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ORIGINAL ARTICLE

Endovenous Treatment for Varicose Veins

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Abstract
There has been a paradigm shift in the treatment of varicose veins in the last three decades. Open surgical techniques, once considered the gold standard for treatment of varicose veins, have largely been replaced by various non-surgical minimally invasive techniques. Currently, multiple thermal and non-thermal treatment techniques are available, and they have similar long-term results of success as compared to open surgical techniques. The advantage lies in avoiding surgical scars, anaesthesia and hospital stay. This review elaborates on the commonly used techniques, although it must be stressed that rapid innovations and newer techniques are constantly being introduced for the effective treatment of varicose veins.

Keywords Varicose veins · Endovenous therapy · Chronic venous disease

Introduction

Almost 60 to 70% of patients with varicose veins are due to venous reflux, with an incompetent saphenofemoral valve and great saphenous vein reflux [1]. The treatment of the cause of venous hypertension is as important as the treatment of the varicosities.

Venous hypertension leads to a broad range of clinical manifestations, ranging from either only symptoms, or to clinical manifestations like varicose veins, reticular veins, telangiectasias, swelling, skin discoloration and ulcerations. Once venous hypertension is present, the venous dysfunction continues to worsen through a vicious cycle. Over time, with more local dilatation, other adjacent valves sequentially fail, and after a series of valves have failed, the entire superficial venous system becomes incompetent. Lower-extremity venous insufficiency is a common medical condition afflicting 25% of women and 15% of men in the USA and Europe.

The drainage of the superficial system takes several pathways. The most important is the great saphenous vein (GSV), responsible for 70–80% of cases. The GSV reflux is due to saphenofemoral junction (SFJ) incompetence. The small saphenous vein (SSV) is affected in about 10% of patients, due to reflux at the saphenopopliteal junction (SPJ). Although less common than GSV reflux, SSV reflux may result in symptoms of equal severity. Isolated anterior saphenous vein reflux occurs in approximately 10% of patients. Another cause of reflux is incompetent perforating veins. In about 10% of the patients, varicose veins appear without affecting one of those four pathways.

Treatment of GSV reflux has traditionally been surgical. However, recurrence in 30–60% of cases has been reported [2]. Surgery is also associated with significant perioperative morbidity. Less invasive surgical treatments, including high ligation of the GSV at the SFJ, have been attempted in the hope that gravitational reflux would be controlled while the vein is preserved for possible use as a bypass graft. Unfortunately, ligation of the GSV alone usually results in recurrent varicose veins. Even when high ligation has been combined with phlebectomy of varicose tributaries or retrograde sclerotherapy, recurrence has been the rule. Therefore, when it is determined that GSV reflux is the principal underlying problem, treatment should involve eliminating this source of reflux with ablation of any associated incompetent venous segments [3]. Though inadequate surgery of the SFJ and progression of the disease are mechanisms that explain some cases of recurrence, another important mechanism is neovascularization around the junction after venous surgery. Neovascularization has been reported to be the principal cause of recurrence with clear histologic evidence. Surgery for the incompetent SSV is even more challenging, with more complications and higher recurrence rates, than for the GSV. The potential for damage to the sural nerve with resulting

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neurological deficit has deterred many vascular surgeons from stripping the SSV routinely. Most commonly, the SSV is ligated only at the SPJ. Recurrence rates of SSV after surgery are about 30–50% at 5 years [4].

Treatment of varicose veins has now evolved from open radical surgery to use of newer endovenous technologies. The clinical success of the endovenous procedures is comparable to high ligation and stripping operations and there are several advantages to surgery.

Endovenous thermal ablative techniques are recognized as less invasive alternatives to open conventional surgery procedures [5]

Endovenous procedures are also associated with rapid recovery and return to daily activity with low risks of infection and hematoma, especially in obese patients if compared with surgery [6].

Postoperative pain is less severe with endovenous ablation than surgical intervention [7].

Hospital stay is longer in surgical patients. Karmota [8] demonstrated a mean hospital stay time of 36 ± 9.2 h in the surgical group, while in the laser group, the mean time was 8 ± 2.6 h. There was a significant difference between both groups in return to daily activity. In surgery groups, it took a mean time of 7.5 ± 1.7 days, while in the laser group, the mean time was 2 ± 1.2 days [8].

Endovenous Therapeutic Options.

The currently available endovenous therapeutic options for treatment include:

1. Thermal ablation techniques
    a. Radiofrequency ablation
    b. Laser thermal ablation
    c. Steam ablation
    d. Microwave treatment
    e. HIFU—high-intensity focussed ultrasound
2. Non-thermal techniques
    a. Sclerotherapy
    b. Mechano-chemical ablation
    c. Medical glue—cyanoacrylate
    d. CLaCS for telangiectasis

Thermal Ablation Techniques

The most used techniques are endovenous laser ablation (ELA) and radiofrequency (RFA) segmental thermal ablation.

Radiofrequency Ablation

In 1999, the RFA first-generation device, *Closure Procedure*, received US FDA approval. This first-generation device used bipolar electrodes mounted on the end of a catheter to deliver radiofrequency (RF) energy to the inner vein wall. The electrodes make direct contact with the vein wall, and the resistive effects of the vein wall tissue cause conversion of the RF energy into heat. The vein wall collagen contraction in response to thermal energy causes immediate vein wall thickening and reduction in the lumen diameter. The endothelial destruction causes an inflammatory response, which finally results in fibrosis and permanent vein occlusion. The treatment protocol for this first-generation device was delivering a treatment temperature of 85 °C, with a pullback speed of 3 cm/min.

The second-generation device was *VNUS ClosureFast*. With the introduction of the ClosureFast RF ablation catheter, the elimination of the slow pullback and the implementation of segmental treatment at 120 °C markedly improved the ablation procedure. Controlled heating of the vein by conduction avoids vein perforations even with high dosing of thermal energy. The postprocedure inflammation is also minimal (Fig. 1).

In the ClosureFast technique, the length of the conduction element is 7 cm, and a temperature of 120 °C is maintained for a period of 20-s cycles. At the saphenofemoral junction, two cycles of RF energy are delivered averaging an LEED of 116.2 ± 11.6 J/cm, to ensure good vein closure at this critical site. Distal to this, a single cycle is used delivering LEED of 68.2 ± 17.5 J/cm. In 2008, Proebstle [9] reported the occlusion rate at 99.6% at 2 years, and 70% of treated patients did not require any postoperative analgesia (Fig. 2).

