

Endovenous treatment options in patients with chronic venous disease and lower limb ulcers

KEY WORDS

- ▶ Chronic venous disease
- ▶ Venous leg ulcers
- ▶ Endovenous treatments
- ▶ NICE guidance

Chronic venous disease (CVD) is a major cause of patient distress and an enormous clinical and financial burden to healthcare providers. Although CVD encompasses a spectrum of venous disorders (ranging from varicose veins to intractable venous ulceration), superficial venous reflux is a common finding. Early treatment can also prevent or slow progression to more advanced stages of CVD. A range of minimally invasive endovenous treatments is now available for superficial venous reflux. Novel treatments such as radiofrequency ablation, laser ablation and foam sclerotherapy have been proven to be effective and are recommended by NICE guidance. However, the national implementation of NICE referral and treatment guidelines for varicose veins remains suboptimal, with many patients not receiving appropriate investigations or treatments. The aim of this article is to discuss the importance of superficial venous reflux, describe modern endovenous treatment options and highlight future challenges in the management of patients with CVD, with or without active ulceration.

Chronic venous disease (CVD) (also known as venous insufficiency) refers to a wide spectrum of disorders ranging from uncomplicated thread or varicose veins, to severe intractable venous ulceration. CVD is common and widely accepted as an enormous cause of patient morbidity, distress and health service expense (Van den Oever et al, 1998; Robertson et al, 2008). Large population based studies have demonstrated that venous disease is present in up to a third of adults, with venous skin changes or ulceration present in 5–7% of the adult population (Rabe et al, 2012; Wittens et al, 2015) (*Figure 1*). The burden of CVD is likely to rise dramatically in the coming years. This is primarily due to dramatic increases in population age and obesity, both of which are risk factors for the development and progression of venous disorders and ulceration (Rabe et al, 2003; Padberg et al, 2003).

While the cost-effectiveness for interventions to treat venous disease has been demonstrated unequivocally (and supported by national/international guidelines) (Gohel et al, 2010), the pathways for referral and treatment of patients with CVD and ulceration remain poorly developed. There is widespread perception that the management

of patients with CVD is too often reactive (once complications have developed), rather than preventative. The aim of this article is to explore the rationale for treating superficial venous reflux and discuss some novel and minimally invasive treatment options that are now available for this important patient group.

PATHOPHYSIOLOGY OF CHRONIC VENOUS DISEASE

While our understanding of CVD pathophysiology is far from complete, there is widespread consensus that the manifestations of venous disease are caused by chronic venous hypertension in the leg (Nicolaidis et al, 1993). Chronic venous hypertension occurs due to an inability of the calf muscle pump to maintain normal venous function in the presence of one or more factors contributing to high venous pressure. These factors include venous reflux (affecting superficial and/or deep veins), deep venous occlusive disease (usually after deep vein thrombosis), ankle stiffness or muscle weakness (causing impairment of calf muscle pump function), immobility and prolonged dependency (*Figure 2*).

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Table 1. Summary of clinical stage of CEAP classification	
CEAP clinical stage	Description
C0	Absence of any signs of venous disease
C1	Reticular veins
C2	Truncal varicose veins
C3	Oedema
C4a	Skin changes (eczema, pigmentation)
C4b	Lipodermatosclerosis, atrophie blanche
C5	Healed ulceration
C6	Open ulceration



Figure 1. Photograph of medial malleolus area in patient with CVD. Evidence of varicose veins, skin pigmentation and healed venous ulceration.

The precise manifestation of CVD varies dramatically between patients and it remains a mystery that patients with very similar patterns of venous disease, may have wildly different clinical presentations. The Clinical aEtiological Anatomical Pathophysiological (CEAP) classification was revised in 2004 and offers a useful descriptive tool for CVD severity (Eklöf et al, 2004). The clinical stage of CEAP has been adopted widely and is summarised in *Table 1*.

