodiki E. The current status of air-plethysmography in evaluating non-thrombotic iliac vein lesions. *Phlebology.* 2018;33(1):3–4. doi:10.1177/0268355516687866
68. Whiteley MS, Dos Santos SJ, Harrison CC, Holdstock JM, Lopez AJ. Transvaginal duplex ultrasonography appears to be the gold standard investigation for the haemodynamic evaluation of pelvic venous reflux in the ovarian and internal iliac veins in women. *Phlebology.* 2015;30(10):706–713. doi:10.1177/0268355514554638
69. White A, Holdstock J. Ultrasound assessment of pelvic venous reflux. *Indian J Vasc Endovasc Surg.* 2018;5(4):234–243. doi:10.4103/ijves.ijves_84_18
70. Malgor RD, Adrahtas D, Spentzouris G, Gasparis AP, Tassiopoulos AK, Labropoulos N. The role of duplex ultrasound in the workup of pelvic congestion syndrome. *J Vasc Surg Venous Lymphat Disord.* 2014;2(1):34–38. doi:10.1016/j.jvsv.2013.06.004
71. Gavrilov SG, Vasilyev AV, Moskalenko YP, Mishakina NY. Diagnostic value of pelvic venography in female patients with pelvic varicose veins and vulvar varicosities. *Int Angiol.* 2020;39(6):452–460. doi:10.23736/S0392-9590.20.04402-8
72. Beckett D, Dos Santos SJ, Dabbs EB, Shiangoli I, Price BA, Whiteley MS. Anatomical abnormalities of the pelvic venous system and their implications for endovascular management of pelvic venous reflux. *Phlebology.* 2018;33(8):567–574. doi:10.1177/0268355517735727
73. Dos Santos SJ, Holdstock JM, Harrison CC, Lopez AJ, Whiteley MS. Ovarian vein diameter cannot be used as an indicator of ovarian venous reflux. *Eur J Vasc Endovasc Surg.* 2015;49(1):90–94. doi:10.1016/j.ejvs.2014.10.013
74. Laurent R, Gilly R, Frileux C. Clinical evaluation of a venotropic drug in man. *Example of Daflon 500 Mg Int Angiol.* 1988;7(2 Suppl):39–43.
75. Ramelet AA. Clinical benefits of Daflon 500 mg in the most severe stages of chronic venous insufficiency. *Angiology.* 2001;52(Suppl 1):S49–56. doi:10.1177/0003319701052001S07
76. Guillot B, Guilhou JJ, de Champvallins M, Mallet C, Moccatti D, Pointel JP. A long term treatment with a venotropic drug. Results on efficacy and safety of Daflon 500 mg in chronic venous insufficiency. *Int Angiol.* 1989;8(4 Suppl):67–71.
77. Boisseau MR, de La Giclais B. Chronic venous diseases: roles of various pathophysiological factors. *Clin Hemorheol Microcirc.* 2004;31(1):67–74.
78. Michiels C, Bouaziz N, Remacle J. Role of the endothelium and blood stasis in the development of varicose veins. *Int Angiol.* 2002;21(2 Suppl 1):18–25.
79. Mlosek RK, Woźniak W, Gruszecki L, Stapa RZ. The use of a novel method of endovenous steam ablation in treatment of great saphenous vein insufficiency: own experiences. *Phlebology.* 2014;29(1):58–65. doi:10.1258/phleb.2012.012092
80. Milleret R, Huot L, Nicolini P, et al. Great saphenous vein ablation with steam injection: results of a multicentre study. *Eur J Vasc Endovasc Surg.* 2013;45(4):391–396. PMID: 23410966. doi:10.1016/j.ejvs.2013.01.027
81. Yang L, Wang XP, Su WJ, Zhang Y, Wang Y. Randomized clinical trial of endovenous microwave ablation combined with high ligation versus conventional surgery for varicose veins. *Eur J Vasc Endovasc Surg.* 2013;46(4):473–479. doi:10.1016/j.ejvs.2013.07.004
82. Ashpittel HF, Dabbs EB, Salguero FJ, Nemchand JL, La Ragione RM, Whiteley MS. Histopathologic differences in the endovenous laser ablation between jacketed and radial fibers, in an ex vivo dominant extrafascial tributary of the great saphenous vein in an in vitro model, using histology and immunohistochemistry. *J Vasc Surg Venous Lymphat Disord.* 2019;7(2):234–245. doi:10.1016/j.jvsv.2018.09.017