Fig. 1 The Closure RFA generator and catheter

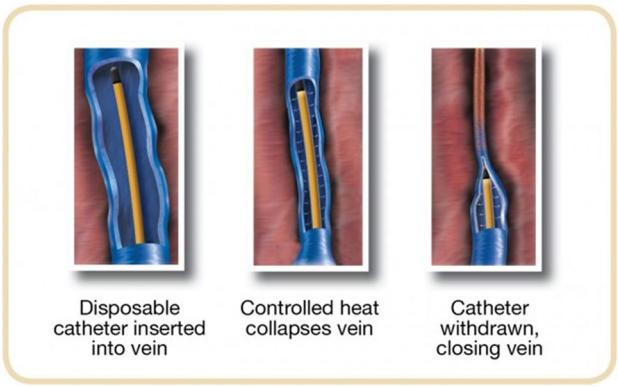

Fig. 2 The ClosureFast technique

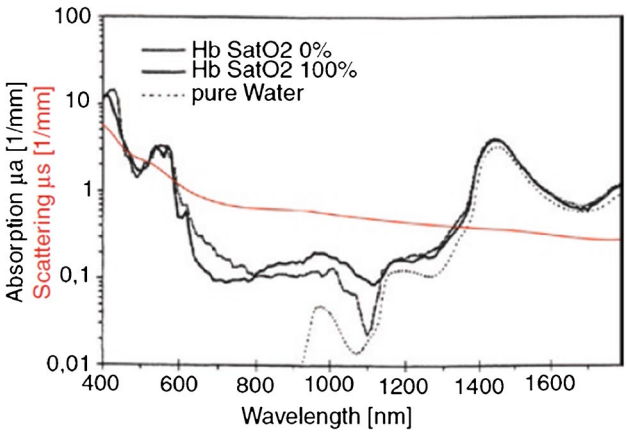

Fig. 3 Absorption and scattering (*red*) coefficients of blood relative to wavelength

Endovenous Laser Ablation (EVLA)

Endovenous laser ablation (EVLA) works by means of thermal destruction of venous tissues. Laser energy is delivered to the desired incompetent segment inside the vein through a laser fibre that has been passed through a sheath to the desired location.

When using laser light, heat is generated within the zone of optical penetration by direct absorption of laser energy. Without absorption, there is no energy transfer to the tissue and the tissue is left unaffected by the light.

Several wavelengths have been proposed: 810, 940, 980, 1064, 1320 and 1470 nanomicrons. Wavelengths of 1470–1500 nm are preferentially absorbed by water [10–15], and currently the most popular is the 1470-nm laser wavelength (Fig. 3).

While using the laser, it is essential that the vein is emptied of blood, because:

1. The blood around the fibre tip reduces the transmission of light to the biological target of EVLA: the venous wall [16].
2. If the laser light energy is entirely absorbed by the blood, the initial success rate will be mainly due to a thrombotic effect; later, thrombus dissolution will lead to recanalization, as clearly demonstrated by Proebstle et al. [16].
3. The presence of blood induces carbonization at the fibre tip and often melting of the glass fibre tip. The carbon layer rapidly forming at the tip absorbs most of the light energy and converts it into heat, radically altering the laser/tissue interaction process.

The equipment used for endovenous laser procedure:

a Diode laser: 810-, 940-, 980- and 1470-nm wavelengths
b Nd:YAG laser: 1320-nm wavelengths
c Sheaths of 35, 45 and 65 cm lengths should be available to accommodate different vein lengths
d Six hundred–micron diameter laser fibre (bare tip or covered tip, or radial) is placed through the sheath and deployed at the target site under ultrasound control.

The Laser Procedure

Under ultrasound guidance, the great saphenous vein is identified just below the knee joint, usually at the distal-most site of reflux. A wheal of local anaesthesia on the skin access site is delivered, and the vein is percutaneously cannulated with an 18-gauge Seldinger needle. For smaller veins, a 21-gauge needle is used. A 0.035-inch guidewire is passed through the 18-gauge needle and advanced into the vein under ultrasound guidance into the deep femoral vein. For tortuous veins, a hydrophilic guidewire is preferred. A 5-French sheath is then introduced over the guidewire, and the tip of the fibre is placed proximal to the saphenofemoral junction. The guidewire is removed, and the laser fibre is introduced into the sheath, protruding about 2 cm from its tip. The assembly is then pulled back, under ultrasound guidance, so that the tip of the laser fibre is 2 cm away from the saphenofemoral junction (Fig. 4).

The next step is to deliver perivenous tumescent anaesthesia. This offers several benefits. It acts as a heat sink; by circumferentially surrounding the target vein with fluid, the heat transferred by the laser fibre to the vein wall will not damage the surrounding tissues and nerves. Secondly, the tumescent anaesthesia compresses the vein, and empties out the blood, bringing the laser catheter into direct contact with the inner vein wall. Finally, the fluid also has an analgesic effect. Tumescent anaesthetic solution is prepared by adding 50 ml of 1% lidocaine with 1:100,000

