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Endovenous management of varicose veins

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Abstract:

Varicose veins are a very common condition and have been the subject of a recent proliferation of treatment modalities. The advent of the endovenous treatment era has led to a confusing array of different techniques which can be daunting when making the transition from traditional surgery. All modalities offer excellent results in the right situation and each has their own treatment profile. Thermal ablation techniques have matured and have a reassuring and reliable outcome, but the arrival of non-thermal techniques has delivered further options for both patient and surgeon. This article provides an overview of the different treatment devices and modalities available to the modern superficial vein surgeon and details the currently available evidence and summation analysis to help surgeons to make an appropriate treatment choice for their patients.

Keywords:

Endovenous ablation, varicose veins, venous disease, radiofrequency, sclerotherapy, cyanoacrylate

Introduction

Varicose veins are a common condition affecting up to one-third of the population, with detrimental effects on the quality of life (QoL).[1-2] Until the past decade, the traditional technique of saphenofemoral or saphenopopliteal ligation with or without vein stripping has been the gold standard treatment of truncal saphenous incompetence. This usually necessitates either general or regional anaesthesia.[3] Although surgery provides good outcomes, it is associated with ecchymosis, hematoma, tenderness,[4] infection, nerve injury, delayed return to normal activity[3-5] and routinely necessitates narcotic analgesia.[3]

In response to the need for less invasive treatment, endovenous treatments, namely radio-frequency ablation (RFA) and endovenous laser ablation (EVLA) have been developed. These have led to a reduction in morbidity compared with open surgery,[4-6] by reducing postoperative pain, providing faster recovery time, improving QoL and lowering complication rates.[7-8]

More recently, new non-thermal, non-tumescent (NTNTs) treatments have been developed to overcome the shortcomings associated with thermal ablation. Both thermal and non-thermal treatments are discussed in this review.

Thermal-Tumescent Ablative Management

Since 1999, endovenous thermal ablation, in the form of RFA and EVLA have been developed. More recently, endovenous microwave ablation (EMA) and steam vein sclerosis (SVS) have also been introduced. Their mechanism of action involves using heat to cause thermal damage to the venous wall.

Radio-frequency ablation (RFA)

The practice of RFA utilizes radio-frequency waves to produce thermal energy (85-120°C) resulting in endothelial damage and sealing of the incompetent vein (Figure 1). In 1999, the U.S. Food and Drug Administration (FDA) approved RFA for treatment of the great saphenous vein (GSV).[3]

Clinical results

In 2000, Goldman and Amiry[9] reported their early experience with RFA utilizing the Closure catheter (VNUS Technologies, Sunnyvale, CA, USA). This initial trial included 10 patients (12 limbs) with GSV incompetence, and all patients were assessed at 3 and 6 months. The

results demonstrated complete obliteration of the GSV with no evidence of recurrence. They concluded that RFA of an incompetent GSV can be easily accomplished and is efficacious.

In 2007, the second generation of this device was introduced (ClosureFast, Medtronic, Minnesota, USA),[10] which allowed segmental ablation of incompetent truncal veins. Proebstle et al. [11] published the first clinical series of 252 legs treated using this new device, a complete occlusion rate and no reflux within treated vein observed in 92.6% and 95.7%, respectively, after 3-years follow-up.[12] At 5 years follow-up GSV occlusion rate was 91.9%, and there was a significant improvement in Venous Clinical Severity Score (VCSS) from 3.9 at baseline to 1.3 ($p<0.001$).[13]

Zuniga and coworkers[14] in 2012 reported on the superiority of the ClosureFast™ catheter in terms of GSV obliteration (98% *vs* 88%; $p <0.001$) and rate of deep vein thrombosis (DVT) (0% *vs* 3.5%; $p <0.001$) against the ClosurePlus™ catheter.

The EVOLVeS prospective multicenter randomized study compared RFA with high ligation and stripping (HL/S). In total, 84 patients were treated. Occlusion and recurrence rates were similar in both groups at 2 years follow-up. The authors reported faster recovery times and superior QoL scores, less postoperative pain and fewer adverse events in the RFA group.[15]

Bipolar radiofrequency-induced thermotherapy technology - RFiTT (Olympus Surgical Technologies Europe/Celon AG Teltow, Germany) is an alternative radiofrequency ablation catheter (Figure 2). The RFiTT was initially used for treating primary and metastatic liver lesions.[16] The mechanism of action of the bipolar arrangement of electrodes in veins enables resistive heating which results in ablation and vein occlusion. An industry sponsored study recommends power sitting of 18-20 Watt with withdrawal velocity ≥1.5 s/cm. This system is claimed to be able to treat truncal varicose veins with and without tumescence.[5]

In order to investigate the effectiveness of the RFiTT system, Braithwaite et al.[5] conducted a multi-center non-randomized study in which 462 patients (56.5% CEAP class 3 or worse) were enrolled and received their treatment either under general anesthesia or tumescent fluid injection. Mean followed-up period was 290±84 days. Average pullback rate and average output power were 1.8±1.3 s/cm and 23±3W, respectively. Complete occlusion rate of 98.4% was observed with a power setting on the RFiTT generator of 18W and 20W. The authors concluded that the RFiTT system is effective with a low rate of procedure-related postoperative complications. Longer term follow-up, as well as larger comparative studies, are needed to fully investigate the RFiTT system.

