Medical Policy Manual

Varicose Vein Treatment

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based on all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Varicose veins are dilated, tortuous veins that may cause pain or skin ulcers; however, the majority of treatment is done for cosmetic reasons. Invasive treatment may include surgical removal and/or destruction using lasers, heat, or injection of sclerosing solution.

MEDICAL POLICY CRITERIA

NOTES:

- Member contracts for covered services vary. Member contract language takes precedence over medical policy. In addition, when there is a contract denial for treatment of varicose veins, the denial not only includes treatment but also the associated duplex scans (i.e. CPT 93970 or 93971) for treatment planning.

POLICY CRITERIA

- This policy only addresses treatment of the superficial system veins of the lower extremity (e.g., long and short saphenous veins, saphenous tributaries, and associated lower extremity perforator veins) and upper extremity varices including sclerotherapy and vulvar varices.
Embolization, ablation, and sclerotherapy of the ovarian, internal iliac, or gonadal veins for treatment of pelvic congestion syndrome or varicoceles are addressed separately (see Cross References below).

I All of the following **general criteria** (see Policy Guidelines) must be met for varicose vein treatment to be considered for coverage:

**A** At least one or more of the following indications must be documented to be present:

1. Functional impairment, attributed to varicose veins, which limits performance of instrumental activities of daily living (ADL). Instrumental ADL are defined as feeding, bathing, dressing, grooming, meal preparation, household chores, and occupational tasks that are required as a daily part of job functioning. Clinical records **must specifically document** ALL of the following:
   a. The specific instrumental ADL that is impaired; and
   b. A description of how performance of the instrumental ADL is limited

2. Ultrasound documented recurrent attacks of superficial phlebitis.

3. Recurrent or persistent hemorrhage from ruptured varix.

4. Ulceration from venous stasis where incompetent varices are a significant contributing factor.

**B** There is clinical documentation that ongoing medically supervised conservative therapy, including use of compression (minimum 20 mmHg) stockings (or compression wrap when stockings cannot be utilized), has been utilized for a minimum of three months, is currently being utilized, and did not successfully treat the patient’s indication(s) or clinical condition. **Clinical documentation must include all of the following:**

1. History of present illness, physical examination, and conservative therapy treatment plan. **Note:** There are a number of different classification scales for compression stockings; for consistency, this policy requires that units of compression be documented in mmHg.

2. Progress notes from a treating provider of at least 1 office visit after at least 3 months of conservative therapy documenting patient compliance with conservative therapy, including the use of compression (minimum 20 mmHg) stockings, is currently being utilized, and the patient response. For example, compression stockings should be worn daily while the patient is out of bed. *Unna boot or compression wrap* may be utilized in lieu of compression stockings when there is documentation of an open venous stasis ulcer of the leg to be treated.

3. For requests for additional treatment sessions, three months of conservative therapy must have been utilized after the most recent varicose vein procedure, and have not successfully treated the patient’s symptoms.

**C** Incompetence in the superficial system veins (e.g., long and short saphenous veins, perforator veins, and saphenous tributaries) must be supported by
complete venous imaging study documentation obtained no more than 6 months prior to the request for coverage with the diameter of the vein and the reflux in seconds measured at multiple levels in the thigh and calf. Note: for requests for additional treatment sessions after previous varicose vein procedures, additional imaging is not required so long as imaging is submitted that was performed no more than 6 months prior to the current request for coverage. Remeasurement must be done as part of a complete venous study.

D Clear, interpretable photographs are required on any affected areas of the leg, e.g., protruding varicose veins or ulcers and must be consistent with the submitted clinical description

II Procedures

A Ligation/stripping and phlebectomy (i.e., stab, hook, transilluminated powered)

1. Ligation/stripping and phlebectomy of incompetent superficial system veins (including the long and short saphenous veins and saphenous tributaries including accessory saphenous veins) and varicose veins 4 mm or greater in diameter may be considered medically necessary when all of the following criteria are met:

   a. The incompetent superficial veins proximal to the vein to be treated either have been treated or are being treated concurrently.
   
   b. All of Criteria I. (A-D) above are met.
   
   c. For ligation/stripping of the long and short saphenous veins, significant incompetence exceeding 0.5 seconds is demonstrated at the saphenofemoral junction (SFJ) and thigh, or at the saphenopopliteal junction (SPJ) and calf.

2. If criteria II.A.1. above are not met, ligation/stripping or phlebectomy is considered not medically necessary.

B Endovenous ablation

1. Endovenous radiofrequency or laser ablation of incompetent long or short saphenous veins may be considered medically necessary when all of the following are met:

   a. Minimum vein diameters where treatment is requested:

      i. Long saphenous vein diameter 5.5 mm or greater throughout the segment to be ablated, measured via ultrasound at the SFJ (or proximal thigh), mid-thigh, and knee (or above knee); (If below knee ablation requested mid-calf measurement also necessary); or

      ii. Short saphenous vein diameter is 4 mm or greater throughout the segment to be ablated, measured via ultrasound at the SPJ and mid-calf.

   b. Significant incompetence exceeding 0.5 seconds throughout the segment to be ablated, is demonstrated at the SFJ and thigh, or at the SPJ and calf.

   c. Clinical documentation that all incompetent segments of the same
A vein will be treated in the same session.

d. All of Criteria I. (A-D) above are met.

2. If criteria II.B.1. above are not met, endovenous radiofrequency or laser ablation of incompetent long or short saphenous veins is considered **not medically necessary**.

3. Endovenous laser or radiofrequency ablation of the entire incompetent saphenous vein usually can be accomplished in a single treatment session. Multiple separate sessions for ablation of segments of a continuous vein are considered **not medically necessary**. Although additional procedures, including ligation or sclerotherapy, performed in the same treatment session on the same ablated saphenous vein are considered included components of the ablation procedure, procedures on other saphenous venous systems may be distinct procedural services.

4. Endovenous laser or radiofrequency ablation is considered **investigational** for all of the following:

   a. Cryoablation of any vein

   b. Radiofrequency or laser ablation of veins other than the long or short saphenous veins, including but not limited to the following:

      i. accessory saphenous veins

      ii. branch tributaries

      iii. varicose veins

      iv. perforator veins

   c. Ablation of saphenous and other veins (i.e., vulvar varices)

   d. Mechanochemical ablation of any vein

   e. Microwave ablation of any vein

   f. Steam injection ablation of any vein

**C Sclerotherapy**

1. Sclerotherapy (liquid, foam, or microfoam) of the following superficial system veins, short saphenous vein, and saphenous tributaries including accessory saphenous veins, and varicose veins 4 mm or greater in diameter may be considered **medically necessary** when both of the following criteria are met:

   a. If related superficial system veins proximal to the incompetent vein to be treated are incompetent, those incompetent proximal veins either have been treated or are being treated concurrently

   b. All of Criteria I. (A-D) above are met.

2. If criteria II.C.1. above are not met, sclerotherapy is considered **not medically necessary**.

3. Ultrasound guidance (see Policy Guidelines) for liquid, foam, or microfoam sclerotherapy of varicose veins **other than** the following superficial system veins...
veins; the short saphenous vein and saphenous tributaries including accessory saphenous veins is considered **not medically necessary**.

4. Sclerotherapy is considered **investigational** for the following:
   a. Vulvar, including labial and buttock varices
   b. Upper extremity varices
   c. The long saphenous vein
   d. The perforator veins

5. Sclerotherapy of small (less than 4 mm in diameter) superficial reticular veins and/or telangiectasias (spider veins) is considered **cosmetic**.

### III Treatment sessions (see Policy Guidelines): the medical necessity of each treatment session must be established. Subject to other applicable criteria, treatment sessions may be considered **medically necessary** when one of the following criteria are met (A, B or C):

   A Initial treatment, single session; OR
   B Initial treatment including endovenous ablation: either a single bilateral session or two treatment sessions (a separate session for each of the right and left legs); OR
   C Subsequent treatment when the clinical outcome of prior treatment(s) during three months subsequent to prior treatment(s) has been established and documented and criteria I.A.-D. are met in addition to either criteria 1. or 2. below:
   1. Single session; or
   2. For subsequent treatment including bilateral endovenous ablation, either a single bilateral session or two treatment sessions (a separate session for each of the right and left legs).

### IV If Criteria I. A-D above are not met, varicose vein treatment is considered **not medically necessary**.

### V Follow-up venous studies performed within 6 months following the most recent ipsilateral treatment, in the absence of complications, are considered **not medically necessary**, including but not limited to routine confirmation studies following endovenous ablation.

### VI Use of endovenous glue/adhesive (e.g. cyanoacrylate adhesives) is considered **investigational** for all indications.