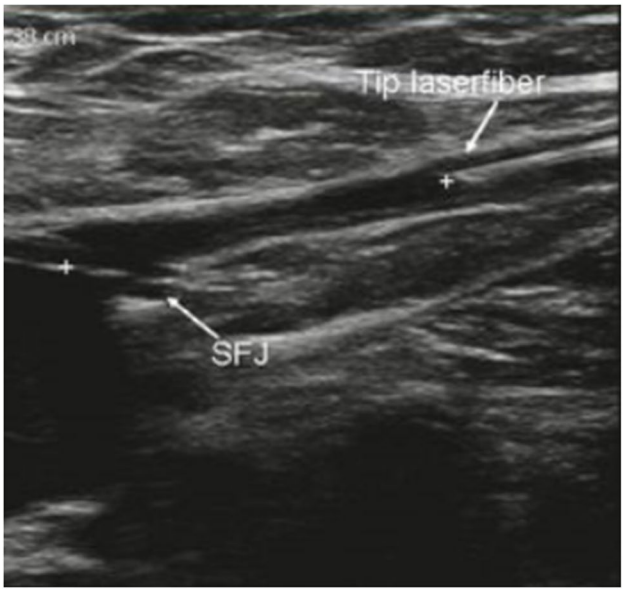

Fig. 4 Tip of laser fibre placed 2 cm away from SF junction

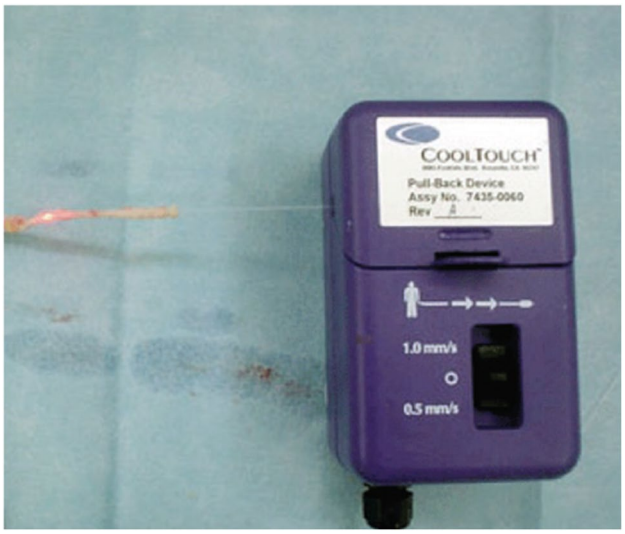

Fig. 5 Automated pullback device

epinephrine in 500 ml of normal saline. Ten cubic centimetres of bicarbonate is added as a buffer.

The pullback protocol for the endovenous procedure is not standardised since multiple wavelengths exist, and no absolute energy protocols have been established. As per popular protocols, the linear endovenous energy density (LEED) should be between 60 and 80 J/cm. The pullback speed is measured in millimetres per second.

The laser has adjustable power outputs. One watt of energy delivers 1 J of energy per second, and 10 watts will deliver 10 J/s. With the laser set at 10 watts, for most veins, the results are very satisfactory. To treat a saphenous vein of 40 cm length, at an LEED of 60 J/cm, the total energy to be delivered will be 2400 J. At the power of 10 watts, the total time for energy delivery will be 240 s. Therefore, the pullback speed will be 1.7 mm per second. An automated pullback device has been developed to assist in a uniform pullback speed, to deliver uniform laser energy to the vein wall along its length (Fig. 5).

Once laser energy has been delivered to the entire vein length, the laser and sheath are removed together as one entity.

A compression bandage is then placed from the foot to the groin, to be removed after 24 to 48 h as per physician preference.

It is important to make sure that the tip of the laser fibre is not abutting against the vein wall. In such a case, perforation of the vein wall will occur, with resultant burn injury and ecchymosis. The introduction of the radial laser fibre has ensured that the laser energy is delivered circumferentially instead of a forward direction, thereby preventing vein perforation (Fig. 6).

Recently, the 1940 laser wavelength laser fibre has been introduced and has increasingly been used to perform endovenous ablation for varicose veins. Since the absorption coefficient of both blood and water increases with the increasing wavelength, it is assumed that treatment would be possible with lower power regardless of the main absorption site, blood, water, or vein wall. When lower power and LEED are used, the resulting thermal damage to the normal perivenous normal tissue also decreases, and early recovery may be expected with less postprocedural pain. A 1-month closure rate of 100% was demonstrated in a prospective observational study of 89 patients with 160 incompetent saphenous veins using a 1940-nm diode laser and bare fibre

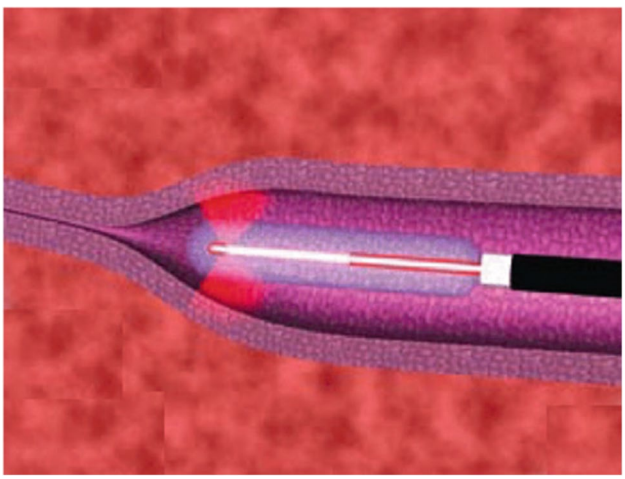

Fig. 6 Radial laser fibre

by Park [17]. The laser's power was set to 4.5 W with a mean linear endovenous energy density of 50.4 J/cm.

Over medium- to long-term time follow-up also, the 1940 nm laser proved to be safe and effective in venous segments up to 10 mm in diameter. Forty-one patients were treated with a 1940 laser fibre delivering an average LEED of 45.3 J/cm, with an average follow-up period of 803 days. The immediate success rate was 100% and the late success rate was 95.1% [18].

The initial results of the use of 1940 laser therapy are encouraging, although more long-term studies of larger groups of patients are awaited.

Results of Endovenous Thermal Ablation

Both RFA and ELA are less invasive than junctional ligation and saphenous stripping. EVTA is safely and effectively performed using local anaesthesia in an office setting, requiring about 45 to 75 min to perform. Patient satisfaction has been reported to be very high following both procedures.

Anatomical outcome must include occlusion of the treated segment, early failure (complete or segmental), or late recanalization. Anatomical success with ELA and RFA has been reported between 85 and 100%. Most of the EVTA recanalisation occurs in the first 6 months, and all in the first 12 months following EVTA in all series. This suggests that the recanalization may be due to insufficient thermal energy delivery to the target vein wall, with resultant vein thrombosis rather than cicatrisation. The thrombosis is then followed by recanalization.

In EVTA, the procedure is performed about 2 cm away from the saphenofemoral junction. This proximal patent stump of the GSV is usually connected to a saphenous tributary, which over a period may reflux and be the source of a clinical recurrence.

Patients with a high body mass index have a higher rate of failure; the reason is unclear, although these obese patients are known to have a higher central venous pressure and higher frequency of chronic venous disease.