The mechanisms that lead from venous hypertension to eventual skin ulceration are widely debated, with a variety of theories having been proposed (fibrin cuff, growth factor trapping, white cell trap and others) (Burnand et al, 1982; Falanga and Eaglstein, 1993; Coleridge Smith et al, 1988). Nevertheless, the primary aim of treatments for patients with CVD is (where possible) to eliminate or reduce the causes of venous hypertension in the leg. This can be achieved with leg elevation

and compression therapy, but concordance with both of these measures is notoriously poor (Carpentier et al, 2011). Addressing any underlying superficial venous reflux is a key component of the multidisciplinary management to provide an effective and durable treatment for CVD.

THE IMPORTANCE OF SUPERFICIAL VENOUS REFLUX

With the widespread availability of colour venous duplex scanning, our understanding of venous disease has advanced dramatically. The leg contains deep veins (crural, popliteal, femoral), superficial veins (great saphenous, small saphenous, tributaries) and veins that connect the deep and superficial veins (perforators). Normal venous function in the legs relies on blood flow towards the heart (up the leg, against gravity). Venous blood flow is stimulated by the calf muscle pump (activated by walking and calf muscle contraction). Healthy deep and superficial veins also contain a series of 'one-way' valves, which keep the venous blood flowing from the leg to the heart (*Figure 3*). Failure of these valves, results in blood flow in the wrong direction (down the leg)

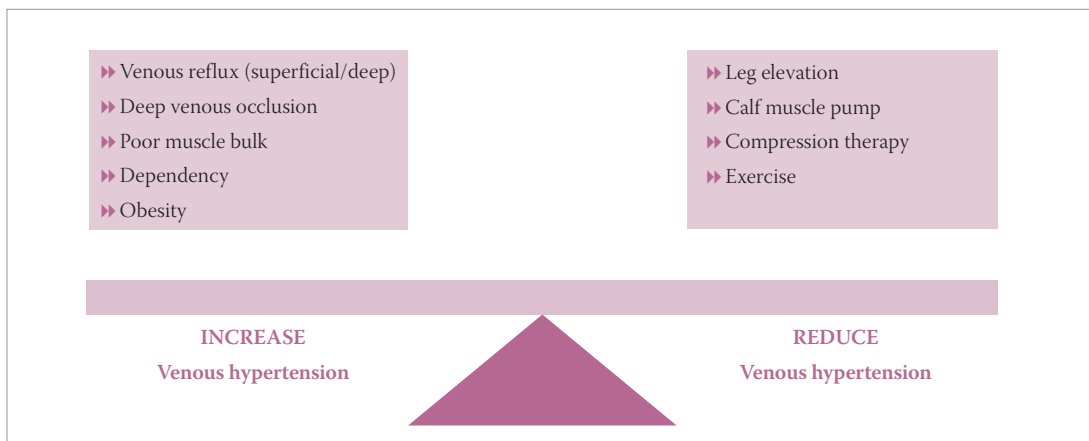


Figure 2. Factors influencing to chronic venous hypertension

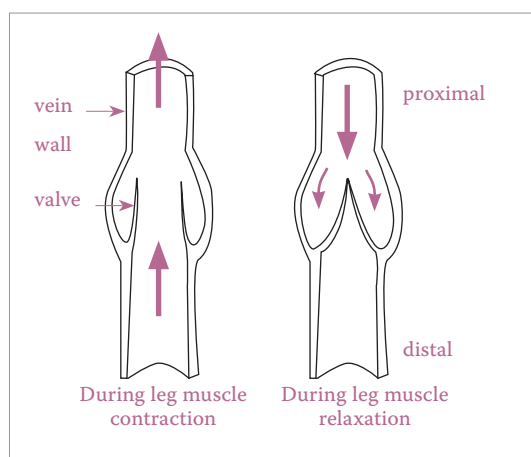


Figure 3. Depiction of a venous valve. The valve opens to allow flow towards the heart, but closes to prevent reverse flow (venous reflux)

and is known as venous reflux or incompetence. Venous reflux in superficial veins is often described as 'varicose veins', even in the absence of visible prominent veins.