**NOTE:** A summary of the supporting rationale for the policy criteria is at the end of the policy.

**POLICY GUIDELINES**

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History of present illness, physical examination, and impact on activities of daily living (ADL) (including the specific ADL) impaired, how it impacts performance, and what is done to alleviate it)
- Complete duplex studies including vein names with measurements of seconds of reflux and average vein diameters. A complete venous study includes a minimum of the following:
  - Deep veins: common femoral, mid-femoral, and popliteal
  - Long saphenous vein: SFJ, mid-thigh, knee, and mid-calf
  - Short saphenous vein: SPJ, and mid-calf
  - Perforators: site with seconds of reflux and diameters
  - Branch tributaries: site with seconds of reflux and diameters
  - Varicose veins (varices): diameters
- Photos (clear and interpretable quality)
- Conservative therapy treatment plan (including units of compression stocking strength documented in mmHg)
- Results of monitoring conservative therapy, including documentation of medical supervision and timeframe of conservative therapy
- Procedures requested:
  - Specific veins to be treated
  - Number of treatment session(s) being requested
  - If bilateral endovenous ablation is requested, document whether a bilateral or two unilateral sessions are being requested
  - Specify the veins to be treated in each session
  - For ablations, specify how all incompetent segments of the same vein are to be treated

**Treatment Sessions**

Each treatment session should address as much abnormality as is appropriate and reasonable and may include more than one vein and/or modality.

**CROSS REFERENCES**

1. [Cosmetic and Reconstructive Surgery](#), Surgery, Policy No. 12
2. [Ovarian Internal Iliac, and Gonadal Vein Embolization as a Treatment of Pelvic Congestion Syndrome](#), Surgery, Policy No. 147

**BACKGROUND**

The venous system of the lower extremities consists of the superficial system (e.g., long and short saphenous veins and accessory or tributary veins that travel in parallel with the long and short saphenous veins) and the deep system (e.g., popliteal and femoral veins). These two parallel systems are interconnected via perforator veins and at the saphenofemoral and the saphenopopliteal junctions.

**Note:** The long and short saphenous veins are also known as the great or greater and the small or lesser saphenous veins, respectively. This policy uses the nomenclature long saphenous vein and short saphenous vein as these terms are consistent with current CPT nomenclature.

One-way valves are present within all veins to direct the return of blood up the lower limb. Larger varicose veins, many protruding above the surface of the skin, typically are related to valve incompetence. As the venous pressure in the deep system is generally greater than that of the superficial system, valve incompetence leads to increased hydrostatic pressure.
transmitted to the unsupported superficial vein system. Backflow (venous reflux) with pooling of blood ultimately results in varicosities. In addition, clusters of varicosities may appear related to incompetent perforating veins, such as Hunter and Dodd, located in the mid- and distal thigh, respectively and/or associated with incompetence at the saphenofemoral junction. In some instances, the valvular incompetence may be isolated to a perforator vein, such as the Boyd perforating vein located in the anteromedial calf. These varicosities are often not associated with saphenous vein incompetence since the perforating veins in the lower part of the leg do not communicate directly with the saphenous vein.

Although many varicose veins are asymptomatic, when present, symptoms include itching, burning, heaviness, fatigue, and pain. In addition, chronic venous insufficiency secondary to venous reflux can lead to peripheral edema, hemorrhage, thrombophlebitis, venous ulceration, and chronic skin changes. In an effort to improve the consistency in diagnosing chronic venous disorders, particularly for patient selection in clinical trials, an international consensus committee developed CEAP classification.[1] In this system, classification is based on clinical manifestations (C), etiology (E), anatomical distribution (A), and underlying pathophysiology (P). (See Appendix 1)

Note: The term "varicose veins" does not apply to the telangiectatic dermal veins, which may be described as "spider veins" or "broken blood vessels." While abnormal in appearance, these veins typically are not associated with any symptoms, such as pain or heaviness, and their treatment is considered cosmetic.

TREATMENT OF SUPERFICIAL VARICOSE VEINS

Conservative Therapy

Treatment of venous reflux/venous insufficiency is aimed at reducing abnormal pressure transmission from the deep to the superficial veins. Varicose veins can usually be treated with non-surgical measures. Symptoms often decrease when the legs are elevated periodically, when prolonged standing is avoided, and when elastic compression stockings are worn.

Operative Therapy

If conservative treatment measures fail, additional treatment options typically focus first on identifying and correcting the site of reflux, and second on redirecting venous flow through veins with intact valves. Thus conventional surgical treatment of varicosities is based on the following three principles:

- Control of the most proximal point of reflux, typically at the saphenofemoral junction, as identified by preoperative Doppler ultrasonography. Surgical ligation and division of the saphenofemoral or saphenopopliteal junction is performed to treat the valvular incompetence.

- Removal or occlusion by ablation of the refluxing long and/or short saphenous vein from the circulation. The classic strategy for isolation is vein stripping in conjunction with vein ligation and division.

- Removal or occlusion of the refluxing varicose tributaries. Strategies for removal include phlebectomy (i.e., ligation/division/stripping, powered phlebectomy, or stab avulsion) or occlusion by injection sclerotherapy; either at the time of the initial treatment, or subsequently. Over the years various different minimally invasive alternatives to ligation...
and stripping have been investigated, including sclerotherapy and thermal ablation using radiofrequency energy (high frequency radiowaves), laser energy, or cryoablation (also called cryotherapy).

**Endovenous Ablation**

The objective of endovenous ablation techniques is to cause injury to the vessel, causing retraction and subsequent fibrotic occlusion of the vein.

**Thermal Ablation**

Three endovenous thermal ablation techniques have been investigated as minimally invasive alternatives to vein ligation and stripping.

- **Radiofrequency (RF) ablation** is performed by means of a specially designed catheter inserted through a small incision in the distal medial thigh to within 1-2 cm of the saphenofemoral junction. High frequency radio waves (200-300 kHz) are delivered through the catheter electrode and cause direct heating of the vessel wall, causing the vein to collapse. The catheter is slowly withdrawn, closing the vein.

- **Laser ablation** is performed similarly; a laser fiber is introduced into the saphenous vein under ultrasound guidance; the laser is activated and slowly removed along the course of the saphenous vein. Laser ablation may be referred to as endovenous laser ablation (EVLA) or endovenous laser treatment (EVLT).

- **Cryoablation** uses extreme cold to cause injury to the vessel. Technical developments since thermal ablation procedures were initially introduced include the use of perivenous tumescent anesthesia which allows treatment of veins larger than 12 mm in diameter and helps to protect adjacent tissue from thermal damage during treatment of the lesser saphenous vein.

- **There are two technologies that are not available in the United States:**
  - **Microwave ablation** is performed via endovenous catheter using microwave energy to heat the vessel walls.
  - **Steam ablation** is catheter-based endovenous thermal ablation that uses high pressure pulses of steam to heat the vein to 120°C.

**Mechanochemical Ablation**

Endovenous mechanochemical ablation (MOCA) utilizes both sclerotherapy and mechanical damage to the lumen. Following ultrasound imaging, a disposable catheter with a motor drive is inserted into the distal end of the target vein and advanced to the saphenofemoral junction. As the catheter is pulled back, a wire rotates at 3500 rpm within the lumen of the vein, abrading the lumen. At the same time, a liquid sclerosant (sodium tetradecyl sulphate) is infused near the rotating wire. It is proposed that mechanical ablation allows for better efficacy of the sclerosant, without the need for the tumescent anesthesia used in thermal ablation.

**Cyanoacrylate Adhesive**

Cyanoacrylate adhesive is a clear, free-flowing liqueat that polymerizes in the vessel via an anionic mechanism (i.e. polymerizes into a solid material upon contact with body fluids or
tissues). The adhesive is gradually injected along the length of the vein in conjunction with ultrasound and manual compression. The acute coaptation halts blood flow through the vein until the implanted adhesive becomes fibrotically encapsulated and establishes chronic occlusion of the treated vein. Cyanoacrylate glue has been used as a surgical adhesive and sealant for a variety of indications, including gastrointestinal bleeding, embolization of brain arteriovenous malformations, and to seal surgical incisions or other skin wounds.

**Sclerotherapy**

The objective of sclerotherapy is to destroy the endothelium of the target vessel by injecting an irritant solution (either a detergent, osmotic solution, or a chemical irritant), ultimately resulting in the complete obliteration of the vessel. The success of the treatment depends on accurate injection of the vessel, an adequate injectant volume and concentration of sclerosant, and post-procedure compression. Compression theoretically results in direct apposition of the treated vein walls to provide more effective fibrosis and may decrease the extent of the thrombosis formation.