83. Vuylsteke ME, Thomis S, Mahieu P, Mordon S, Fourneau I. Endovenous laser ablation of the great saphenous vein using a bare fibre versus a tulip fibre: a randomised clinical trial. *Eur J Vasc Endovasc Surg.* 2012;44(6):587–592. PMID: 23084274. doi:10.1016/j.ejvs.2012.09.003
84. Minaev VP, Minaev NV, Bogachev VY, Kaperiz KA, Yusupov VI. Endovenous laser coagulation: asymmetrical heat transfer (modeling in water). *Lasers Med Sci.* 2021;36(8):1599–1608. doi:10.1007/s10103-020-03184-y
85. Woźniak W, Kielar M, Mlosek RK, Ciostek P. Comparative analysis of five-year outcomes of lower extremity varicose vein therapy using monopolar and segmental radiofrequency ablation. *Int Angiol.* 2018;37(6):457–464. doi:10.23736/S0392-9590.18.03954-8
86. Braithwaite B, Hnatek L, Zierau U, et al. Radiofrequency-induced thermal therapy: results of a European multicentre study of resistive ablation of incompetent truncal varicose veins. *Phlebology.* 2013;28(1):38–46. doi:10.1258/phleb.2012.012013
87. Garcia-Madrid C, Pastor Manrique JO, Sánchez VA, Sala-Planell E. Endovenous radiofrequency ablation (venefit procedure): impact of different energy rates on great saphenous vein shrinkage. *Ann Vasc Surg.* 2013;27(3):314–321. doi:10.1016/j.avsg.2012.06.015

88. The venclose system. Available from: <https://venclose.com/the-venclose-system/>. Accessed November 21, 2021.
89. Proebstle TM, Moehler T, Gül D, Herdemann S. Endovenous treatment of the great saphenous vein using a 1320 nm Nd: yAGlaser causes fewer side effects than using a 940 nm diode laser. *Dermatol Surg*. 2005;31(12):1678–83; discussion 1683–4. doi:10.2310/6350.2005.31308
90. Timperman PE, Sichlau M, Ryu RK. Greater energy delivery improves treatment success of endovenous laser treatment of incompetent saphenous veins. *J Vasc Interv Radiol*. 2004;15(10):1061–1063. doi:10.1097/01.RVI.0000130382.62141.AE
91. Whiteley MS. Endovenous thermal ablation of varicose veins and examination of the use and failings of Linear Endovenous Energy Density (LEED). In: Whiteley MS, Dabbs EB, editors. *Advances in Phlebology and Venous Surgery Volume 1*. Whiteley Publishing (Guildford); 2017: 11–27. ISBN: 978-1908586049.
92. Whiteley MS, Holdstock J. Percutaneous radiofrequency ablations of varicose veins (VNUS closure). In: Greenhalgh RM, editor. *Vascular and Endovascular Challenges*. London: Biba Publishing; 2004:361–381.
93. Whiteley MS. New methods of vein ablation. In: Davies AH, Lees T, Lane IF, editors. *Venous Disease Simplified*. UK: Harley; 2006:113–130.
94. Davies HO, Popplewell M, Darvall K, Bate G, Bradbury AW. A review of randomised controlled trials comparing ultrasound-guided foam sclerotherapy with endothermal ablation for the treatment of great saphenous varicose veins. *Phlebology*. 2016;31(4):234–240. doi:10.1177/0268355515595194
95. Whiteley MS, Dos Santos SJ, Fernandez-Hart TJ, Lee CT, Li JM. Media damage following detergent sclerotherapy appears to be secondary to the induction of inflammation and apoptosis: an immunohistochemical study elucidating previous histological observations. *Eur J Vasc Endovasc Surg*. 2016;51(3):421–428. doi:10.1016/j.ejvs.2015.11.011
96. Hamann SAS, Giang J, De Maeseneer MGR, Nijsten TEC, van den Bos RR. Editor's choice - five year results of great saphenous vein treatment: a meta-analysis. *Eur J Vasc Endovasc Surg*. 2017;54(6):760–770. doi:10.1016/j.ejvs.2017.08.034
