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Current therapy for primary varicose veins

Assessment and treatment options for patients with varicose veins have improved with the availability of office-based ultrasound and recent technical advances.

ABSTRACT: Chronic venous disease encompasses a broad range of conditions from minor telangiectasia to varicose veins to severe venous insufficiency with venous ulcers. The common underlying mechanism for chronic venous disease is congestion and stasis caused by reversal of venous flow and valve failure. Patients with primary varicose veins have venous congestion limited to the superficial venous system, which means that removal of the affected superficial vessels is curative. Patients with secondary varicose veins have dysfunction of the deep venous system, and the more complex treatment they require is not addressed in this article. In patients with primary varicose veins, valve failure is thought to result from hereditary weakness in the valve leaflets, prolonged standing, hormonal effects, minor direct trauma, or superficial phlebitis. Although the natural history of varicose veins is usually benign, many patients do experience symptoms of achy legs and edema. Treatment options include conservative measures such as compression therapy and leg elevation as well as more invasive vein procedures including sclerotherapy, vein surgery, stab avulsion, and endovenous ablation. While surgery with high ligation and stripping remains the gold standard for treating varicose veins, endovenous procedures have some advantages, including the use of local rather than general anesthetic, earlier return to normal activities, a reduction in periprocedural discomfort, and improved cosmetic appearance. Ultimately, the best treatment is the one tailored to the individual patient based on vein anatomy, symptoms, comorbidities, and preference.

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Patients with varicose veins (VV) have serpiginous or worm-like raised superficial veins in a lower extremity (**Figure 1**). Indications for treatment include leg pain, persistent edema, skin damage, and healed or active venous ulcer. The availability of office-based ultrasound and recent technical advances have vastly improved the assessment and treatment options for VV patients. Both conservative and more invasive interventions may be considered, depending on the individual patient.

Epidemiology and pathophysiology

Chronic venous disease encompasses a broad range of conditions from minor telangiectasia (so-called spider veins) to varicose veins to severe venous insufficiency with venous ulcers. An estimated 10% to 30% of adults are affected by VV. The prevalence of VV is higher in industrialized countries, but can affect patients of any ethnicity. Most studies have found VV to affect women more often than men, with a twofold to threefold predominance. This difference is presumed to

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be due to the effect of pregnancy and possibly to vein-dilating hormonal influences. Other risk factors for developing VV include older age, positive family history, obesity, and a standing occupation.

The common underlying mechanism for chronic venous disease is congestion and stasis caused by reversal of venous flow and valve failure. There are several theories regarding pathogenesis. The current predominant theory posits that weakness in the vein wall causes vessel dilatation, which leads to valve failure and reflux flow.[1] Normally, venous return in the leg consists of blood traveling through one-way valves from the feet to the heart, and from superficial veins to the deep veins. Anatomically, the pathways are through the saphenous and perforator veins. Valve failure in the great saphenous vein (GSV) or small saphenous vein (SSV) causes pooling and congestion of blood in the superficial leg veins when the patient is in a standing or sitting position. Over time, this congestion forces the veins to dilate, elongate, and develop varicosities. GSV and SSV reflux are the most common anatomical reason for VV.

Primary versus secondary varicose veins

In most patients, there is no specific disease process to account for vein wall weakness. Patients in this large group are categorized as having primary VV, and any valve failure is thought to be attributable to hereditary weakness in the valve leaflets, prolonged standing, hormonal effects, minor direct trauma, or superficial phlebitis. By contrast, the small group of patients with secondary VV have a history of deep vein thrombosis (DVT) in the affected leg. Venous reflux in secondary VV is more severe and is due to the damaging inflammatory effect of the blood clots on the valves of the deep veins. Venous obstruction may also result from residual clots. Patients with secondary VV tend to have severe symptoms of leg edema and skin changes from venous insufficiency with or without prominent varicose vein formation. The management strategy for secondary VV is quite different from the strategy for primary VV. This is because patients with primary VV have venous congestion limited to the superficial venous system, which means that removal of the offending superficial vessels is curative. Patients with secondary VV have dysfunction of the deep venous system, which means that treatment cannot simply aim to eliminate the superficial varicose veins but must also control the underlying deep venous problem, a topic beyond the scope of this article.