Sclerotherapy is an accepted and effective treatment of telangiectatic vessels. Historically, larger veins and very tortuous veins were not considered to be good candidates for sclerotherapy. Technical improvements in sclerotherapy, including the routine use of Duplex ultrasound to target refluxing vessels, luminal compression of the vein with anesthetics, and foam sclerosant in place of liquid sclerosant, have improved its effectiveness in these veins. Other concerns have arisen with these expanded uses of sclerotherapy. For example, use of sclerotherapy in the treatment of varicose tributaries without prior ligation, with or without vein stripping creates issues regarding its effectiveness in the absence of the control of the point of reflux and isolation of the refluxing saphenous vein. Sclerotherapy of the long saphenous vein raises issues regarding appropriate volume and concentration of the sclerosant and the ability to provide adequate post-procedure compression. Moreover, the use of sclerotherapy, as opposed to the physical removal of the vein with stripping, raises the issue of recurrence due to recanalization.

**TREATMENT OF PERFORATOR VEINS**

Perforator veins cross through the fascia and connect the deep and superficial venous systems. Incompetent perforating veins were originally addressed with an open surgical procedure, called the Linton procedure, which involved a long medial calf incision to expose all posterior, medial, and paramedial perforators. While this procedure was associated with healing of ulcers, it was largely abandoned due to a high incidence of wound complications. The Linton procedure was subsequently modified by using a series of perpendicular skin flaps instead of a longitudinal skin flap to provide access to incompetent perforator veins in the lower part of the leg. The modified Linton procedure may be occasionally utilized for the closure of incompetent perforator veins that cannot be reached by less invasive procedures. Subfascial endoscopic perforator surgery (SEPS) is a less-invasive surgical procedure for treatment of incompetent perforators and has been reported since the mid-1980s. Guided by Duplex ultrasound scanning, small incisions are made in the skin and the perforating veins are clipped or divided by endoscopic scissors. The operation can be performed as an outpatient procedure. Endovenous ablation of incompetent perforator veins with sclerotherapy and radiofrequency has also been reported.

**OTHER**
Deep vein valve repair or reconstruction and replacement are being investigated.
Venous “glue” or “superglue” is not cleared for use in the United States. This is an adhesive delivered via endovenous catheter as a method for sealing the vein.

**REGULATORY STATUS**

The following devices have received specific U.S. Food and Drug Administration (FDA) marketing clearance for the endovenous treatment of superficial vein reflux:

- **The VenaSeal™ (Medtronic) Closure System** was FDA approved in 2015. The system includes a liquid adhesive, catheter, guidewire, dispenser gun and tips, and syringes. The clear liquid adhesive, cyanoacrylate adhesive, is injected into the diseased vein and polymerizes into a solid material to permanently seal the vein.

- **The CERMAVEIN Steam Vein Sclerosis (SVS™) system** is being studied outside of the United States but does **not** have FDA approval or clearance for marketing.

- **The ClariVein® Infusion Catheter (Vascular Insights)** received marketing clearance through the 510(k) process in 2008 (K071468). It is used for mechanochemical ablation. Predicate devices were listed as the Trellis® Infusion System (K013635) and the Slip-Cath® Infusion Catheter (K882796). The system includes an infusion catheter, motor drive, stopcock and syringe and is intended for the infusion of physician-specific agents in the peripheral vasculature.

- **Polidocanol** is an injectable sclerosing agent that may be used for intravenous treatment of varicose veins.
  - **Varithena® (Biocompatibles, Inc, a BTG group company), formerly Varisolve®,** is a polidocanol sclerosant microfoam made with a proprietary gas mix that is dispersed from a canister with a controlled density and more consistent bubble size. FDA approval in 2013 was for the treatment of incompetent great saphenous veins, accessory saphenous veins, and visible varicosities of the great saphenous vein system above and below the knee.
  - **In 2010, Asclera® (Merz North America, Inc)** is an injectable solution with FDA approval for the treatment of uncomplicated spider veins (varicose veins ≤ 1mm in diameter) and reticular veins (varicose veins 1-3 mm in diameter) in the lower extremities.

- **A modified Erbe Erbokryo® cryosurgical unit (Erbe USA) received FDA clearance for marketing in 2005.** A variety of clinical indications are listed, including cryostripping of varicose veins of the lower limbs.

- **The Trivex system** is a device for transilluminated powered phlebectomy that received FDA clearance through the 510(k) process in October 2003. According to the label, the intended use is for “ambulatory phlebectomy procedures for the resection and ablation of varicose veins.”

- **In 2002, the Diomed 810 nm surgical laser and EVLT ™ (endovenous laser therapy) procedure kit** received FDA clearance through the 510(k) process, "... for use in the
endovascular coagulation of the greater saphenous vein of the thigh in patients with superficial vein reflux."

- In 1999, the VNUS® Closure™ system (a radiofrequency device) received FDA clearance through the 510(k) process for "endovascular coagulation of blood vessels in patients with superficial vein reflux." The VNUS RFS and RFSFlex devices received FDA clearance in 2005 for “use in vessel and tissue coagulation including: treatment of incompetent (i.e., refluxing) perforator and tributary veins. The modified VNUS® ClosureFAST™ Intravascular Catheter received FDA clearance through the 510(k) process in 2008.

### EVIDENCE SUMMARY

Outcomes of interest for venous interventions include symptom control, healing and recurrence, recannulation of the vein, and neovascularization. Recannulation (recanalization) is the restoration of the lumen of a vein after it has been occluded; this occurs more frequently following treatment with endovenous techniques. Neovascularization is the proliferation of new blood vessels in tissue, and occurs more frequently following vein stripping. Direct comparisons of durability for endovenous and surgical procedures are complicated by these different mechanisms of recurrence. Relevant safety outcomes include the incidence of paresthesia, thermal skin injury, thrombus formation, thrombophlebitis, wound infection, and transient neurologic effects.

### ENDOVENOUS ABLATION

Endovenous ablation of varicose veins has been proposed as an alternative to ligation and/or stripping. Outcomes of interest include short and long term functional improvement and recurrence rates related either to recannulization of the saphenous vein or neovascularization. In terms of safety, relevant outcomes include the incidence of paresthesias, thermal skin or nerve injuries, thrombus formation, thrombophlebitis, and wound infection.

#### Vein Diameter

There is currently no standardized range for saphenous vein diameter most likely to be associated with severe symptoms or for which endovenous ablation is recommended. In studies of the correlation between long saphenous vein diameter and the presence or absence of reflux, the best cutoff measurement to predict reflux varied between studies from 5.05 mm to 7.3 mm.[2-5] Sensitivity and specificity ranged from 76% to 87% and 60% to 87%, respectively. It is important to note that there is heterogeneity among the populations included in the studies. In addition, there was heterogeneity between studies in measurement techniques (e.g., location, position).

#### Laser Ablation Compared to Radiofrequency Ablation

He (2017) conducted a systematic review which evaluated the effectiveness and safety of endovenous laser ablation compared to radiofrequency ablation for the treatment of varicose veins.[6] The systematic review included a total of 12 studies (N=1,577) (10 RCTs and 2 nonrandomized studies). The meta-analysis of the combined studies concluded that there were no significant differences in effectiveness and safety outcomes between the two groups.
An additional study by Woźniak (2016) also evaluated laser ablation compared to radiofrequency ablation. The study included 510 adults with five year follow-up and reported similar conclusions to He (2017) summarized above.

**Laser Ablation and Radiofrequency Ablation Compared to Ligation and Stripping**

**Systematic Reviews**

A number of systematic reviews of randomized controlled trials (RCTs) comparing various types of ablation to surgical treatment have been published. These review consistently reported moderate quality of evidence. Most of the reviews compared endovenous laser ablation (EVLA), radiofrequency ablation (RFA), and surgical treatment of varicose veins. Overall, these techniques had similar, statistically significant improvement in function and in pain relief compared to preoperative scores. RFA and EVLA had low rates of technical procedure failure rates, and short-term recannulization rates. Adverse effects were generally minor for all techniques. Though intraoperative pain was not reported, EVLA consistently resulted in significantly greater pain and bruising when compared to RFA for one to two weeks following the procedure. RFA had significantly more occurrences of superficial phlebitis. Recanalization was similar for EVLA and RFA at one-year follow-up.

The primary limitation of the current evidence is the lack of long-term data on recanalization rates for ablation techniques and neovascularization rates for ligation and stripping. In addition, many of the available studies used first-generation technology and, therefore, do not provide data on newer devices. For example, newer laser technology may result in decreased pain during and after the procedure. Newer RFA technology (e.g., ClosureFast RF catheter) may result in higher rates of vein occlusion.