Complications

Almost all side effects of EVTA are minor.

Ecchymosis over the treated segments of the vein frequently occurs and can last for up to 3 weeks.

After about a week of EVTA, the treated vein may develop a feeling of tightness like that of a strained muscle. This is self-limited and responds to anti-inflammatory drugs. Both these side effects are more common with EVLA than RFA.

Superficial phlebitis may occur in about 5% of patients.

More significant adverse effects include neurological injuries, skin burns and deep vein thrombosis. These are known to occur more commonly in low volume centres. The nerves at highest risk include the saphenous nerve adjacent to the GSV below the mid-calf perforating vein, and the sural nerve adjacent to the SSV in the mid- and lower calf.

Laser Crossectomy

It is now known that a long residual saphenofemoral stump promotes recurrence [19, 20]. When endovenous thermal ablation of the great saphenous veins is performed a distance away from the saphenofemoral junction, it does not occlude the origin of the anterior accessory great saphenous vein (AAGSV) and recurrence preferentially occurs via the anterior accessory saphenous vein [21–23].

It is postulated that once the GSV is ablated, flow is then directed to the AAGSV. Due to inherent defects in vein wall or valves, resultant insufficiency occurs. Prior to GSV ablation, refluxing flow preferentially follows the larger diameter GSV.

In the REVATA study, new AAGSV insufficiency occurred in 40 patients (24%) after the original procedure of GSV ablation [24].

Therefore, the recent trend is towards performing an endovenous crossectomy, i.e. the treatment of the long saphenous vein is carried out up to the saphenofemoral junction, which again was not previously possible with bare fibres, but which is no longer a problem with the modern radially radiating laser fibres and modern RFA techniques [25].

Laser crossectomy of the GSV has been established as a more effective method of preventing secondary anterior accessory great saphenous vein (AAGSV) reflux than treatment modalities which leave stumps. A randomised controlled study was published comparing the technique with infra-epigastric closure was published by Ragg [26].

The aim of the randomised study was to compare infra-epigastric to femoral-level laser ablation, using identical device and techniques. Two hundred forty consecutive patients with GSV insufficiency were included. One hundred twenty patients in group A underwent laser crossectomy—defined as EVLA starting at the femoral vein level—while 120 patients in group B were treated with EVLA starting below the epigastric vein junction. "Primary GSV occlusion was obtained in all cases. Using ablation from the femoral level (group A), the outlet of AAGSV was covered in 118/120 cases (98.3%). In group B, the entry to the AAGSV was covered in only 13 of 120 cases (10.8%). Within the 2-year follow-up, AAGSV insufficiency was recorded in five of the patients (4.2%) after laser crossectomy (group A) and 26 of the patients (21.7%) in group B ($p > 0.01$).

In conclusion, laser crossectomy may be helpful in preventing long-term recurrences. However, the use of radial laser fibres, proper positioning of the laser fibre at the junction and operator experience are necessary to prevent EHIT in these cases.

EHIT—Endovenous Heat-Induced Thrombosis

EHIT refers to the postprocedural propagation of thrombus after an endothermal ablation (e.g. RFA or EVLA). The definition for EHIT is based on a specific relationship between the superficial vein that is being treated and the contiguous deep vein.

With the popularisation of RFA and laser in the treatment of varicose veins, Hingorani et al. [27] reported venous thrombosis (DVT) of the common femoral vein on postprocedure surveillance ultrasound in 2004. Later publications started referring to these postoperative thrombi, ranging in incidence from 0 to 8% [28–30] as thrombus extension rather than DVT as it was believed that they represented a distinct phenomenon [31, 32].

Although the occurrence of superficial thrombus within the treated vein segment is a normal ultrasound finding, its propagation into a deep vein may pose a risk for the development of symptomatic DVT and pulmonary embolism (PE) [30, 33].

In 2006, Kabnick [34] first introduced the term endothermal heat-induced thrombosis (EHIT), defining it as the propagation of thrombus into the deep vein contiguous with the ablated superficial vein. This definition has been widely adopted to describe this clinical entity. From a diagnostic and clinical standpoint, EHIT is an entity separate from classic DVT. EHIT, for the most part, has a distinct sonographic appearance, behaves like a stable thrombus, and often regresses spontaneously after a few weeks of observation or a short course of anticoagulation.

Most EHITs are asymptomatic, and the diagnosis is usually detected by postprocedure duplex ultrasound examinations performed anywhere from 24 to 72 h to 1 to 2 weeks after the procedure, depending on the local ultrasound surveillance protocol. It is currently believed that most EHITs develop within 72 h, but postprocedure surveillance ultrasound scans may occasionally identify an EHIT after 7 days and even up to 4 weeks after endovenous ablation [35, 36].

Based on current literature, practitioners report that the overall rate of DVT after endovenous ablations is < 1%, and EHIT is three to four times more likely to occur than non-EHIT DVT [35, 36]. Classic DVTs do not retract or resolve as early as EHITs and are likely to be due to other eliciting factors, such as excessive immobilization, ill-fitted compression hosiery or activation of the coagulation cascade during endothermal ablation at a remote location [37].

Two EHIT classification schemes are present in the literature: the Kabnick classification [34] and the Lawrence classification [37]. The current classification of types of EHIT is a combination of the Kabnick and Lawrence classifications as advised by the American Venous Forum and the Society for Vascular Surgery (Table 1).

Multiple studies have evaluated the risk factors and, by extension, the modes of prevention for EHIT. In general, the evidence for risk factors and modes of prevention was limited and lacked reproducibility. Some of the risk factors identified included diameter, age and a history of thromboembolic disease, among other factors. Regarding prevention of EHIT, there were no significant findings with the use of chemical prophylaxis, the use of compression, or the distance of ablation from the deep vein junction, although there was a trend towards a decreased rate of EHIT II when treatment was initiated > 2.5 cm from the deep vein junction.

The management of EHIT remains controversial considering its presumed benign natural history compared with conventional DVT. Specifically, patients are often asymptomatic, and the progression to PE is rarely reported. In addition, there is no conclusive evidence to support the theory that treating EHIT reduces the incidence of PE (Table 2).