97. Lim SY, Tan JX, D'Cruz RT, Syn N, Chong TT, Tang TY. Catheter-directed foam sclerotherapy, an alternative to ultrasound-guided foam sclerotherapy for varicose vein treatment: a systematic review and meta-analysis. *Phlebology*. 2020;35(6):369–383. doi:10.1177/0268355519898309
98. Cavezzi A, Mosti G, Campana F, Tessari L, Bastiani L, Urso SU. Catheter foam sclerotherapy of the great saphenous vein, with perisaphenous tumescence infiltration and saphenous irrigation. *Eur J Vasc Endovasc Surg*. 2017;54(5):629–635. Erratum in: *Eur J Vasc Endovasc Surg*. 2018 Mar 21. doi:10.1016/j.ejvs.2017.08.004
99. Myers KA, Roberts S. Evaluation of published reports of foam sclerotherapy: what do we know conclusively? *Phlebology*. 2009;24(6):275–280. doi:10.1258/phleb.2009.009048
100. Palm MD, Guiha IC, Goldman MP. Foam sclerotherapy for reticular veins and nontruncal varicose veins of the legs: a retrospective review of outcomes and adverse effects. *Dermatol Surg*. 2010;36(Suppl 2):1026–1033. doi:10.1111/j.1524-4725.2010.01496.x
101. Kahraman N, Demir D. Efficacy of foam sclerotherapy accompanied by near infrared light and duplex ultrasonography in treatment of symptomatic recurrent varicose veins: a retrospective cohort study. *J Surg Med*. 2019;3. doi:10.28982/josam.517231
102. Whiteley AM, Holdstock JM, Whiteley MS. Symptomatic recurrent varicose veins due to primary avaluvar varicose anomalies (PAVA): a previously unreported cause of recurrence. *SAGE Open Med Case Rep*. 2018;6:2050313X18777166. doi:10.1177/2050313X18777166
103. Brittenden J, Cooper D, Dimitrova M, et al. Five-year outcomes of a randomized trial of treatments for varicose veins. *N Engl J Med*. 2019;381(10):912–922. doi:10.1056/NEJMoal805186
104. Vähäaho S, Halmesmäki K, Albäck A, Saarinen E, Venermo M. Five-year follow-up of a randomized clinical trial comparing open surgery, foam sclerotherapy and endovenous laser ablation for great saphenous varicose veins. *Br J Surg*. 2018;105(6):686–691. doi:10.1002/bjs.10757
105. Lawaetz M, Serup J, Lawaetz B, et al. Comparison of endovenous ablation techniques, foam sclerotherapy and surgical stripping for great saphenous varicose veins. Extended 5-year follow-up of a RCT. *Int Angiol*. 2017;36(3):281–288. doi:10.23736/S0392-9590.17.03827-5
106. Venermo M, Saarinen J, Eskelinen E, et al. Finnish Venous Study Collaborators. Randomized clinical trial comparing surgery, endovenous laser ablation and ultrasound-guided foam sclerotherapy for the treatment of great saphenous varicose veins. *Br J Surg*. 2016;103(11):1438–1444. doi:10.1002/bjs.10260
107. Sinabulya H, Östmyren R, Blomgren L. Editor's choice - mid-term outcomes of endovenous laser ablation in patients with active and healed venous ulcers: a follow-up study. *Eur J Vasc Endovasc Surg*. 2017;53(5):710–716. PMID: 28408089. doi:10.1016/j.ejvs.2017.02.028
108. Bush RG. New technique to heal venous ulcers: terminal interruption of the reflux source (TIRS). *Perspect Vasc Surg Endovasc Ther*. 2010;22(3):194–199. doi:10.1177/1531003510387637
109. Hauer G. Die endoskopische subfasziale Diszision der Perforansvenen-vorläufige Mitteilung [Endoscopic subfascial dissection of perforating veins—preliminary report]. *Vasa*. 1985;14(1):59–61. German.
110. Kianifard B, Browning L, Holdstock JM, Whiteley MS. Surgical technique and preliminary results of perforator vein closure - TRLOP (Transluminal Occlusion of perforators). *Br J Surg*. 2002;89:508.