Reasons to treat varicose veins

The natural history of primary VV is usually benign; many patients do, however, experience symptoms from their veins. Even patients who claim to have no symptoms will often feel better using compression stockings or after having their veins removed. Classic symptoms associated with VV include achy legs and lower leg swelling toward the latter part of the day. The symptoms worsen with prolonged standing and are relieved with leg elevation. Some patients develop superficial thrombophlebitis, or inflamed blood clot, which can be quite painful. More severe presentations for VV include stasis dermatitis, skin pigmentation (**Figure 2**), skin hardening (detmatosclerosis), atrophie blanche, varicose bleeding, and skin ulceration (**Figure 3**). These severe manifestations are commonly referred to

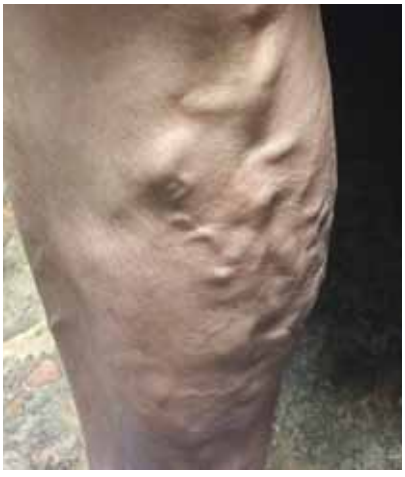

Figure 1. Leg with primary varicose veins.

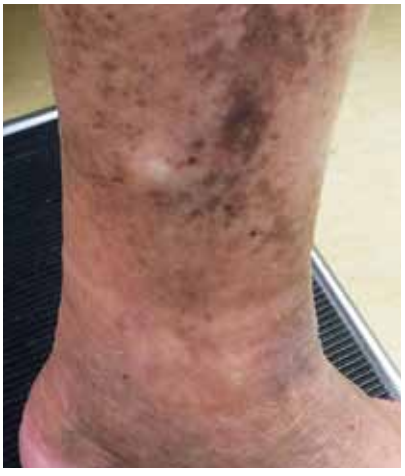

Figure 2. Chronic venous stasis pigmentation.

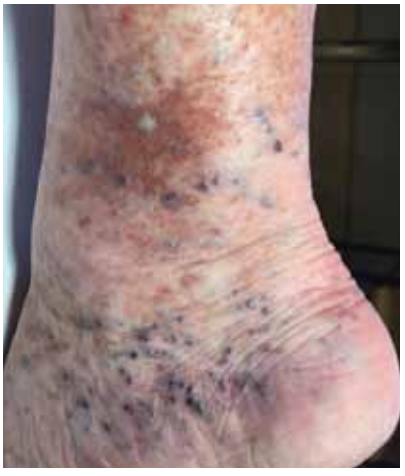

Figure 3. Healed venous ulcer.

as findings of chronic venous insufficiency. The severity of varicose veins is scored according to the revised clinical, etiologic, anatomic, and pathophysiologic (CEAP) classification system developed by the American Venous Forum (**Table 1**).[2] Indications for treatment include leg pain, persistent edema (C3), skin damage (C4), and healed (C5) or active venous ulcer (C6). Some patients may also seek treatment to improve the cosmetic appearance of their legs.

Conservative treatment

A number of conservative options can be used to treat VV. These include compression therapy, leg elevation, weight loss, and pharmacotherapy.

Compression therapy

In the past, graduated compression stockings were generally considered first-line treatment for patients with varicose veins. This has changed recently with guidelines from the Society for Vascular Surgery and the American Venous Forum now recommending against stockings as primary therapy in patients who are candidates for definitive vein surgery or ablation.[3]

The rationale for stocking use is to offer external support in combating the venous stasis within veins. Laboratory studies have shown improvement in venous flow velocities and cutaneous microcirculation.[3] Clinical studies on compression stockings have shown symptom improvement, ulcer healing, and ulcer prevention, even in patients with class C5 to C6 disease.[4] Different levels of compression are available: 10 to 15 mm Hg, 20 to 30 mm Hg, 30 to 40 mm Hg, and 40 to 50 mm Hg (**Table 2**). With the exception of the lowest strength stockings (10 to 15 mm Hg), all require a prescription. The highest strength stocking (40 to 50 mm Hg) are rarely used for treating venous disease and are usually reserved for patients with the most severe recurrent disease or lymphedema.