In conclusion, thrombus extension into the adjacent deep vein is the most recognized potentially clinically significant entity. The current consensus is that surveillance duplex ultrasound should be considered for these clinical entities (EHIT II and III). Treatment should be tailored to the patient, taking the risks and benefits into account. Ongoing data collection from prospective studies and registries will allow the refinement of diagnosis and treatment protocols.

Table 1 Endovenous heat-induced thrombosis. Kabnick et al. [38]

Class	Definition
I	Thrombus without propagation into the deep vein a. Peripheral to superficial epigastric vein b. Central to superficial epigastric vein, up to and including the deep vein junction
II	Thrombus propagation into the adjacent deep vein but comprising <50% of the deep vein lumen
III	Thrombus propagation into the adjacent deep vein but comprising >50% of the deep vein lumen
IV	Occlusive deep vein thrombus contiguous with the treated superficial vein

Table 2 Treatment of EHIT—AVF/SVS recommendations 2021 [39]

EHIT class	Treatment recommendation	Strength of recommendation and level of evidence
I	No treatment or surveillance	2C
II	No treatment, weekly surveillance until thrombus resolution, in high-risk patients consider antiplatelet therapy vs anticoagulation. Discontinue treatment following thrombus retraction or resolution	2C
III	Therapeutic anticoagulation, weekly surveillance. Discontinue treatment following thrombus retraction or resolution	1B
IV	Treatment should be individualized, taking into account risks and benefits to patient. Reference may be made to CHEST GUIDELINES for treatment of DVT	1A

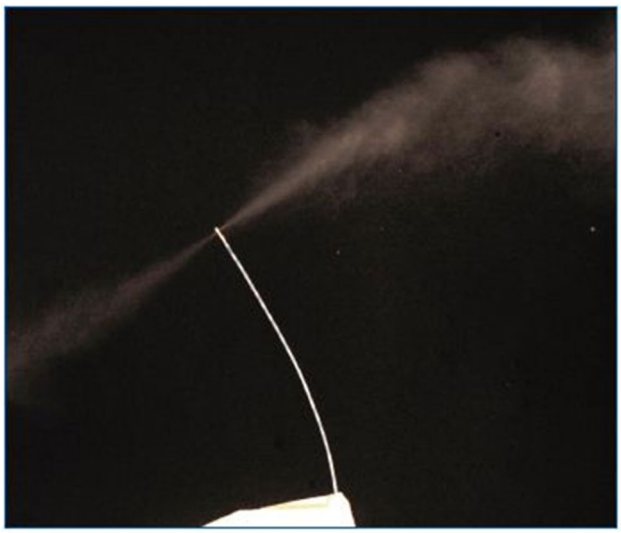

Fig. 7 Steam is ejected from two areas at the tip of the catheter

Steam Ablation

Endovenous steam ablation (EVSA) is a new method of thermal vein ablation that works by heating the venous structure with steam to a maximum temperature of 120 °C.

The procedure is very similar to EVLA and can be performed with the patient under local tumescent anaesthesia in an outpatient setting (Fig. 7).

The vein is punctured with a 16-gauge needle or cannula under ultrasound guidance. The GSV is usually entered at the distal site of reflux, at or just above knee level because access is easy at this site and the risk of nerve injury is low. The SSV is usually punctured halfway or at a position in the distal third of the calf, depending on vein diameter and extent of reflux. After puncturing the vein, the steam catheter (1.2-mm diameter) is passed through the hollow needle into the vein, and the echo-dense tip of the catheter is then carefully positioned 3 cm from the junction, under ultrasound guidance. About 250 to 500 mL (depending on the length of vein treated) of tumescent anaesthesia is administered into the perivenous space under ultrasound guidance. After activation, the catheter releases small "puffs" of steam and is pulled back in a stepwise fashion. At the first activation, 3 cm below the saphenofemoral or saphenopopliteal junction, four puffs of steam should be administered, while exerting gentle manual pressure on the junction. Further along the vein, two or three puffs of steam can be administered at 1 cm intervals depending on vein diameter. For the first 4 cm of treatment, manual compression of the junction should still be applied as the steam can reach several centimetres beyond the catheter tip. After the procedure, patients are advised to wear thigh-length medical elastic compression stockings (pressure range 25–35 mm Hg) for 1 week and to mobilize immediately after the treatment.

The main limitation of steam ablation is the lack of evidence; only three reports on steam ablation have been published to date [40–42].

Microwave Ablation

In 2009, Subwongcharoen [43] found that endovenous microwave ablation (EVMWA) appeared to be another extremely safe and effective technique for the treatment of varicose veins and the best ablation effect could be obtained with microwave generator with 50-W power setting. EVMWA uses dielectric hysteresis to produce direct volume heating of tissue. The microwave probe is more flexible than laser fibre, and it can be smoothly inserted into the vessel and reach the SFJ without the help of a catheter and guidewire. The microwave generator can produce much higher energy than that of the laser generator. The occlusion rate of target veins depends on the thoroughness of endothelial damage, which correlates positively to the thermal energy received by the vein wall. Due to more energy provided by the microwave, the occlusion rate after EVMWA is significantly higher than that due to EVLA. The microwave energy is delivered circumferentially away from the fibre tip, and therefore the fibre need not be in direct contact with the vein wall. The temperature at the tip of the microwave probe is usually around 80 °C, (as compared to 800 °C with EVLA)

which seldom creates an ulceration, and even perforation, and therefore the incidence of ecchymosis is very minimal [44] (Fig. 8).

High-Intensity Focussed Ultrasound (HIFU)

This is a new, disruptive technology for the treatment of varicose veins. An ultrasound transducer applied to the skin above the vein and the beam is focused on the target vein, using a linear ultrasound array to obtain an image of the target vein in real time. The focused ultrasound generates heat at a precise point deep into the skin. During each treatment cycle, a small volume of vein tissue is ablated at about 85–90 °C, which causes permanent closure of the incompetent vein by fibrosis. Due to the heat, some patients do require small amounts of local anaesthesia to be injected at the point of heating. The HIFU procedure does not require cannulation of the vein and indeed nothing is inserted into the target vein at all. There is no need for an operating theatre and, as nothing is introduced into the vein itself, this procedure can be performed in a clean clinical room.