The most recent systematic review is an updated Cochrane review from 2014, which compared RFA, EVLA, and foam sclerotherapy versus ligation/stripping for saphenous vein varices. Included in the review were 13 randomized studies with a combined total of 3081 patients. The overall quality of the evidence was moderate. For EVLA versus surgery, there were no significant differences between the treatment groups for clinician noted or symptomatic recurrence, or for recanalization. Neovascularization and technical failure were reduced in the laser group (OR=0.05, p<0.001; and OR=0.29, p<0.001, respectively). For RFA versus surgery, there were no significant differences between the groups in clinician noted recurrence, recanalization, neovascularization, or technical failure. The authors concluded that sclerotherapy, EVLA, and RFA were at least as effective as surgery in the treatment of long saphenous vein varicose veins.

**Radiofrequency Ablation of Varicose Veins**

**Systematic Reviews**

In 2016, Boersma et al. published results from a systematic review and meta-analysis that compared the anatomical success rates and complication rates of six treatment modalities for small saphenous vein incompetence: surgery, endovenous laser ablation (EVLA), radiofrequency ablation (RFA), ultrasound-guided foam sclerotherapy (UGFS), steam ablation, and mechanochemical endovenous ablation (MOCA). Although the review included 49 articles (five RCTs and 44 cohort studies), nine were specific to RFA and were cohort studies. The pooled anatomical success rate for RFA in 386 incompetent small saphenous veins was 97.1% (95% CI 94.3% to 99.9%). RFA had a relatively low neurological complication rate.
(mean 9.7%) when compared to the overall neurological complication rate (mean 19.6%) of the six treatment modalities.

In 2012, a systematic review of RCTs and meta-analysis was published that compared the clinical outcomes of endovenous laser ablation (EVLA), radiofrequency ablation (RFA). The review included 28 RCTs and reported no significant difference in primary failure and clinical recurrence with EVLA and RFA compared with surgery. The advantages of the endovenous ablation techniques over surgery were a lower rate of wound infections and hematoma, and a shorter recovery period.

**Randomized Controlled Trials (RCTs)**

No new RCTs on RFA of varicose veins have been published since the systematic review.

**Nonrandomized Trials**

Several case series have reported on endoluminal radiofrequency ablation. The largest was reported by Merchant and colleagues, who analyzed the four-year data collected in the ongoing Closure Study Group registry focusing on the treatment of reflux of the long saphenous vein. Data were available on 890 patients and 1,078 limbs treated at 32 centers. Clinical and duplex ultrasound follow-up was performed at one-week, six-months, and yearly for four-years. The vein occlusion rates were 91% at one week and 88.8% at four-years, although only 98 limbs had been followed up to the four-year mark. These results suggest that radiofrequency ablation results in durable occlusion. Radiofrequency ablation has typically been limited to vessels less than 12 mm in diameter. The rationale behind this patient selection criterion is that the electrodes must remain in direct contact with the vein wall during treatment and the largest diameter of the deployed radiofrequency electrodes is 12 mm. The authors noted that exsanguinations, perivenous tumescent infiltration, and external compression may promote electrode and vessel wall contact such that larger veins can be treated. However, in this large case series, there were only 58 limbs with vein sizes larger than 12 mm, and only 29 available for follow-up at six-months or one-year. While the occlusion rate was similar to that seen in smaller vessels, long-term data are inadequate to determine if this effect is durable.

In 2005, Merchant and Pichot also reported the 5-year Closure Study Group registry data. There were 1222 limbs in 1006 patients treated at 34 centers with radiofrequency ablation of various levels of the long saphenous vein, the short saphenous vein, and the accessory saphenous vein. At five-year follow-up using duplex ultrasound examination, 185 limbs were considered failures due to nonocclusion (12.4%), recanalization of a previously occluded vein (69.7%), or groin reflux of a vein with occluded trunk (17.8%). In the latter group, the groin reflux often involved an accessory vein. Logistic regression analysis of risk factors of gender, age, body mass index [BMI], vein diameter, and catheter pullback speed showed that each unit increase in BMI over 25 was associated with increasing risk of long-term failure. In addition, a catheter pull-back speed over the standard speed of 3 cm/min was associated with failure to occlude or recanalization. The authors pointed out that this anatomical failure did not necessarily result in clinical failure; most patients experienced initial symptom relief that was maintained over 5 years.

**Laser Ablation of Varicose Veins**

**Systematic Reviews**
In 2016 Boersma et al. published results from a systematic review and meta-analysis that compared the anatomical success rates and complication rates of six treatment modalities for small saphenous vein incompetence, as discussed above. The review included 28 articles specific to EVLA, and included both RCT’s and cohort studies. The pooled anatomical success rate for EVLA in 2,950 incompetent small saphenous veins was 98.5% (95% CI 97.7% to 99.2%). EVLA had a low neurological complication rate (mean 4.8%) when compared to the overall neurological complication rate (mean 19.6%) of the six treatment modalities. The authors concluded that EVLA should be a preferred treatment in small saphenous vein incompetence.

A systematic review of endovenous laser ablation (EVLA) versus surgery was published in 2009. Fifty-nine studies were included, with seven studies that directly compared EVLA and surgery. Randomized and nonrandomized studies directly comparing outcomes for EVLA or surgery were included for the assessment of safety or effectiveness, while case series with a minimum patient population of 100 were included for the assessment of safety alone. For all studies, it was calculated that 5,759 patients (6,702 limbs) were treated with EVLA and 6,395 patients (7,727 limbs) underwent surgery. Few differences were apparent between treatments with respect to clinical effectiveness outcomes, although long-term follow-up was lacking. Nonclinical effectiveness outcomes generally favored EVLA over surgery in the first two months after treatment. The authors concluded that while EVLA offers short-term benefits and appears to be as clinically effective as surgery up to 12 months after treatment, clinical trials with a minimum of three years of follow-up are required to establish the enduring effectiveness of EVLA.

Similarly, the 2012 systematic review with meta-analysis summarized above under radiofrequency ablation also reported no significant difference in primary failure and clinical recurrence with EVLA compared with surgery.

Randomized Controlled Trials

The following RCTs on EVLA of the long saphenous vein were published since the systematic reviews summarized above:

In 2015, van der Velden et al. published results from a five-year follow-up comparing conventional surgery, endovenous laser ablation, and ultrasound-guided foam sclerotherapy in patients with great saphenous varicose veins. A total of 224 legs were included (69 conventional surgery, 78 EVLA, and 77 UGFS), and 193 were evaluated at final follow up (86.2%). At the five year follow-up, the Kaplan-Meier analysis showed obliteration or absence of the great saphenous vein in 85% of patients who underwent conventional surgery and 77% of patients who underwent EVLA (not significantly different). Grade I neovascularization was higher in the conventional surgery group (27% vs 3%, p<0.001), while grade II neovascularization was similar in the two groups (17% vs 13%).

In 2014, Brittenden et al. reported a multicenter randomized trial that compared foam sclerotherapy, EVLA, and surgical treatment in 798 patients. The study was funded by U.K.’s Health Technology Assessment Programme of the National Institute for Health Research. Veins greater than 15 mm were excluded from the study. At the six week follow-up visit, patients who were assigned to treatment with foam or laser had the option of treatment with foam for any residual varicosities; this was performed in 38% of patients in the foam group and 31% of patients in the EVLA group. Six months after treatment, mean disease-specific quality of life was slightly worse after sclerotherapy than after surgery (p=0.006), and
there were more residual varicose veins, although the differences were small. Disease-specific quality of life was similar for the laser and surgery groups. The frequency of procedural complications was similar for the foam sclerotherapy (6%) and surgery (7%) groups, but was lower in the laser group (1%). The rate of complications at 6 months (primarily lumpiness and skin staining), was highest for the sclerotherapy group.

In 2013, Biemans et al. published results from the MAGNA trial, which randomized 223 consecutive patients (240 legs) with long saphenous vein reflux to EVLA, ligation and stripping, or physician compounded foam sclerotherapy (1 ml aethoxysclerol 3#: 3ml air).[20] At one-year follow-up, the anatomic success rates were similar between EVLA and stripping (88.5% and 88.2%, respectively), which were superior to foam sclerotherapy (72.2%). Ten percent of the stripping group showed neovascularization. Health-related quality of life improved in all groups. The CEAP classification improved in all groups with no significant difference between the groups. Transient adverse events were reported in 11 patients after stripping, seven after EVLA, and five after sclerotherapy.

The ongoing, and largest randomized study on EVLA, comparing endovenous laser ablation with costectomy and stripping of the great saphenous vein (RELACS), schedule to follow patients for five years, randomized 400 patients to EVLA performed by a surgeon at one site or to ligation and stripping performed by a different surgeon at a second location.[21] Fifty-four patients withdrew from the study after receiving the randomization result (from an independent site), due primarily to preference for the other treatment. At the two year follow-up there was no significant difference between the groups for clinically recurrent varicose veins, medical condition on the Homburg Varicose Vein Severity Score, or disease-related quality of life. Saphenofemoral reflux was detected by ultrasonography more frequently after EVLA (17.8% vs 1.3%). At 5-year follow-up, Kaplan-Meier analysis showed obliteration or absence of the great saphenous vein in 85% of patients who underwent conventional surgery and 77% of patients who underwent EVLA (not significantly different). 15 Grade I neovascularization was higher in the conventional surgery group (27% vs 3%, p<0.001), while grade II neovascularization was similar in the 2 groups (17% vs 13%).