The majority of patients with CVD have venous reflux. This is commonly seen in superficial veins (>50% of patients), sometimes in the deep veins alone and frequently in both superficial and deep veins. This is important as superficial venous reflux can be ablated readily using a range of minimally invasive thermal and non-thermal ablation techniques, which are durable and well tolerated. These procedures are performed using local anaesthesia alone and offer an excellent, long-term strategy for reducing chronic venous hypertension. This is particularly relevant given the poor patient concordance with leg elevation and compression therapy.

The clinical evidence for treating superficial venous reflux is unequivocal. Clinical outcomes, patient reported outcomes (quality of life) and health economic outcomes have all been shown to improve after treatment of superficial venous reflux in patients with symptomatic CVD (Marsden et al, 2013). Treatment of superficial reflux in pre-ulcerative CVD (CEAP grades C2–C4) results in significant patient quality of life improvements and can slow or prevent progression to more advanced venous disease and ulcers (Pannier and Rabe, 2012).

The importance of treating superficial venous reflux in patients with chronic venous ulcers is worthy of specific mention, not least as venous ulceration is an enormous source of patient distress and health service/societal expense (Ruckley,

1997). Superficial venous surgery has been shown to reduce ulcer recurrence rates by around 50% at 3 years (Gohel et al, 2007). There may also be a benefit in terms of faster ulcer healing, particularly in patients who are not concordant with optimal compression therapy (Kulkarni et al, 2013). The impact of minimally invasive varicose vein interventions on ulcer healing is being evaluated in the NIHR HTA funded EVRA study, which is currently in progress (www.evrastudy.com). Overall, there is a clear and cogent case for diagnosing and treating superficial venous reflux in patients with CVD.

MODERN OPTIONS FOR TREATMENT OF SUPERFICIAL VENOUS REFLUX

The aim of traditional and modern treatments for superficial venous reflux is the same: to remove or obliterate all incompetent superficial veins. Surgical ligation and 'stripping' of varicose veins had been the mainstay of treatment for over a century and is an effective treatment (Michaels et al, 2006). However, operations were usually performed using general anaesthesia and associated with bruising, wound complications, pain and long recovery periods before patients could return to normal activity (Brittenden et al, 2015). Consequently, many patients (particularly the elderly) with CVD were unwilling or unfit for traditional varicose vein stripping.

The desire (and necessity) to develop less invasive procedures led to the introduction of a range of keyhole (or 'endovenous') techniques. These interventions involve cannulation of the vein to be treated (usually under ultrasound guidance) followed by ablation of the vein using heat, chemicals or other modalities in order to close the venous channel. These local anaesthetic, 'walk-in, walk-out' procedures have become increasingly widespread over the last decade and revolutionised the management of patients with superficial venous reflux. This choice is certainly welcome for clinicians and patients, for whom the treatment strategy can now be tailored to their individual circumstances and preferences.

Endovenous thermal ablation

Thermal ablation is the most commonly used endovenous approach. The two main types of thermal ablation are radiofrequency ablation (RFA) and endovenous laser ablation (EVLA); one or other of these interventions is available in the majority of vascular units in the United Kingdom.