The current device (Sonovein) is large, cumbersome and expensive, and treatment is slow in long truncal veins, as very small amounts of vein tissue are ablated during each cycle. The Sonovein HIFU equipment automatically detects the depth of the vein from the skin surface, and adjusts the maximum energy that can be delivered, to protect the skin. This, combined with a skin cooling delay which is computed within the device, prevents any thermal skin damage. Each pulse of HIFU lasts for 8 s, and then there is a variable delay to ensure skin temperature is normal before a further pulse.

Encouraging results in the initial 5 cases have been reported by Whitely [45], although further modifications in equipment and treatment techniques are needed to determine the benefit of this procedure in varicose veins.

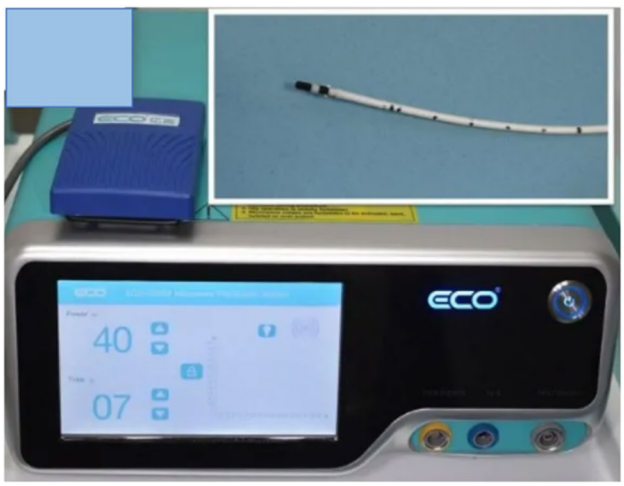

Fig. 8 The microwave machine with fibre and foot pedal

Non-Thermal Ablation Techniques

Chemical Ablation (Sclerotherapy)

Sclerotherapy is a technique which employs chemical cauterants to sclerify and obliterates vascular tissue. It was first described in 1939 by S. McAusland who injected froth, produced by shaking a rubber-capped bottle filled with sodium morrhuate, into spider veins.

The mechanism of action of sclerosing solutions is directed towards complete destruction of the endothelial cells lining the venous lumen, exposure of subendothelial collagen fibres and ultimately the formation of a fibrotic cord.

The most important qualities that a sclerosant should possess are safety, efficacy and lack of untoward side effects. Also, the ability to produce durable and repeatable results, painless treatments, accurate placement with ultrasound guidance, ease of availability and low cost.

The efficacy of sclerosant agents is a function of concentration and vein diameter. If the vein diameter is larger than 3 mm, liquid sclerosants will not reach the vein wall, due to dilution in blood. Sclerosants in the form of foam are more efficacious than liquid, and more easily monitored with ultrasound imaging. Foam will fill a vein up to 12 mm in diameter, offering better contact with the vein wall. Cabrera has published a clinical series of 500 lower limbs treated with foam sclerotherapy, with 81% of great saphenous veins remaining occluded at 3 years. In this series, 86% of patients required one session, 11% required two sessions and 3% required three sessions of therapy [46].

Type of Sclerosants

They are classified according to their primary mechanism of action.

1. Detergent sclerosants

These are the most popular in clinical use. Although they are generally safe, they can produce serious allergic reactions, and can also lead to superficial and deep venous thrombosis, thrombophlebitis, pulmonary emboli, tissue necrosis and matting.

(a) Sodium tetradecyl sulphate: due to its potency, it is particularly effective for the treatment of large incompetent and refluxing veins. Dilute concentrations (up to 0.1%) is used for the treatment of spider and reticular

veins. The main disadvantage of using STS is its ability to cause tissue necrosis on extravasation into the skin. This is also dose-dependent.

(b) Polidocanol: it is the most widely used sclerosant worldwide. It has the lowest incidence of extravasation-related tissue necrosis of any detergent. Since it is a local anaesthetic, it does not produce any discomfort if injected peri vascularly.

2. Osmotic sclerosants

Hypertonic saline (HS) is the most used agent. When used in its pure form, there is a complete absence of any allergic reaction. However, it can cause significant tissue necrosis if injected extravascularly. Unlike detergents, the effects of osmotic solutions are confined to small, localised areas. HS is a good substitute for the treatment of telangiectasia in patients with significant allergies, who are not suitable candidates for use of detergent sclerosants.

3. Chemical sclerosants

Glycerine and chromated glycerin fall into this category of sclerosants. Their effects involve both chemical denaturation and detergent effects. They are mainly used for the treatment of telangiectasia. While the efficacy of glycerine is the same as polidocanol, glycerine is more viscous and difficult to inject into tiny veins. It is suggested by some that the incidence of pigmentation with the use of glycerine is less than that produced by other sclerosants.

Foam Sclerotherapy

Detergent foam sclerosants are three or four times more potent than equivalent concentrations of liquid sclerosants.

Advantages of foam:

- Increase in the effective surface area of foam
- Displacement of blood from the treated veins, which produces prolonged undiluted intimal contact
- Increased vasospasm and sclerosis of veins at a distance from the injection site
- Can be used in lower concentrations and lower volumes, with lesser risk of tissue necrosis and allergic reactions.
- More visible on ultrasound imaging

For large veins associated with significant reflux, a combination of foam sclerotherapy, surgical treatment, endovenous laser or radiofrequency ablation may be used in combination to deliver a superior result.

Disadvantage of foam:

- Takes time to prepare
- Deteriorates quickly at room temperature
- Generally, not suitable for the treatment of small reticular veins and telangiectasia.
- Increased incidence of pigmentation and matting
- In patients with patent foramen ovale, it can lead to visual disturbances, amaurosis and stroke. (Use of CO_2 instead of room air for preparing foam may decrease the risk of embolization)
- Recurrent thrombi and thrombophlebitis in the treated vessels may occur for up to 2 months in some patients.

Lorenzo Tessari's Tourbillon technique for producing foam is the most frequently reported in the English literature. Two plastic disposable syringes are connected by a three-way stopcock. The foam is formed by mixing one part of the liquid sclerosant with 4 or 5 parts of air, through 20 passes between the two syringes with the hub at a 30° rotation. This rotation narrows the stopcock passage generating high turbulence, which produces a high-quality micro-foam. Instead of air, CO_2 may be used to produce foam, which ensures more stable foam bubbles, and decreases the incidence of complications due to cerebral embolization of foam (Fig. 9).