Table 1. Clinical classification of varicose vein severity from revised CEAP* system developed by the American Venous Forum.[2]

Clinical score	Clinical signs
C0	No visible or palpable veins
C1	Telangiectases (diameter < 1 mm) or reticular veins (diameter 1–3 mm)
C2	Varicose veins (diameter > 3 mm)
C3	Edema
C4	Pigmentation or venous eczema, lipodermatosclerosis or atrophie blanche
C5	Healed venous ulcer
C6	Active venous ulcer

*CEAP = clinical, etiologic, anatomic, pathophysiologic

Table 2. Compression stocking guide.

Stocking strength	Indication
10–15 mm Hg	C1–C2 disease; mild edema; achy legs; DVT prevention
20–30 mm Hg	C1–C3 disease; mild to moderate VV; superficial phlebitis; post-sclerotherapy
30–40 mm Hg	C3–C6 disease; moderate to severe VV; edema; skin pigmentation; venous ulcers; DVT; post-thrombotic syndrome; mild to moderate lymphedema
40–50 mm Hg	C5–C6 disease; severe lymphedema

The major challenge with compression therapy is patient compliance. Since stockings do not cure varicose veins, the patient must wear them daily and indefinitely, and must buy new stockings every 6 to12 months. Wearing stockings can be difficult, particularly for older patients and those affected by obesity or arthritis. Many patients find the stockings intolerable during warm weather. Compression stockings, therefore, should remain the conservative treatment of choice for patients who are not candidates for direct venous interventions, or should be considered as secondary therapy for patients who are candidates for saphenous vein interventions such as surgery with high ligation and stripping or endovenous ablation.

Leg elevation

The simple maneuver of leg elevation can relieve symptoms of varicose veins by promoting venous return in the leg with the assistance of gravity.[3] For leg elevation to be effective, the affected leg should be raised higher than the heart several times a day for a minimum of 30 minutes. Leg elevation may be particularly useful for elderly patients who have trouble with compression stockings and are sufficiently mobile to elevate legs regularly on their own. However, this strategy is impractical for many active working patients who do not have the time to assume the elevation position frequently for prolonged periods.

Weight loss

Many epidemiological studies have reported on an association between obesity and VV.[3] The pathophysiology linking obesity to VV is thought to involve the increased outflow venous pressure in leg veins caused by the increased intra-abdominal pressure experienced by obese patients. Studies looking at treatment of morbidly

obese patients with bariatric surgery have also shown improved signs and symptoms of chronic venous disease after weight loss. Although high-level evidence is lacking, study findings suggest that weight loss in obese patients can be helpful in improving symptoms of varicose veins.

Pharmacological therapy

Multiple clinical trials and a Cochrane review indicate that a heterogeneous group of plant-based venoactive drugs may benefit patients with symptomatic varicose veins (**Table 3**).[5,6] Clinical trials have found improvements in pain, heaviness, cramps, restless legs, sensation of swelling, and paresthesia. Most of the drugs studied have been shown to increase venous tone by mechanisms related to enhancing the noradrenaline pathway, increasing capillary resistance, and reducing capillary filtration. Micronized purified flavonoid fraction (MPFF) has been shown to improve lymphatic flow, decrease blood viscosity, and reduce release of inflammatory mediators. Rutosides, escin, proanthocynidines, and MPFF have been shown to treat leg edema effectively. MPFF has also been shown to improve venous ulcer healing. In Canada, some of these plant-based drugs are sold as vein health supplements in the natural health section of pharmacies or health supplement specialty stores. Although generally positive results have been reported, the clinical trials involving these plant-based medications have been small. These medications should be considered as supplementary to other therapies such as compression therapy, sclerotherapy, and surgery. Most of these medications have been found to be safe and are sold over the counter.

Pentoxifylline is a prescription drug more commonly used for patients with arterial claudication, but is also shown to accelerate healing of venous ulcers[7] by inhibiting neutrophil activation and reducing the release of superoxide free radicals. While generally well tolerated, pentoxifylline may cause GI upset and should be prescribed in reduced doses for patients with severe renal impairment (creatinine clearance less than 20 mL/min).