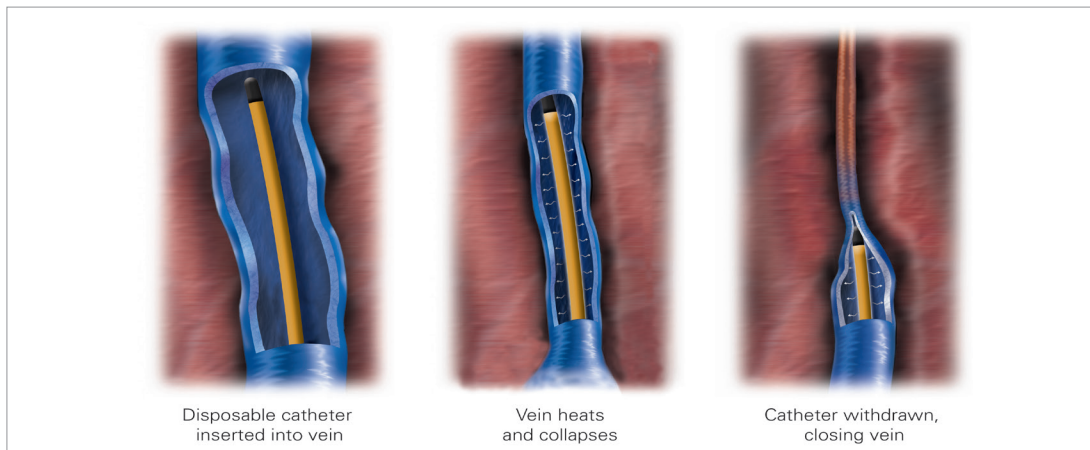


Figure 4. ClosureFast™ radiofrequency ablation catheter in vein (© Covidien)

Both RFA and EVLA are commonly used for the ablation of refluxing saphenous veins and excellent medium-term success rates have been reported in prospective and randomised clinical studies (Marsden et al, 2013). Now considered the gold standard for varicose vein interventions, endovenous thermal techniques have largely replaced varicose vein stripping operations.

Under local anaesthesia (often in a treatment room/modified office setting), the vein to be treated is cannulated and the radiofrequency or laser fibre is carefully positioned at least 2cm from the junction with the deep vein (saphenofemoral or saphenopopliteal). A dilute local anaesthetic is then injected around the vein (known as 'tumescence anaesthesia') before heating the vein wall to close the venous lumen (Figure 4). The entire procedure can be completed in 20–30 minutes. Patients are usually asked to wear a stocking for a week after the procedure, but can usually return to normal activity within a few days, or sooner.

Ultrasound guided foam sclerotherapy (UGFS)

Rather than using thermal ablation of the veins, UGFS is an endovenous technique for chemical ablation of the incompetent superficial veins. After cannulation of the veins to be ablated, a foam sclerosant mix is injected. The foam mixture can be obtained ready-made, but the majority of specialists mix liquid sclerosant with air (using a 3-way tap) to create a foamy emulsion for injection (Figure 5). The technique is cheap, well tolerated and particularly useful for elderly patients with chronic venous ulcers (who may not tolerate tumescence anaesthetic injection) or patients where RFA or EVLA are not deemed feasible.

As with other endovenous interventions, the risks are low with UGFS. However, patients often

experience some post-procedure phlebitis and may get brown pigmentation of the skin over the treated veins. Finally, some patients may experience transient visual disturbances and there have been reports of stroke after UGFS (Cavezzi and Parsi, 2012). While this may be alarming, such events are extremely rare. It is the author's practice to avoid foam sclerotherapy in patients known to have a 'hole in the heart' (such as patent foramen ovale) or those with severe migraines, as there is some evidence that visual disturbances after UGFS may be more likely in these patients.

Other non-thermal ablation techniques

The treatment of CVD has become an area for great innovation and industry attention in recent years. As a result, a number of novel and exciting non-thermal interventions have been developed and are available. Mechanochemical ablation (ClariVein®) is an endovenous procedure using a combination of vein wall damage (using a rapidly rotating filament) and sclerosant injection to close the refluxing superficial vein (Deijen et al, 2015).

Another exciting development is the use of cyanoacrylate glue (VenaSeal® Closure System) to close the venous lumen (Morrison et al, 2015).



Figure 5. Production of foam using the 'Tessari technique' (Tessari et al, 2001). Liquid sclerosant and air are mixed together using two syringes and a 3-way tap to produce a foamy emulsion for injection.

Both of these non-thermal techniques can be performed without tumescent anaesthetic, which is often the most uncomfortable stage of RFA and EVLA procedures. Early outcomes are extremely promising, leading many specialists to believe that non-thermal endovenous ablation may be the ideal modalities for treating superficial venous reflux in years to come.

GUIDELINES FOR REFERRAL AND TREATMENT OF CVD

The rapid expansion in choice of treatments for varicose veins, has inevitably led to confusion for patients and healthcare professionals. This has been exacerbated by major inconsistencies in rationing policies and treatment pathways between and within regions.