In 2012 Rasmussen et al. reported the five year follow-up data comparing EVLA (n=121) with ligation and stripping (n=68).[22] Data was available on 98% of the patients. There was no significant difference between the two groups for clinical recurrence (EVLA 36%, stripping 35%) or in the percentage of reoperations (EVLA 38.6%, stripping 37.7%).

Literature on isolated treatment of the anterior accessory saphenous vein is limited. In a 2009 study, outcomes from a cohort of 33 patients who underwent EVLA of the anterior accessory saphenous vein were compared with 33 matched controls undergoing EVLA of the greater saphenous vein.[23] In 21 of the patients (64%) in the accessory saphenous vein group there had been no previous treatment of the greater saphenous vein. At 12-month follow-up there was no evidence of reflux in these patients, and the treated accessory saphenous vein was not visible with ultrasound. The Aberdeen Varicose Vein Symptom Severity Score had improved in both groups, with no significant difference between the two groups. Patient satisfaction scores were also similar.

Nonrandomized Trials

The bulk of the clinical trials on laser ablation of varicose veins are case series[24-28] and registry data[15]. Using historical controls for comparison is difficult since treatment outcomes are variably reported. There are no consistent definitions of success versus failure, either
based on patient or clinical assessment. In general, recurrence rates after ligation and stripping are estimated at around 20%. Doppler or Duplex ultrasound are perhaps the most objective form of assessment of recurrence, but many of the reports of the long term outcomes of ligation and stripping did not use ultrasound studies for postoperative assessment. Only two studies have reported objective results of ligation and stripping at 12 and 24 months. Jones and colleagues reported on the results of a study that randomized 100 patients with varicose veins to undergo either ligation alone or ligation in conjunction with stripping.[29] The results of the ligation and stripping group are relevant to this discussion. At one year, reflux was detected in 9% of patients, rising to 26% at two years. Rutgers and Kitslaar reported on the results of a trial that randomized 181 limbs to undergo either ligation and stripping or ligation combined with sclerotherapy.[30] At two years, Doppler ultrasound demonstrated reflux in approximately 10% of patients, increasing to 15% at three years. Therefore, based on this crude assessment, the reflux rate of 13% for radiofrequency ablation at one year[31] and 6% for laser ablation at two years[24] is roughly comparable to the reflux rate of 9-10% reported by Jones et al and Rutgers and Kitslaar.

**Cryoablation**[32]

Disselhoff and colleagues reported two and five year outcomes from a randomized trial that compared cryostripping with EVLA.[33,34] One hundred and twenty patients were included with symptomatic uncomplicated varicose veins (CEAP C2) with saphenofemoral incompetence and greater saphenous vein reflux. At 10 days after treatment, EVLA had better results than cryostripping with respect to pain score over the first 10 days (2.9 vs. 4.4), resumption of normal activity (75% vs. 45%) and induration (15% vs. 52%). At the two year follow-up, freedom from recurrent incompetence was observed in 77% of patients after EVLA and 66% of patients after cryostripping (not significantly different). At five years, 36.7% of patients were lost to follow-up; freedom from incompetence and neovascularization was found in 62% of patients treated with EVLA and 51% of patients treated with cryostripping (not significantly different). Neovascularization was more common after cryostripping, but incompetent tributaries were more common after EVLA. There was no significant difference between groups in the Venous Clinical Severity Score or Aberdeen Varicose Vein Severity Score at either two or five years.

Klem and colleagues published results from a randomized trial in 2009 that found endovenous cryoablation (n=249) to be inferior to conventional stripping (n=245) for treating patients with symptomatic varicose veins.[35] The percentage of patients with greater saphenous vein remaining was 44% in the endovenous cryoablation group and 15% in the conventional stripping group. The Aberdeen Varicose Vein Questionnaire also showed better results for conventional stripping (score of 11.7) in comparison with cryoablation (score of 8.0). There were no differences between the groups in SF-36 subscores, and neural damage was the same (12%) in both groups.

**Cyanoacrylate Ablation**

Bozkurt (2016) conducted a one year prospective comparative study (n=310) evaluating cyanoacrylate glue compared to endovenous laser ablation for venous insufficiency.[36] The authors concluded that periprocedural pain, ecchymosis, permanent paresthesia were less in the cyanoacrylate ablation group. There were no significant differences in closure rates at 12 months follow-up. In addition, there were no significant differences in severity scores nor the
Aberdeen Varicose Vein Questionnaire. Additional studies are needed to evaluate the effectiveness and safety of this technique.

**Mechanochemical Ablation**

**Systematic Review**

In 2016 Boersma et al. published results from a systematic review and meta-analysis that compared the anatomical success rates and complication rates of six treatment modalities for small saphenous vein incompetence, as discussed above. The review included just one study on mechanochemical ablation (MOCA), and although the authors reported an anatomical success rate of 94%, more research is needed to determine these effects.

**Randomized Controlled Trials**

In 2014, Bootun et al. published early one month results from an ongoing study comparing 119 patients randomized to mechanochemical ablation (MCA) (n=60) or RFA (n=59). The maximum and average pain scores were significantly lower during MCA compared to RFA (p<0.001). At one month follow-up, both groups showed complete or proximal occlusion rates of 92%, though data were available for only 67% of participants. These preliminary outcomes do not permit conclusions due to methodological limitations including the short-term follow-up and incomplete data. The authors noted that data from longer follow-up is being collected.

**Nonrandomized Studies**

The remainder of the evidence on MCA of varicose veins is limited to nonrandomized series and cohort studies. In the only comparative study, van Eekeren and colleagues compared postoperative pain and early quality of life in 68 patients treated with either RFA or MCA of great saphenous veins. Patients who did not want to be treated with MCA were offered treatment with RFA; this study design could potentially lead to selection bias. There was no significant between-group difference in procedure-related pain. Compared with RFA, patients treated with MCA had a 14.3 mm reduction in pain measured on a 100 mm visual analog scale (VAS) measured over the first 3 postoperative days (6.2 vs. 20.5) and a 13.8 mm reduction in pain (4.8 vs. 18.6 mm; p<.001) over the first two weeks. MCA patients treated also had a significantly earlier return to normal activities (1.2 vs. 2.4 days) and return to work (3.3 vs. 5.6 days; p=.02). There was a similar improvement in quality of life for the two groups when measured at six weeks. Longer studies are required to determine the durability of these effects.

**Microwave Ablation**

This technique has not been approved or cleared for marketing by the FDA. Two clinical trial reports were found. The first, a preliminary randomized trial, compared endovenous microwave ablation (EMA) with high ligation and stripping (HLS). At 24-months follow-up, there was no significant difference in outcomes between the two groups. The second, a retrospective comparison between laser (n=163 limbs in 138 patients) and microwave (n=143 limbs in 121 patients) ablation of the greater saphenous vein, found significantly lower ecchymosis, skin burn, and paresthesia in the laser ablation. However, the recanalization rate was significantly higher in the laser ablation group at one week and six months postoperatively (p<0.01). Loss to follow-up at 24-months was about 19% in each group.

**Steam Ablation**
This technique has not been approved or cleared for marketing by the FDA. There is currently no published clinical trial evidence on this technique.

**SCLEROTHERAPY**

In general, reported outcomes of uncontrolled studies have varied for sclerotherapy, as have the periods of follow-up. In many studies the outcomes are reported in terms of cure rates, but the criteria for cure or failure are poorly defined. Studies have also reported subjective patient-assessed outcomes or physician assessment, both of which may be poorly defined. More recent studies included results of Doppler or duplex ultrasonography; however, the relationship between finding ultrasonographic evidence of recurrent reflux and clinical symptoms is uncertain. Finally, it should be noted that sclerotherapy of the long saphenous vein is a fundamentally different approach than stripping. With stripping, recurrences are likely related to an incomplete surgical procedure or to revascularization. With sclerotherapy, recurrences may be additionally related to recanalization of an incompletely fibrosed saphenous vein.

Below is a summary of articles that are representative of the current published evidence. The results of these studies have established ligation and stripping as the gold standard treatments for saphenofemoral incompetence, due to the improved long-term recurrence rates. Sclerotherapy is used primarily as an adjunct to treat varicose tributaries.

**Systematic Reviews**

In 2016 Boersma et al. published results from a systematic review and meta-analysis that compared the anatomical success rates and complication rates of six treatment modalities for small saphenous vein incompetence, as discussed above.[9] The review included just six articles specific to ultrasound-guided foam sclerotherapy (UGFS). The pooled anatomical success rate for UGFS in 494 incompetent small saphenous veins was 63.6% (95% CI 47.1% to 80.1%); however, more research is needed to determine these effects.