Currently, the American Venous Forum practice guidelines[3] assign a weak recommendation for using venoactive drugs with other therapies for symptomatic varicose veins patients, and a strong recommendation for using pentoxifylline as adjuvant therapy when prescribing compression for patients with venous ulcers.

Table 3. Venoactive substances commonly available as health supplements.

Substance	Source
Diosmin	Citrus spp.; *Sophora japonica*
Rutin	*Sophora japonica*
Micronized purified flavonoid fraction (MPFF)	*Rutaceae aurantiae*
Escin	*Aesculus hippocastanum* (horse chestnut)
Hesperidin	Citrus spp.
Proanthocyanidins	Grapes, apples
Pycnogenol	*Pinus pinaster* (pine tree bark)
Troxerutin	Eucalyptus spp.; *Fagopyrum esculentum* (buckwheat)
Ruscus	*Ruscus aculeatus* (Butcher's broom)

Vein procedures

An assortment of more invasive procedures that aim to destroy or remove the varicose veins and their underlying source of superficial venous reflux may be used to treat VV. These procedures include sclerotherapy, vein surgery, stab avulsion, and endovenous ablation. In well-selected patients, these procedures can be used in combination or alone to render the patient varicose vein free. To ensure excellent outcome, the use of office-based duplex ultrasound is crucial when selecting appropriate patients for these procedures.

Sclerotherapy

Sclerotherapy involves the injection of a locally irritating medication into the vein to induce endothelial damage, inflammation, fibrosis, occlusion, and eventually absorption of the offending smaller vessels from a non-saphenous source or the residual veins after treatment of saphenous vein reflux. The most commonly used sclerosants can be divided into two groups: osmotic agents and detergents.[8] Osmotic agents such as hypertonic saline and sodium chloride with dextrose (Sclerodex) cause cell death by dehydrating the endothelial cells through osmosis, and are used primarily for occluding smaller veins. Detergents such as sodium tetradecyl sulfate and polidocanol are stronger sclerosants used for treating larger veins, and work by denaturing cell surface proteins to cause endothelial damage and vein thrombosis. A major recent advance in sclerotherapy is the use of foam created by mixing a detergent sclerosant with air or carbon dioxide, which extends the contact time between the drug and endothelial surface. Foaming of the detergent significantly enhances its potency and allows for treatment of large veins. However, the potency of foam sclerotherapy is also associated with increased risk of phlebitis. As well, large volumes of

foam sclerosant may cause embolization to the lungs, eyes, and brain. More rarely, foam sclerotherapy can cause chest pain, visual disturbance, and even stroke.[9] In general, foam sclerotherapy should be performed with ultrasound guidance and using minimal volumes to avoid complications. Although studies have reported successful treatment of saphenous vein reflux with foam sclerotherapy, large randomized clinical trials have shown it to be vastly inferior to surgery and endovenous ablation because of a high VV recurrence rate.[10] Commonly cited complications of sclerotherapy include hyperpigmentation, vein matting, thrombophlebitis, allergic reaction, skin irritation, and ulceration. In general, the risk of complications increases with increases in the potency and volume of the sclerosant given.

Vein surgery

For many years the gold standard for treating VV has been vein surgery with high ligation and stripping of the great saphenous vein or small saphenous vein combined with excision of larger varicose veins. The success of this procedure requires clear visualization of the offending refluxing vein with duplex ultrasound. In patients with GSV reflux, the GSV is removed from the saphenous femoral junction at the groin to the level just below the knee. For patients with SSV reflux, the SSV is removed from the popliteal fossa to the mid or lower calf level where it gives rise to the varicosities. Large varicose veins or refluxing perforator veins may be excised at the same time, but it is not necessary to remove all of the offending veins as remaining veins usually shrink in size after the underlying source of reflux is removed.

High ligation and stripping surgery is highly effective treatment for patients with VV. Although performed under general anesthesia or a regional block, the surgery is usually done as a day procedure and is well tolerated by most patients. On average, patients require 1 to 2 weeks off work for convalescence. Complications associated with open venous surgery include infection (1% to 2%), DVT (1%), and sensory nerve injury causing paresthesia (10% to 20%). The recurrence rate for VV is 10% to 20%. Recurrent VV can usually be treated with ultrasound-guided sclerotherapy.