Endovenous Laser Ablation (EVLA)

In 1999, Dr. Carlos Boné first reported on EVLA as a treatment of varicose veins and truncal varicosities at the International Union of Phlebology.[17] EVLA using an 810-nm device received U.S FDA approval in January 2000.[3] The mechanism of action of laser ablation is generation of non-thrombotic vein occlusion by heating the vein wall, leading to wall thickening, vessel contraction and eventual endo-fibrosis.[18]

Clinical results

Navarro et al.[17] published the first clinical trial of EVLA use to treat 44 GSVs using a wavelength of 810-nm. Their data showed 100% of GSV were occluded at a mean follow-up of 4.2 months, with no significant complications.

EVLA of the GSV with wavelengths longer than 810-nm gives rise to thrombotic vessel occlusion and have been associated with reduced postoperative pain. A study involving the use of a 940-nm wavelength on 31 limbs with GSV incompetence was published in 2002. On day 1, 7, and 28, successful closure was demonstrated in 97% of limbs with one limb incompletely occluded, and two limbs (6%) had thrombophlebitis[19]. Min et al.[18] evaluated 490 patients (499 limbs) undergoing EVLA for incompetent GSVs. Patients were followed for up to 17 months (range: 1 to 39 months). Occlusion rates were 98%, 97% and 93.4%, at 1 month, 1 year and 2 years, respectively. Bruising was observed in 24% and thrombophlebitis in 5%.[18]

A prospective randomized study compared 1920-nm wavelength EVLA to 1470-nm wavelength EVLA with the primary outcome measure of venous occlusion rates at one-year follow-up. In total, 67 patients were recruited with 48 limbs receiving 1920-nm and 42 limbs 1470-nm laser to treat their GSVs. Results at 1-year follow-up showed that patients treated with the 1470-nm catheter had higher occlusion rates compared to the 1920-nm system (94.7% *vs* 87.5%; p=0.05). Patients who were treated with the 1920-nm EVLA catheter had less ecchymosis, induration and less analgesic use. However, both groups showed a similar improvement in CEAP and VCSS.[20]

Two studies have reported that using a low Linear endovenous energy density (LEED) (< 80 J/cm) in the management of incompetent saphenous veins is associated with less adverse events.[21-22]

Comparison of RFA and EVLA

In a prospective randomized study, 810-nm wavelength EVLA (BioLITEC system, Biolitec AG, Germany) was compared with RFA (Olympus Celon RFiTT system, Teltow, Germany) in 66 patients (87 legs), with outcome measures of post-procedural pain and bruising. This study showed a significantly lower level of pain in the RFA arm of the study on days 2-11, as measured by a 10-cm visual analogue

scale (VAS). The degree of bruising was also significantly less in the RFA group on days 3-9. However, occlusion rate in the EVLA group was equivalent to the RFA group at nine months follow-up (78% *vs* 74%). Both treatment options produced a similar improvement in the patients' mean QoL (3.78 *vs* 3.55; p=0.74), the success of treatment and time to return to normal activity.[23]

Lower pain scores with RFA was confirmed in another randomized controlled trial (RCT) of RFA (VNUS®ClosureFast™ system) *vs* EVLA. However, time to resume normal activities and QoL improvement were equivalent.[24]

A prospective, double-blind, randomized trial was performed to compare the endovenous treatment of primary GSV in 159 patients, using either RFA or 810 nm EVLT. Post-procedural duplex ultrasound at 1 week revealed complete occlusion in both groups (100%). No significant adverse event were reported. RFA had less postoperative pain and bruising. However, both methods again showed comparable outcomes in terms of venous occlusion rates (97% for RFA and 96% for EVLT at 3 months follow-up), QoL, and return to normal activities.[25]

Steam Vein Sclerosis (SVS)

SVS is a new method of endothermal ablation, and the objective of this method is to provide more favorable treatment with fewer side effects than the traditional technique of thermal ablation (Figure 3). The SVS catheter delivers steam (maximal 120°C) that causes endothelial destruction followed by fibrosis.