Comparison of Foam Sclerotherapy with Endovenous Laser Ablation

A review of randomised controlled trials comparing ultrasound-guided foam sclerotherapy with endothermal ablation for the treatment of great saphenous varicose veins was published by Davies et al. [47]. It was found that although anatomical success appeared higher with endothermal ablation than ultrasound-guided foam sclerotherapy, clinical success and patient-reported outcome measures were similar.

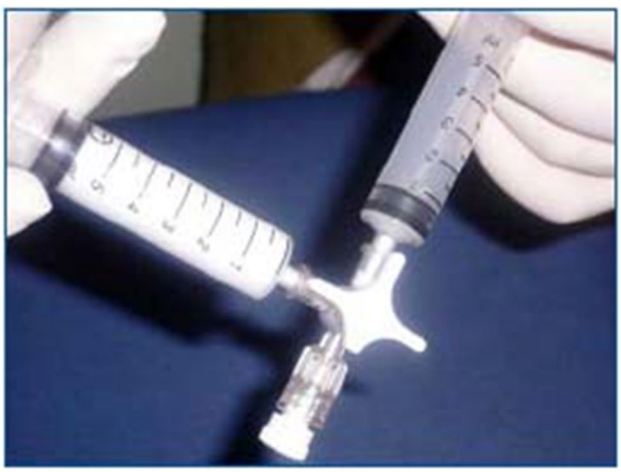

Fig. 9 Tessari's method of producing foam

Morbidity and complication rates were very low and not significantly different between endothermal ablation and ultrasound-guided foam sclerotherapy. Ultrasound-guided foam sclerotherapy was consistently less expensive than endothermal ablation.

Different techniques for treatment with foam sclerotherapy also matter. A randomised controlled trial has been published on comparison between catheter-directed foam sclerotherapy with tumescence of the great saphenous vein versus ultrasound-guided foam sclerotherapy [48]. The conclusion was that catheter-directed foam sclerotherapy with tumescence was better than usual ultrasound-guided foam sclerotherapy as it reached higher full success rate of the treated great saphenous vein and as a lower number of patients required retreatment sessions in the short term. Both methods proved to be safe and improved the quality of life.

Mechano-Chemical Ablation (MOCA)

Newer systems have now been developed for the treatment of varicose veins, which do not need the use of tumescent anaesthesia. One of the first to be introduced was ClariVein. ClariVein is a specialty infusion catheter for the occlusion of incompetent veins in patients with superficial venous reflux. The ClariVein catheter is introduced through a micro-introducer set, placed 2 to 3 cm away from the SFJ or SPF under ultrasound guidance. ClariVein has a rotating tip that agitates and sensitizes the endothelium. Simultaneously, a sclerosant drug is sprayed from the tip of the catheter ensuring precise longitudinal and radial drug delivery, occluding the vein. The 3-French ClariVein catheter is easily identified under vascular imaging and incorporates a cartridge for secure fastening to the motor drive unit (Figs. 10 and 11).

Multiple speed settings allow for rotating tip and dispersion ball to rotate between approximately 2000 and 3500 RPM.

Fig. 10 ClariVein catheter

Fig. 11 Motor drive unit

Non-thermal techniques such as mechanical occlusion chemically assisted endovenous ablation (MOCA) allow treatment of entire trunks with single anaesthetic injections. The early outcomes show similar results at year 1 compared with endothermal ablation [49].

A multicentre randomised controlled trial comparing radiofrequency ablation and mechanico-chemical occlusion of varicose veins using Clarivein has been reported [50]. Patients undergoing local anaesthetic endovenous ablation for primary varicose veins were randomised to either MOCA or RFA. Pain scores using Visual Analogue Scale and number scale (0–10) during truncal ablation were recorded. Patients were reviewed at 1 and 6 months with clinical score quality of life scores and duplex ultrasound assessment of the treated leg. A total of 170 patients were recruited over a 21-month period from 240 screened. It was concluded that pain secondary to truncal ablation is less painful with MOCA than RFA with similar short-term technical, quality of life and safety outcomes.

Cyanoacrylate Glue Therapy for Varicose Veins

In a quest to minimize the invasiveness, non-thermal techniques that do not require tumescent anaesthesia have been developed in the last decade. These new non-thermal, tumescent-less techniques are well tolerated and result in equivalent outcomes compared with endothermal ablations. VenaSeal, one such technique, utilizes a proprietary cyanoacrylate glue to occlude the saphenous vein. Cyanoacrylate glue has long been used in the management of intracranial arteriovenous malformations, pelvic variceal and gastric variceal treatments. VenaSeal, a proprietary cyanoacrylate glue, is an n-butyl cyanoacrylate with unique properties, including quick polymerization upon contact with blood and high viscosity. These properties help prevent embolization.

VenaSeal cyanoacrylate glue is also designed to be pliable and to allow flexion and torsion once solidified.

Indications for using cyanoacrylate glue treatment are no different from the indications for other ablative therapies. However, it is important to discuss procedural outcomes and set appropriate expectations with the patient. In asymptomatic patients with documented reflux, the goal is to improve cosmesis. In symptomatic patients, the goal is to improve symptoms, speed up ulcer healing and reduce recurrence rates. As per the FDA-approved instructions for use document, absolute contraindications include previous hypersensitivity reactions to cyanoacrylate glue or cyanoacrylates, acute superficial thrombophlebitis, thrombophlebitis migrans and the presence of acute sepsis.

The VenaSeal closure system procedure pack is a self-contained sterile, single-patient kit comprised of the cyanoacrylate glue and the cyanoacrylate glue delivery system components, including a glue disperser gun, 5 mL of the cyanoacrylate glue in a small bottle, 5-F delivery catheter, 7-F introducer/dilator, 2 dispenser tips (blunt tip needles), two 3-mL syringes and a 0.035″ J-wire guidewire (Fig. 12).