111. Elias S, Peden E. Ultrasound-guided percutaneous ablation for the treatment of perforating vein incompetence. *Vascular*. 2007;15(5):281–289. doi:10.2310/6670.2007.00068
112. O'Donnell TF. Letter regarding: “The role of perforators in chronic venous insufficiency” by TF O'Donnell. *Phlebology*. 2010;25:3–10. *Phlebology*. 2010 Dec;25(6):314; author reply 315-6. doi:10.1258/phleb.2010.010013
113. Toonder IM, Lam YL, Lawson J, Wittens CH. Cyanoacrylate adhesive perforator embolization (CAPE) of incompetent perforating veins of the leg, a feasibility study. *Phlebology*. 2014;29(1 suppl):49–54. doi:10.1177/0268355514529696
114. de Waard MM, der Kinderen DJ. Duplex ultrasonography-guided foam sclerotherapy of incompetent perforator veins in a patient with bilateral venous leg ulcers. *Dermatol Surg*. 2005;31(5):580–583. doi:10.1111/j.1524-4725.2005.31167
115. Dillavou ED, Harlander-Locke M, Labropoulos N, Elias S, Ozsvath KJ. Current state of the treatment of perforating veins. *J Vasc Surg Venous Lymphat Disord*. 2016;4(1):131–135. doi:10.1016/j.jvsv.2015.03.009
116. Ratnam LA, Marsh P, Holdstock JM, et al. Pelvic vein embolisation in the management of varicose veins. *Cardiovasc Intervent Radiol*. 2008;31(6):1159–1164. doi:10.1007/s00270-008-9402-9
117. Guirrola JA, Sánchez-Ballester M, Sierre S, Lahuerta C, Mayoral V, De Gregorio MA. A randomized trial of endovascular embolization treatment in pelvic congestion syndrome: fibered platinum coils versus vascular plugs with 1-year clinical outcomes. *J Vasc Interv Radiol*. 2018;29(1):45–53. doi:10.1016/j.jvir.2017.09.011

118. Gandini R, Konda D, Abrignani S, et al. Treatment of symptomatic high-flow female varicoceles with stop-flow foam sclerotherapy. *Cardiovasc Intervent Radiol*. 2014;37(5):1259–1267. doi:10.1007/s00270-013-0760-6
119. Ahuja RS, Garg T, Sudheendra D. Management of patients when superficial venous disease arises from pelvic escape points. *Semin Intervent Radiol*. 2021;38(2):226–232. doi:10.1055/s-0041-1729744
120. Lemasle P, Greiner M. Duplex ultrasound investigation in pelvic congestion syndrome: technique and results. *Phlebology*. 2017;24(2):79–87.
121. van Eekeren RR, Boersma D, Konijn V, de Vries JP, Reijnen MM. Postoperative pain and early quality of life after radiofrequency ablation and mechanochemical endovenous ablation of incompetent great saphenous veins. *J Vasc Surg*. 2013;57(2):445–450. doi:10.1016/j.jvs.2012.07.049
122. Alozai T, Huizing E, Schreve M, et al. A systematic review and meta-analysis of mechanochemical endovenous ablation using Flebogrif for varicose veins: a summary of evidence. *J Vasc Surg Venous Lymphat Disord*. 2021:S2213-333X(21)00289-4. doi:10.1016/j.jvs.2021.05.010
123. Lam YL, De Maeseneer M, Lawson J, De Borst GJ, Boersma D. Expert review on the VenaSeal[®] system for endovenous cyano-acrylate adhesive ablation of incompetent saphenous trunks in patients with varicose veins. *Expert Rev Med Devices*. 2017;14(10):755–762. doi:10.1080/17434440.2017.1378093
124. Yavuz T, Acar AN, Aydn H, Ekingen E. A retrospective study of a new n-butyl-2-cyanoacrylate glue ablation catheter incorporated with application guiding light for the treatment of venous insufficiency: twelve-month results. *Vascular*. 2018;26(5):547–555. doi:10.1177/1708538118770548
125. Hirsch T. Varicose vein therapy and nerve lesions. *Vasa*. 2017;46(2):96–100. doi:10.1024/0301-1526/a000588
126. Lane T, Bootun R, Dharmarajah B, et al. A multi-centre randomised controlled trial comparing radiofrequency and mechanical occlusion chemically assisted ablation of varicose veins - Final results of the Venefit versus ClariVein for varicose veins trial. *Phlebology*. 2017;32(2):89–98. doi:10.1177/0268355516651026
127. van Eekeren RR, Hillebrands JL, van der Sloot K, de Vries JP, Zeebregts CJ, Reijnen MM. Histological observations one year after mechanochemical endovenous ablation of the great saphenous vein. *J Endovasc Ther*. 2014;21(3):429–433. doi:10.1583/13-4588MR.1
128. Boersma D, van Haelst ST, van Eekeren RR, et al. Macroscopic and histologic analysis of vessel wall reaction after mechanochemical endovenous ablation using the ClariVein OC device in an animal model. *Eur J Vasc Endovasc Surg*. 2017;53(2):290–298. doi:10.1016/j.ejvs.2016.11.024