NICE guidelines

In 2013, the National Institute for Health and Care Excellence (NICE) produced guidelines for the referral, assessment and management of patients with varicose veins in the legs (Marsden et al., 2013). Referral to a vascular service is recommended for patients with:

- ▶▶ bleeding varicose veins (immediate referral)
- ▶▶ symptomatic primary or symptomatic recurrent varicose veins
- ▶▶ superficial thrombophlebitis or lower limb venous skin changes (such as eczema or pigmentation)
- ▶▶ a venous leg ulcer, not healed within 2 weeks
- ▶▶ a healed venous leg ulcer.

All patients should undergo colour venous duplex scanning to define the extent of venous reflux and for those patients with superficial venous reflux, the guidance recommends that specialists should:

- ▶▶ offer endovenous thermal ablation (RFA or EVLA)
- ▶▶ if endovenous thermal ablation is unsuitable, offer UGFS
- ▶▶ if UGFS is unsuitable, offer traditional surgery.

Importantly, the NICE guidance recommends that compression stockings should not be offered to patients unless interventional treatments are unsuitable. This guidance is in stark contrast to the traditional approach of compression therapy as the primary treatment modality for venous disease.

The main recommendations made in the NICE guidelines have also been reinforced by recently

published guidelines from the European Society for Vascular Surgery (ESVS) (Wittens et al, 2015), where endovenous thermal ablation is also recommended as the first-line treatment for patients with superficial venous reflux.

CURRENT AND FUTURE CHALLENGES IN THE TREATMENT OF CVD

The management of patients with CVD has been enhanced by strong therapeutic innovation, supported by good quality clinical evidence. As described in NICE and other clinical guidelines, there are a number of safe, well tolerated and highly effective treatments available for patients with superficial venous reflux. The treatment of patients with symptoms, skin changes or ulceration (active or healed) is beneficial and cost-effective. However, there is a strong perception among primary and secondary care healthcare professionals that many patients with advanced CVD are not considered for assessment or treatment of superficial venous reflux.

Despite the scientific evidence and guidelines supporting superficial venous interventions, there is a failure of implementation. Factors that may be contributing to this include:

1. A lack of understanding of the benefits of treating varicose veins among patients and healthcare professionals
2. Financial constraints, potentially acting as a disincentive to patient referral or treatment (despite the proven cost-effectiveness)
3. Inconsistency in commissioning guidelines between regions, which may not concur with NICE guidance
4. The absence of proactive screening initiatives to identify and refer patients with CVD
5. Poor dissemination of evidence and guidelines to overworked front-line clinical staff
6. A lack of formal audit to quantify the lack of implementation of evidence-based NICE guidance.

Clearly, the current financial climate may inhibit the development of new services and interventions. However, the treatment of superficial venous reflux in patients with CVD has been proven to be cost-effective, as defined by national thresholds. Moreover, any efforts by healthcare policy makers and commissioners to reduce varicose vein interventions to save money would be short-sighted, as the progression to more advanced (and more expensive) stages of CVD is inexorable (Pannier and Rabe, 2012).

Perhaps the greatest challenge for healthcare professionals involved with CVD is to improve and refine patient pathways of care, particularly at the interface between primary and secondary care services. Links between community nursing teams, primary care doctors and hospital vascular services should be developed, so that patients can be managed in a seamless manner. The development and adoption of local anaesthetic endovenous interventions may offer a unique opportunity to deliver venous interventions in the community, in a more patient centred manner. This can only act to improve communication between hospital and non-hospital healthcare staff and promote easier access to specialist investigations and treatments. Healthcare staff should be encouraged to innovate and develop new models of care for patients with CVD, to improve the outcomes for this important patient group.

CONCLUSIONS

The importance of chronic venous disease and the treatment of superficial venous reflux is clear. Novel, endovenous interventions have replaced varicose vein stripping as the gold standard for care and are recommended as first-line treatments in NICE guidance. Innovative pathways and models of care are needed to improve collaboration between primary and secondary care settings and improve patient access to appropriate assessment and treatments. Greater implementation of endovenous procedures will improve patient quality of life in the short-term, but may also reduce the burden of complicated venous disease and ulceration in years to come.

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