Stab avulsion

Stab avulsion is a surgical procedure for removing varicose veins through multiple small incisions (less than 1 cm) under local anesthetic. This procedure is used when the refluxing saphenous vein is normal or has already been removed or ablated, and is particularly useful for patients with large veins or perforator veins that are not suitable for sclerotherapy. Sometimes stab avulsion is performed instead of saphenous vein stripping in frail patients to minimize the extent of surgical intervention. In this setting, stab avulsion is less effective than vein stripping and more prone to VV recurrence.

Endovenous ablation

Endovenous ablation is a minimally invasive ultrasound-guided procedure designed to close the saphenous and perforator veins without removing them. Endovenous procedures are usually performed in the office setting under local anesthetic, and each begins with insertion of a small catheter that traverses the entire refluxing saphenous vein. A variety of vein closure methods are then delivered through the catheter to close the vein under ultrasound guidance.

Currently, the methods used to close veins include endovenous laser ablation (EVLA), radiofrequency ablation (RFA), mechanical-chemical ablation (MOCA), and n-butyl-2 cyanoacrylate closure (n-BCA) (**Table 4**). EVLA and RFA are heat-based methods that cauterize the inside of the vein wall. MOCA achieves vein closure with simultaneous use of mechanical and chemical methods: a fine wire spins to damage the inner wall of the vein while a sclerosant is injected to make the vein thrombose and close down. n-BCA achieves closure using medical grade cyanoacrylate (superglue). These methods can be further categorized according to whether they require tumescent anesthetic (TA), a method to anesthetize the entire target vein by injecting a large volume of very dilute local anesthetic. TA is required for EVLA and RFA since applying heat to the vein is painful. TA is not required for MOCA and n-BCA since both procedures cause minimal discomfort and anesthetic at the catheter entry site is all that is needed.

Table 4. Endovenous methods for ablation of saphenous vein.

Method	Mechanism	Requires tumescent anesthetic
EVLA (endovenous laser ablation)	Laser heat burns inside of vein	Yes
RFA (radiofrequency ablation)	Radiofrequency heat burns inside of vein	Yes
MOCA (mechanical-chemical ablation)	Simultaneous use of spinning wire and sclerosant damages vein	No
n-BCA (cyanoacrylate closure)	Medical superglue occludes vein	No

Therapies compared

Several randomized trials have compared vein surgery with various endovenous ablation procedures. Van der Velden and colleagues looked at 5-year results comparing surgery, EVLA, and foam sclerotherapy in VV patients with GSV reflux and found conventional surgery and EVLA to be more effective than foam for closing the saphenous veins.[11] They also found improved quality of life scores.[11] O'Donnell and colleagues completed a meta-analysis of randomized trials that compared surgery and endovenous ablation (either EVLA or RFA) of the GSV and found no difference in varicose vein recurrence.[12] Koramaz and colleagues completed a retrospective comparison of follow-up data for patients treated with n-BCA and EVLA and found no difference in efficacy between the two modalities. There were, however, fewer adverse reactions such as pigmentation and phlebitis after n-BCA compared with EVLA.[13] In a randomized clinical trial comparing MOCA and RFA, Bootun and colleagues found no difference in closure rate or quality of life, but early results indicated MOCA is the less painful of the two procedures.[14] In general, these studies suggest that endovenous procedures are equally effective for treating VV patients with GSV or SSV reflux when compared with surgery.

Surgery with high ligation and stripping remains the gold standard for treating VV, with excellent anatomical long-term results that are unsurpassed by any of the new modalities. However, there are several advantages to endovenous procedures, including the use of local rather than general anesthetic, earlier return to normal activities, a reduction in periprocedural discomfort, and improved cosmetic appearance. Among endovenous closure procedures, those not requiring tumescent anesthetic may also be associated with a further reduction in short-term discomfort.

Conclusion

Varicose veins can be successfully managed using a wide array of treatment options. Office-based ultrasound has greatly improved clinical assessment and therapeutic options. No single treatment has been found to be appropriate for all patients. Sometimes multiple modalities are needed to address the different veins in the same patient. The best treatment modality is the one tailored to the individual based on vein anatomy, symptoms, comorbidities, and patient preference.

Competing interests

None declared.

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