As noted above, the updated 2014 Cochrane review included comparisons of sclerotherapy and ligation and stripping.[8] There was no significant difference between sclerotherapy and surgery in the rate of recurrence as rated by clinicians (odds ratio [OR], 1.74; p=0.06) or for symptomatic recurrence (OR=1.28). The authors concluded that sclerotherapy, EVLA, and RFA were at least as effective as surgery in the treatment of long saphenous vein varicose veins.

A systematic review from 2008 found that foam sclerotherapy of varicose veins is associated with a higher recurrence rate in patients with saphenofemoral incompetence compared to the rates of endovenous laser therapy or radiofrequency obliteration, while a 2009 systematic review suggested that outcomes from sclerotherapy are worse than those of surgery (ligation and stripping) for saphenous vein reflux.[46,47]

**Randomized Controlled Trials**

Several controlled trials comparing sclerotherapy of varicose tributaries or the saphenous vein, with and without associated ligation and stripping, have reported that the absence of ligation and stripping was associated with an increased frequency of recurrence. These trials are difficult to interpret due to the lack of clarity about which vein—either the varicose tributaries or the saphenous vein itself—have undergone sclerotherapy. Nonetheless, these trials established the importance of control of the site of reflux (ligation) and isolation of the refluxing portion of the saphenous vein (stripping). The following are examples of these studies:
Results from the five year follow up published by van der Velden et al. in 2015 study, as previously mentioned under EVLA, also examined ultrasound-guided foam sclerotherapy in 77 legs.[17] The authors found obliteration or absence of the greater saphenous vein was observed in only 23% of patients treated with sclerotherapy compared to 85% of patients who underwent conventional surgery and 77% of patients who underwent EVLA. Thirty-two percent of legs treated initially with sclerotherapy required one or more reinterventions during follow-up compared with 10% in the conventional surgery and EVLA groups. However, clinically relevant grade II neovascularization was higher in the conventional surgery and EVLA groups (17% and 13%, respectively), compared with the sclerotherapy group (4%). EuroQol-5D scores improved equally in all groups.

In 2015, King et al. published results from the VANISH-1 study, a manufacturer-funded multicenter placebo RCT undertaken to evaluate the efficacy of relief of symptoms and safety of Varithena (0.5%, 1%, and 2%) compared with 0.125% (control) and placebo.[48] Seven-hundred and eighty patients were screened; 279 patients met the study criteria and were treated with either placebo (n=56), or Varithena 0.125% (n=57), 0.5% (n=51), 1% (n=52), or 2% (n=63). Patients rated the duration and intensity of nine symptoms and activity levels during the previous 24 hours using the VVSymQscore instrument. At week eight VVSymQscores for pool Varithena (0.5% +1%+2%) patients were significantly superior to placebo (p=<.001), and VVSymQscores decreased significantly (p<.001) from baseline at eight weeks for all Varithena individual doses. There were no serious AE’s and no PE’s; however, patients receiving higher Varithena dose concentrations (1% and 2%) had higher rates of treatment-emergent AE’s, which occurred in ≥ 3% of patients. The most common kinds of treatment-emergent AE’s included pain, superficial thrombophlebitis, and hematoma at the injection site.

Microfoam sclerotherapy was studied in the 2014 VANISH-2 study, an ongoing five year manufacturer-funded pivotal double-blind RCT undertaken to obtain FDA marketing approval for Varithena microfoam (BTG).[49] The study compared 0.5% or 1.0% polidocanol microfoam with subtherapeutic foam dose (0.125%) and endovenous placebo in 232 patients. The authors reported early eight week follow-up data finding elimination of reflux and/or occlusion of the previously incompetent vein in 85.6% of the combined 0.5% and 1.0% groups, 59.6% in the 0.125% “subtherapeutic” group, and 1.8% of the placebo group. The improvement in the venous clinical severity score was significantly greater in the 0.5% and 1.0% groups (-5.10) compared with placebo (-1.52), but was not reported for the 0.125% group. The 1.0% dose of Varithena was selected for the 2013 FDA approval. Adverse events occurred in 60% of patients receiving foam sclerotherapy compared to 39% of placebo; 95% were mild or moderate and transient. The most common adverse events were retained coagulum, leg pain, and superficial thrombophlebitis. Deep vein thrombosis was detected by ultrasound in 2.8% of Varithena-treated patients with 1% having proximal symptomatic thrombi treated with anticoagulants. No pulmonary emboli were detected and no clinically significant cardiac or cardiopulmonary, neurologic, or visual adverse events were reported. In the short-term the rates of occlusion with this microfoam sclerotherapy were similar to those reported for EVLA or stripping. RCTs comparing EVLA or stripping with microfoam sclerotherapy with long-term outcomes are needed to evaluate comparative effectiveness. In 2015, Todd and Wright published an update to the VANISH-2 study and reported on findings at one year.[51] Results at year one showed symptoms improved when compared to week 8 (64% with total VVSymQ scores of 3 or less at week eight vs 85% at year one). Reductions from baseline in the individual symptom scores that compose the VVSymQ score were also demonstrated, with all five HASTI symptoms showing a continued decrease from over time. In addition,
improvements from baseline in appearance as assessed by both the patients themselves (PA-V score) and blinded experts reading standardized photographs (IPR-V score) were maintained, with a small trend toward further improvement between week eight and one year. Ten patients of the 232 in the total population had 12 AEs reported during the long-term follow-up period through year one, including one death; however, all were unrelated to treatment. Of the patients who had venous thrombus AEs during the main eight week trial, none had recurrent venous thrombus AEs, and all clots stabilized or resolved completely. No post-thrombotic syndrome or other clinically important sequelae were reported. No patient developed a new venous thrombus AE in the one year follow-up, and no pulmonary emboli were diagnosed at any time through the one year in this study.

A 2012 study was a noninferiority trial of foam sclerotherapy versus ligation and stripping in 430 patients. Analysis was per protocol. Forty patients (17%) had repeat sclerotherapy. At two years, the probability of clinical recurrence was similar in the two groups (11.3% sclerotherapy vs 9.0% ligation and stripping), although reflux was significantly more frequent in the sclerotherapy group (35% vs 21%). Thrombophlebitis occurred in 7.4% of patients after sclerotherapy. There were two serious adverse events in the sclerotherapy group (deep venous thrombosis and pulmonary emboli) that occurred within one week of treatment.

In 2010 Blaise et al. reported three year follow-up from a multicenter double-blind randomized trial (143 patients) that compared treatment of the greater saphenous vein with either 1% or 3% polidocanol foam. Additional treatment with foam sclerotherapy was carried out at six weeks, three and six months if required to abolish persistent venous reflux. There were 49 additional injections in the 1% polidocanol group and 29 additional injections in the 3% group. At the three year follow-up, venous reflux was observed in 21% of patients in the 1% group and 22% of patients in the 3% polidocanol group.

Neglen and colleagues reported on a "partially randomized" trial that compared the outcomes of three different treatment strategies: 1) sclerotherapy alone; 2) ligation and stripping, or 3) ligation combined with sclerotherapy. It was difficult to determine the target of the sclerotherapy. As described in the article, sclerosant was injected into all points of control (presumably at the junction of the perforator veins) and, "if possible, into the main stem of the long saphenous vein." Thus, it seems that the intent of the sclerotherapy was not the obliteration of the long saphenous vein as an alternative to stripping, but as a treatment of the varicose tributaries. Therefore, among those patients who underwent ligation plus sclerotherapy, this trial tested whether or not stripping could be eliminated from the overall approach. In the group who received sclerotherapy alone, almost 70% of patients self-reported a cure immediately postoperatively, which declined to about 30% after five years. This gradual recurrence rate for sclerotherapy alone is similar to that reported in the above studies. For the ligation and sclerotherapy group, 70% reported a cure immediately postoperatively, dropping to 50% after five years. The best long-term results were reported for the ligation and stripping group, which reported an 80% immediate cure rate, dropping to 70% after five years. The physician assessment of treatment outcome showed greater differences among the three groups. For example, based on physician assessment (observation and foot volumetric measurements), only 5% of the sclerotherapy group were considered cured after 5 years, compared to 10% in the ligation and sclerotherapy group and 60% in the ligation and stripping group.

Rutgers and colleagues reported on a trial that randomized 156 patients with varicose veins and saphenofemoral incompetence to undergo either ligation and stripping or ligation and...
sclerotherapy. The site of sclerotherapy was not described. At the three years follow-up, the cosmetic results were better in those limbs that had undergone stripping. Additionally, the clinical and Doppler ultrasound evidence of reflux was significantly less in those undergoing stripping.