Technical steps for performing the glue procedure:

1. Identify the most caudad point of reflux in the target vein with ultrasound and administer topical anaesthetic.
2. Access the vein using an ultrasound-guided Seldinger technique, and a micro-puncture needle with a 0.018″ wire.
3. Place a 7-F introducer sheath over the 0.018″ wire and pass a dilator into the introducer sheath.
4. Exchange the 0.018″ wire for a 0.035″ J-wire guidewire, pass a 7-F dilator over the guidewire and use a saline-filled syringe to flush the dilator to prevent backwash of any blood into the dilator.
5. Prime a 5-F introducer catheter with cyanoacrylate glue (described above) and advance the catheter to the saphenofemoral junction. Under ultrasound guidance, position the catheter tip 5.0 cm caudal to the saphenofemoral junction.
6. An ultrasound probe is used to apply pressure 2 to 3 cm cephalad to the tip of the catheter.
7. Make two injections with approximately 0.10 mL cyanoacrylate glue (achieved by squeezing the dispenser gun handle for 3 s); these injections should be given 1 cm apart at this location.
8. Maintain pressure with the ultrasound probe for 3 min.
9. Pull the catheter back 3 cm and inject another 0.10 mL of cyanoacrylate glue.
10. Maintain manual compression 30 s.
11. Continue the procedure every 3 cm with cyanoacrylate glue injection and the 30-s ultrasound probe/manual compression sequences until the entire length of the target vein segment is treated.
12. Remove the sheath and catheter and apply compression at the access site until haemostasis is achieved.
13. Apply an adhesive bandage at the access site.
14. Confirm venous occlusion using duplex ultrasound.

Fig. 12 The venaseal kit

Compression therapy is not needed after the procedure unless concomitant phlebectomy or sclerotherapy are performed.

VenaSeal, a cyanoacrylate glue treatment of incompetent truncal veins, has been demonstrated to be a safe and effective treatment. Other than mild phlebitis episodes and rare reports of allergy that are self-limiting. No serious complications, particularly related to venous thrombosis are reported with this technique, making it an attractive option in patients with other comorbidities. Since there is no dosage limit for the cyanoacrylate glue, unlike other non-thermal non-tumescent treatments, such as sclerotherapy, multiple veins can be treated in the same setting. VenaSeal is also an attractive option in patients with a disproportionately large thigh circumference (compared with the calf), which results in sliding of the postprocedure compression garments. Young and active patients, who do not wish to wear postprocedural compression garments, prefer VenaSeal treatment of multiple veins in a single session. Similarly, patients who fear needle sticks also prefer this treatment.

Studies using VenaSeal have demonstrated high anatomic success rates with closure rates > 90% reported at 3 years. Sustained improvements in patient-reported clinical outcomes have been reported for up to 36 months. No major adverse events or thrombotic complications have been reported with this procedure. Phlebitis and skin reactions are the most common minor adverse events.

Another n-butyl-cyanoacrylate-based polymer with limited modifications, Biolas VariClose, received the CE mark in 2013 and several studies have been reported from Turkey. Due to the limited modification, the glue is less viscous and polymerizes much quicker than VenaSeal, which has the potential disadvantage of distal embolization and adhesion of the catheter tip to the vein wall during the procedure. While VenaSeal is a segmental procedure with aliquots delivered every few centimetres, VariClose requires continuous delivery of the low viscous cyanoacrylate glue. The VariClose studies have also reported a high degree of anatomic success (> 95%) at 12 months. The reported phlebitis rates are lower compared with VenaSeal [51].

A review of randomised studies using cyanoacrylate has revealed the short-term and long-term success of glue in the treatment of varicose veins. Bissacco et al. [52] reviewed 1000 NBCA cases in seven studies (two prospective, four retrospective) and found 96.8% of veins occluded at 12 months [50]. Two studies reported NBCA occlusion beyond the 2-year interval, and these were 94.1% at 30 months and 94.7% at 36 months, respectively [53, 54].

EGIT—endovenous glue-induced thrombosis: thrombus extension into the deep vein, known as endovenous glue-induced thrombosis (EGIT), may be a worrisome complication of the procedure.

A study by Cho et al. [55] in 191 patients demonstrated EGIT in 11 patients (5.8%). Of these 11 patients, 63.6% developed EGIT Grade I and 36.4% patients developed EGIT Grade II. The preoperative saphenous vein diameter of < 5 mm was the only risk factor of significance.

Therefore, while the cyanoacrylate procedure is an otherwise safe procedure, EGIT should be considered as a potential risk factor in all cases considered for CAC procedure, especially in presence of small diameter veins.

In summary, cyanoacrylate glue closure is a simple procedure, with consistent procedural steps. No major adverse events have been noted, although cases of thrombosis have been reported in smaller veins. Minor complications include phlebitis episodes and rare reports of allergies to the cyanoacrylate glue. In the hands of experienced endovenous physicians without prior experience, the procedure resulted in good anatomic and clinical success rates, along with a relatively short learning curve.

CLACS Therapy

CLaCS (cryo-laser and cryo-sclerotherapy) is a treatment for leg vein lesions by combining transdermal laser effect and injection sclerotherapy, all under skin cooling (cryo—cold air blown onto the skin at − 20 °C) [56]. The 1064 wavelength Nd-YAG laser causes a selective photo-thermolysis damaging the vein wall and causing the vein to either collapse completely or significantly decrease its lumen. On a second procedure, a dilute concentration of a sclerosing agent is injected where the vein is still open. This combination allows treatment of veins that could otherwise be treated by phlebectomy or foam sclerotherapy—more invasive options. To improve results, CLaCS can be guided by augmented reality [57].

CLaCS is a technique used for cosmetic purposes, and the use of multimodal methods of treatment, expensive equipment and often multiple treatment sessions make it out of financial reach for most individuals.

Conclusion

The "gold standard" for the treatment of insufficient saphenous veins has been ligation plus stripping for the past 100 years. However, this situation has changed in the last few decades with the introduction of multiple thermal and non-thermal endovenous ablation techniques. These techniques, performed under duplex guidance, are proving to be very effective with high initial and long-term success rates. The effectiveness of current endovenous treatments is excellent (> 90%), side effects are mild and serious complications rare. In an era of health technology assessment and cost-effectiveness analyses, treatment-related costs will become increasingly important, and this will remain a crucial issue in the future.

Data Availability Resource material as quoted and personal views.

Declarations

Consent for Publication The views in the article are of the author himself and rely on published material and personal experience.

Conflict of Interest The authors declare no competing interests.

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