129. Whiteley MS, Dos Santos SJ, Lee CT, Li JM. Mechanochemical ablation causes endothelial and medial damage to the vein wall resulting in deeper penetration of sclerosant compared with sclerotherapy alone in extrafascial great saphenous vein using an ex vivo model. *J Vasc Surg Venous Lymphat Disord*. 2017;May(3):370–377. doi:10.1016/j.jvs.2016.12.009
130. Mordhorst A, Yang GK, Chen JC, Lee S, Gagnon J. Ultrasound-guided cyanoacrylate injection for the treatment of incompetent perforator veins. *Phlebology*. 2021;36(9):752–760. doi:10.1177/02683555211015564
131. Nasser H, Ivanics T, Shakaroun D, Lin J. Severe phlebitis-like abnormal reaction following great saphenous vein cyanoacrylate closure. *J Vasc Surg Venous Lymphat Disord*. 2019;Jul(4):578–582. doi:10.1016/j.jvs.2019.03.010
132. Langridge BJ, Onida S, Weir J, Moore H, Lane TR, Davies AH. Cyanoacrylate glue embolisation for varicose veins - A novel complication. *Phlebology*. 2020;35(7):520–523. doi:10.1177/0268355520901662
133. Weaver I, Weaver P. Audit of the efficacy and complications of cyanoacrylate glue embolisation to treat varicose veins in primary care. *J Prim Health Care*. 2019;11(3):249–258. doi:10.1071/HC19001
134. Cho S, Gibson K, Lee SH, Kim SY, Joh JH. Incidence, classification, and risk factors of endovenous glue-induced thrombosis after cyanoacrylate closure of the incompetent saphenous vein. *J Vasc Surg Venous Lymphat Disord*. 2020;8(6):991–998. doi:10.1016/j.jvs.2020.01.009
135. Watanabe S, Nishio S, Tsuji T, Fujita S, Kyo E. Effect of transluminal injection of foam sclerotherapy combined with endovenous thermal ablation of varicose veins. *EJVES Vasc Forum*. 2020;47:83–86. doi:10.1016/j.ejvsr.2019.12.001
136. Liu ZX, Guo PM, Zhang LL, Shi MJ, Wang RH, Meng QY. Efficacy of endovenous laser treatment combined with sclerosing foam in treating varicose veins of the lower extremities. *Adv Ther*. 2019;36(9):2463–2474. doi:10.1007/s12325-019-01011-7
137. Bone Salat C, Fructuos Gomez J. Device for treating truncal and/or collateral varicose veins and a synergistic physio-chemical method for use. United States Patent US9861443B2. 2018 Jan 9.
138. Miller A, Lilach N, Miller R, Kabnick L. A preclinical animal study of a novel, simple, and secure percutaneous vessel occluder for the treatment of varicose veins. *J Vasc Surg Venous Lymphat Disord*. 2017;5(1):114–120. doi:10.1016/j.jvs.2016.09.001
139. Atta I, El Abd A, Fouda H, Sawaby A. Catheter-directed foam sclerotherapy: a new technique for treating varicose veins. *Egypt J Surg*. 2020;39(3):738–744. doi:10.4103/ejs.ejs_61_20
140. Franceschi C. [The conservative and hemodynamic treatment of ambulatory venous insufficiency]. *Phlebologie*. 1989;42(4):567–568. French.
141. Gasior SA, O'Donnell JPM, Aherne TM, et al. Outcomes of saphenous vein intervention in the management of superficial venous incompetence: a systematic review and network meta-analysis. *Ann Surg*. 2021. doi:10.1097/SLA.0000000000004914
142. Pittaluga P, Chastanet S. Treatment of varicose veins by ASVAL: results at 10 years. *Ann Vasc Surg*. 2017;38:E10. doi:10.1016/j.avsg.2016.07.021
143. Whiteley MS. High intensity focused ultrasound (HIFU) for the treatment of varicose veins and venous leg ulcers - a new non-invasive procedure and a potentially disruptive technology. *Curr Med Res Opin*. 2020;36(3):509–512. doi:10.1080/03007995.2019.1699518
144. Encarnacion SN, Onida S, Lane TR, Davies AH. Do we need another modality for truncal vein ablation? *Phlebology*. 2020;35(9):644–646. doi:10.1177/0268355520913390
145. Whiteley MS. Do we need another modality for truncal vein ablation? *Phlebology*. 2020;35(9):736–737. doi:10.1177/0268355520932785
146. Lane TR, Kelleher D, Shepherd AC, Franklin IJ, Davies AH. Ambulatory varicosity avulsion later or synchronized (AVULS): a randomized clinical trial. *Ann Surg*. 2015;261(4):654–661. doi:10.1097/SLA.0000000000000790
147. The College of Phlebology Venous Registry. Available from: www.collegeofphlebology.com/college-of-phlebology-venous-registry/. Accessed November 18, 2021.

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