Nonrandomized Studies

There has also been interest in injecting sclerosant into the saphenous vein either in conjunction with ligation as an alternative to stripping, as a stand-alone procedure, or as an alternative to both ligation and stripping.

Myers et al. published results from a three-year follow-up prospective observational study of sclerotherapy in 489 patients with refluxing saphenous veins and related tributaries. Out of 807 veins treated, 56% were associated with the great saphenous vein and 22% with the small saphenous vein; 22% were tributaries alone. Ultrasound at three to five days after each treatment showed successful occlusion in an average of 1.5 sessions for the group as a whole (65% in one session and 26% in two sessions). The Kaplan-Meier analysis showed three-year survival rates of 83% for tributaries, 53% for great saphenous veins, and 36% for small saphenous veins. These results do not support the use of sclerotherapy for refluxing saphenous veins.

Kanter and Thibault published result from a case series, which included 172 patients with 202 limbs who had varicose veins with associated saphenofemoral incompetence. Using ultrasound guidance, sclerosant was injected into the long saphenous vein 3-4 cm distal to the saphenofemoral junction. Injections were given at 30- to 90-second intervals, proceeding distally as previously injected segments were observed to spasm. Immediately after therapy, a thigh compression stocking was applied. Two weeks after the initial procedure, patients were reevaluated with Duplex ultrasound and were re-treated if found to have persistent reflux. There was a clinical recurrence rate of 22.8% at one year.

Ninja published two case series (1996; 1997) evaluating sclerotherapy for patients with symptomatic vulvar varicosities. The first study included seven women and the second study included five women. Both studies concluded that all patients noticed marked improvements in symptoms after treatment. However, the sample sizes in these two studies were very small and they lacked a comparator group.

Adverse Effects

Although long-term sequelae have not been reported with sclerotherapy, transient adverse effects have been found in up to 8% of patients, including cerebrovascular accidents, transient ischemic attacks, speech and/or visual disturbance, migraine, shortness of breath, dizziness, and numbness. Bubbles appear in the right side of the heart between 9 and 59 seconds after injection and emboli have been detected in the middle cerebral artery following sclerotherapy of saphenous trunks and varices. Deep venous occlusion after ultrasound-guided sclerotherapy has also been reported; risk was found to be greater when treating veins ≥5 mm in diameter (odds ratio of 3.7) and injecting 10 mL or more of foamed sclerosant (odds ratio of 3.6). A systematic review of visual disturbance following sclerotherapy found this adverse effect to be rare and transient; further research was recommended to clarify the mechanism of action of sclerosants.

Sclerotherapy and Endovenous Thermal Ablation
Randomized Controlled Trial

In 2015, Vasquez and Gasparis published results from a manufacturer sponsored multicenter randomized placebo-controlled study. The purpose of the study was to determine the efficacy and safety of Varithena (0.5%, 1.0%) and placebo, each administered with endovenous thermal ablation.[63] A total of 234 patients were screened; 117 patients met the study criteria and received treatment (38 placebo, 39 Varithena 0.5%, and 40 Varithena 1%). Patients were assessed using the Quality of Life/Symptoms (mVEINES-QOL/Sym) questionnaire, Patients Self-Assessment of Visible Varicose Veins (PA-V) and the Independent Photography Review-Visible Varicose Veins (IPR-V) instruments. Efficacy showed baseline scores were greater at week eight for pooled Varithena than for placebo for both IPR-V (−1.2 vs. −0.8 points, p = 0.001) and PA-V (−1.8 vs. −1.6 points, p = 0.16), however, only IPR-V change score reached statistical significance. The comparison of the individual dose concentrations of Variethena (0.5%, 1.0%) with placebo showed a similar pattern for both IPR-V and PA-V scores. Although no patients presented spontaneously with symptoms of thrombus, six patients were found to have venous thrombi, and all occurred during the first eight weeks post treatment. Through six months of follow-up, there were no reports of visual disturbance or migraine among Varithena recipients, no pulmonary emboli, and no AE-related study withdrawals. There was one serious AE, breast cancer, considered unrelated to the study drug.

Other Treatments

FDA approval of the VenaSeal™ Closure System, which uses adhesive, was based on three manufacturer-sponsored clinical studies, one of which was a randomized controlled noninferiority trial. In the VeClose Study, 222 subjects with symptomatic long saphenous vein incompetence were randomized to undergo either the VenaSeal closure (n=108) or RFA (n=114).[64] A three month follow-up was conducted during which no adjunctive procedures were allowed. There were a number of methodological limitations in this study, which include but are not limited to, a 14% loss of data, which was accounted for using various methods such as imputing missing data. While these analyses supported noninferiority, their reliability is unclear. These results require validation in large RCTs with lower rates of data loss and longer-term follow-up.

PRACTICE GUIDELINE SUMMARY

INTERSOCIETAL ACCREDITATION COMMISSION

In 2016, the Intersocietal Accreditation Commission (IAC) published standards and guidelines on vascular testing for accreditation.[65] The IAC has recommendations for peripheral venous testing in section 4B. The guideline for documentation of lower extremity venous duplex for reflux states the following (section 4.7.2B):

4.7.2.1B Transverse grayscale images without and with transducer compressions (when anatomically possible or not contraindicated) must be documented as required by the protocol and must include at a minimum: i. common femoral vein; ii. saphenofemoral junction; iii. mid femoral vein; iv. great saphenous vein; v. popliteal vein;
vi. small saphenous vein.

4.7.2.2B Spectral Doppler waveforms with the extremity(s) in a dependent position, demonstrating baseline flow and response to distal augmentation and if reflux is present, duration of retrograde flow measured with calipers and documented as required by the protocol and must include at a minimum: i. common femoral vein; ii. saphenofemoral junction; iii. great saphenous vein; iv. mid femoral vein; v. popliteal vein; vi. small saphenous vein.

4.7.2.3B Transverse grayscale images of diameter measurement must be documented as required by the protocol and must include at a minimum:

i. saphenofemoral junction;
ii. great saphenous vein at proximal thigh;
iii. great saphenous vein at knee;
iv. small saphenous vein (at saphenopopliteal junction).

ENDOVENOUS ABLATION

Society for Vascular Surgery and the American Venous Forum

The 2011 Society for Vascular surgery (SVS) and the American Venous Form (AVF) clinical practice guidelines on varicose veins and chronic venous disease included recommendations for endovenous radiofrequency or laser ablation for the treatment of incompetent long saphenous veins.[66]

• A Grade 1B recommendation was made in favor of endovenous thermal ablation over foam sclerotherapy and high ligation and stripping due to the reduced convalescence, pain, and morbidity. A Grade 1B recommendation was defined as a strong recommendation based on moderate quality evidence.
• A Grade 1B recommendation was made against treatment of incompetent perforator veins with CEAP class C2, but recommend treating these veins if they are located underneath a healed or active ulcer (Grade 2B recommendation defined as a weak recommendation based on moderate quality evidence.)
• The guideline does not make recommendations for saphenous vein diameter.

The 2014 SVS/AVF guidelines for management of venous ulcers included the following recommendations in favor of standard compressive therapy and ablation of incompetent superficial veins that have axial reflux directed to the bed of the ulcer[67]:

• In a patient with a venous leg ulcer and incompetent superficial veins to 1) improve ulcer healing (Grade 2B recommendation defined as a weak recommendation based on moderate quality evidence), and 2) prevent recurrence (Grade 1C recommendation defined as a strong recommendation based on low- to very low-quality evidence)
• To prevent ulceration in a patient with skin changes at risk for venous leg ulcer, and incompetent superficial veins (Grade 2C recommendation defined as a weak recommendation based on low- to very low-quality evidence)
• To aid in ulcer healing and to prevent recurrence in a patient who also has pathological perforating veins located beneath or associated with the ulcer bed (Grade 2C recommendation defined as a weak recommendation based on low- to very low- quality evidence)
• To prevent ulceration or ulcer recurrence in a patient with skin changes at risk for venous leg ulcer or healed venous ulcer and incompetent superficial veins (Grade 2C recommendation defined as a weak recommendation based on low- to very low-quality evidence).
• If a patient is expected to benefit from pathologic perforator vein ablation, percutaneous ablation with ultrasound-guided sclerotherapy or endovenous RFA or EVLA is recommended over open venous perforator surgery (Grade 1C recommendation defined as a strong recommendation based on low- to very low-quality evidence)

American College of Radiology[32]

The 2012 the American College of Radiology (ACR) published appropriateness criteria for the treatment of lower-extremity venous insufficiency considered endovenous radiofrequency or laser ablation at least as effective as surgery. Cryoablation and mechanochemical ablation are not addressed. The criteria do not include patient selection criteria related to vein size.

Society of Interventional Radiography, Cardiovascular Interventional Radiological Society of Europe, American College of Phlebology, Canadian Interventional Radiology Association[68]

The 2010 the Society of Interventional Radiography (SIR), Cardiovascular Interventional Radiological Society of Europe (CIRSE), American College of Phlebology (ACP), Canadian Interventional Radiology Association (CIRA) published a joint consensus statement on endovenous thermal ablation using either laser or radiofrequency devices under imaging guidance and monitoring an effective treatment of extremity venous reflux and varicose veins under the following conditions:

I. The endovenous treatment of varicose veins may be medically necessary when one of the following indications (A–E) is present:
   A. Persistent symptoms interfering with activities of daily living in spite of conservative/nonsurgical management. Symptoms include aching, cramping, burning, itching, and/or swelling during activity or after prolonged standing.
   B. Significant recurrent attacks of superficial phlebitis
   C. Hemorrhage from a ruptured varix
   D. Ulceration from venous stasis where incompetent varices are a contributing factor
   E. Symptomatic incompetence of the great or small saphenous veins (symptoms as in A above)

II. A trial of conservative, nonoperative treatment has failed. This would include mild exercise, avoidance of prolonged immobility, periodic elevation of legs, and compressive stockings.

III. The patient's anatomy is amenable to endovenous ablation.
SCLEROTHERAPY

Society for Vascular Surgery and the American Venous Forum

The 2011 Society for Vascular Surgery (SVS) and the American Venous Forum (AVF) published practice guidelines and included the following recommendations concerning sclerotherapy in varicose vein treatment:

- Grade 1B (strong recommendation based on moderate quality evidence) recommendation for the use of sclerotherapy to treat varicose tributaries
- Grade 1B recommendation against selective treatment of perforating vein incompetence in patients with simple varicose veins
- Grade 2B (weak recommendation based on moderate quality evidence) for sclerotherapy to treat pathologic perforating veins (i.e., outward flow of $>500$ ms duration and a diameter of $>3.5$ mm) located under healed or active ulcers (CEAP class C5-C6)

The 2014 SVS/AVF guidelines for management of venous ulcers included the following recommendations:

- Grade 1C (Strong recommendation, low quality or very-low quality evidence) For those patients who would benefit from pathologic perforator vein ablation, we recommend treatment by percutaneous techniques that include ultrasound-guided sclerotherapy or endovenous thermal ablation (radiofrequency or laser) over open venous perforator surgery to eliminate the need for incisions in areas of compromise skin.

SUMMARY

There is enough research to determine that treatment of certain symptomatic varicose veins using ligation, phlebectomy, endovenous treatment with radiofrequency or laser ablation, and sclerotherapy may improve short-term clinical outcomes (e.g., pain and return to work). Therefore, these procedures may be considered medically necessary in select patients when the policy criteria are met. Procedures not meeting the policy criteria may be considered not medically necessary. In addition, follow-up venous studies performed within six months following the most recent treatment in the absence of complications is considered not medically necessary.

There is not enough research to show improvement in health outcomes for endovenous ablation or sclerotherapy of the investigational indications listed in the medical policy criteria. Further, the current evidence has limitations including no comparator groups, small study population, and short-term follow-up.

There is not enough research to show that mechanochemical ablation of varicose veins improves patient outcomes and is safe. Therefore, the use of mechanochemical ablation of any vein is considered investigational.

There is not enough research to show that endovenous glues/adhesives improve patient outcomes and is safe. Therefore, the use of endovenous glues/adhesives of any vein is considered investigational.
### Appendix 1: CEAP Classification

| Clinical classification (C) | C0: no visible or palpable signs of venous disease
| C1: telangiectasias or reticular veins
| C2: varicose veins (≥3 mm diameter)
| C3: edema
| C4: skin and subcutaneous tissue changes
| C4a: pigmentation or eczema
| C4b: lipodermatosclerosis or atrophie blanche
| C5: healed venous ulcer
| C6: active venous ulcer

Each clinical class is further characterized by a subscript for symptomatic (S) or asymptomatic (A), for example, C2A or C5S.

| Etiologic classification (E) | Ec: congenital
| Ep: primary
| Es: secondary (postthrombotic)
| En: no venous cause identified

| Anatomic classification (A) | As: superficial veins
| Ap: perforator veins
| Ad: deep veins
| An: no venous location identified

| Pathophysiologic classification | Basic CEAP
| Pr: reflux
| Po: obstruction
| Pr,o: reflux and obstruction
| Pn: no venous pathophysiology identifiable

Advanced CEAP includes the addition of any of following 18 venous segments as locators:

| Superficial veins | Telangiectasias or reticular veins
| Great saphenous vein above knee
| Great saphenous vein below knee
| Small saphenous vein
| Nonsaphenous veins

| Deep veins | Inferior vena cava
| Common iliac vein
| Internal iliac vein
| External iliac vein
| Pelvic: gonadal, broad ligament veins, other
| Common femoral vein
| Deep femoral vein
| Femoral vein
| Popliteal vein
| Crural: anterior tibial, posterior tibial, peroneal veins (all paired)
| Muscular: gastrocnemial, soleal veins, other

| Perforating veins | Thigh
| Calf

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### REFERENCES


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45. Mao, J, Zhang, C, Wang, Z, Gan, S, Li, K. A retrospective study comparing endovenous laser ablation and microwave ablation for great saphenous varicose veins. European
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49. Todd, KL, 3rd, Wright, D. The VANISH-2 study: a randomized, blinded, multicenter study to evaluate the efficacy and safety of polidocanol endovenous microfoam 0.5% and 1.0% compared with placebo for the treatment of saphenofemoral junction incompetence. *Phlebology*. 2014. PMID: 23864535

50. U.S. Food and Drug Administration Center for Drug Evaluation and Research. 205098 Varithena Summary Review. 2013. [cited 03/22/17]; Available from: [http://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/205098Orig1s000SumR.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/205098Orig1s000SumR.pdf)


**CODES**

- There is no specific CPT code for mechanochemical treatment devices (e.g., the ClariVein® device) which should be reported with an unlisted procedure code such as 37799. Per CPT definitions, it is inappropriate to use codes 37241-37244 or 37475-37479 to report this procedure.
- Varithena is not separately reimbursable using any CPT or HCPCS Code.
- There is no specific CPT code for transilluminated powered phlebectomy. Providers might elect to use CPT codes describing stab phlebectomy (37765 or 37766), excision of varicose vein cluster(s) (37785), or unlisted vascular surgery procedure (37799).
- There is no specific CPT for microfoam sclerotherapy. Providers might elect to use CPT codes describing sclerotherapy (36468-36471) or the unlisted vascular surgery procedure code 37799. Use of codes 36475-36476 would be inappropriate as the procedure is not ablation therapy.
<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
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<tr>
<td>CPT</td>
<td>36468</td>
<td>Single or multiple injections of sclerosing solutions, spider veins (telangiectasia); limb or trunk</td>
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<td>36470</td>
<td>Injection of sclerosing solution; single vein</td>
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<td>36471</td>
<td>Injection of sclerosing solution; multiple veins, same leg</td>
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<td></td>
<td>36473</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, mechanochemical; first vein treated</td>
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<td>36474</td>
<td>;subsequent vein(s) treated in a single extremity, each through separate access sites (List separately in addition to code for primary procedure)</td>
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<td>36475</td>
<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, radiofrequency; first vein treated</td>
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<td>Endovenous ablation therapy of incompetent vein, extremity, inclusive of all imaging guidance and monitoring, percutaneous, laser; first vein treated</td>
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<td>37700</td>
<td>Ligation and division of long saphenous vein at saphenofemoral junction, or distal interruptions</td>
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<td>37718</td>
<td>Ligation, division, and stripping, short saphenous vein (for bilateral procedure, use modifier 50)</td>
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<td>37722</td>
<td>Ligation, division, and stripping, long (greater) saphenous veins from saphenofemoral junction to knee or below</td>
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<td>37735</td>
<td>Ligation and division and complete stripping of long or short saphenous veins with radical excision of ulcer and skin graft and/or interruption of communicating veins of lower leg, with excision of deep fascia</td>
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<td>37760</td>
<td>Ligation of perforators veins, subfascial, radical (Linton type) including skin graft, when performed, open, 1 leg</td>
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<td>37761</td>
<td>Ligation of perforator vein(s), subfascial, open, including ultrasound guidance, when performed, 1 leg</td>
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<td>37765</td>
<td>Stab phlebectomy of varicose veins, one extremity; 10-20 stab incisions</td>
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<td>37766</td>
<td>Stab phlebectomy of varicose veins, one extremity; more than 20 incisions</td>
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<td>Ligation and division of short saphenous vein at saphenopopliteal junction (separate procedure)</td>
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Date of Origin: October 1999