Clinical results

Van den Bos et al. [26] demonstrated the non-inferiority of endovenous steam ablation (EVSA) compared to 910-nm EVLA in an RCT (LAST Trial). A total of 217 patients (237 legs) with GSV incompetence, with a mean age of 55 years, were recruited. EVSA was used to treat 117 legs (81 legs received the higher dose regime with a mean 2-3 pulses/cm, and the remainder received a lower dose of 1-2 pulses/cm), and 110 legs were treated using EVLA (using a LEED of 60 J/cm). At 1-year follow-up, the occlusion rate was 92% for EVSA and 96% for EVLA (p=0.331). Superficial thrombophlebitis at 2 weeks was a common complication in both groups (8.5%). In the EVSA group, 2.8% of legs still had thrombophlebitis at 12 weeks follow-up period, and 2 patients had a nerve injury.

At 12 weeks, clinical and QoL scores improved equally in both groups. Patients who were treated with EVSA reported lower post-procedural pain, shorter duration of analgesia use and increased satisfaction with their treatment.[26] Longer term follow-up and larger comparative studies are needed to confirm these early findings.

Endovenous Microwave Ablation (EMA)

EMA is another novel method of thermal vein ablation, which works by generating radio-frequency energy with the MICROTAZE OT-110M machine. It is commonly used in ablation of hepatocellular carcinoma and kidney resection.[7]

Clinical results

Subwongcharoen et al.[7] carried out the first swine model study, showing that EMA was able to cause thermal injury to all layers of the venous and arterial wall. The same research group recruited 20 patients with GSV reflux to assess the clinical efficacy of EMA. Closure rates of GSV was observed to be 100%, 65%, and 65% at 1-week, 6-months and 1-year follow-up, respectively. No significant complications were noted in this study.

In a RCT comparing conventional surgery to EMA for the treatment of GSV incompetence, EMA was shown to be efficacious, with 97% occlusion rate of GSVs in the EMA group, with no recurrence in the surgery group after 1-year follow-up.[6] However, studies comparing it with other endothermal ablation modalities and long-term follow-up are required.

Non-Thermal Non-Tumescent Ablative Methods

Sclerotherapy

Sclerotherapy has been used for decades in varicose vein treatment, using injection of sclerosing agents either in liquid or foam form into the vessel lumen to induce endothelial damage resulting in vein wall fibrosis. The commonly used sclerosing agents are either polidocanol (POL) (usually in 0.5% to 3% concentration) or sodium tetradecyl sulfate (STS) (1% to 3%). In July 2013, the NICE guidelines recommended the use of sclerotherapy as second-line treatment of varicose veins.[29]

Clinical results

Efficacy of foam sclerotherapy (FS) and liquid sclerotherapy (LS) has been investigated in a comparative non-RCT conducted by Yamaki et al.[30] Under ultrasound guidance, 62 patients were injected with either foam or liquid to treat GSV incompetence. Occlusion of saphenous incompetence was achieved in 68% of foam-treated patients and 17.5% of liquid-treated patients after 12 months.

A further study assessed the efficacy and complications of ultrasound-guided foam sclerotherapy (UGFS) with 197 truncal veins treated in 192 patients using POL. At 6-months follow-up, complete occlusion was obtained in 163 legs after the first intervention, 33 legs after a second and 1 leg after a third. Phlebitis and pigmentation were common complications.[31]

In 2006, Coleridge et al.[32] reported 6-month follow-up on 459 patients treated with POL and STS. 88% of the GSV and 82% the short saphenous vein (SSV) had remained obliterated.

A prospective RCT involving more than 580 legs compared 4 treatments: EVLA, RFA, UGFS and surgical stripping for GSVs. At 1-year follow-up, this study showed that UGFS was associated with a higher technical failure (16.3%) compared with other modalities ($p<0.001$). However, both RFA and UGFS were associated with a faster recovery and less postoperative pain compared with EVLA and surgical stripping. The cost of treatment was also lowest in the UGFS group. All 4 groups demonstrated similar improvement in disease-specific QoL and Short Form 36 (SF-36) scores. No major complications were reported.[33] At 5-year follow-up, the UGFS group was also associated with higher GSV recanalization rate. This study also found a higher than expected recurrence rate in the EVLA group and the authors have advocated the need for further trials to investigate this.[34]

The MAGNA RCT has also demonstrated that UGFS is inferior to EVLT and surgery. It randomized 223 patients (240 legs) with GSV reflux to UGFS, EVLT or surgery. Occlusion rates were significantly lower for UGFS (72.2%) compared with EVLT (88.5%) and surgery (88.2%) at 1-year follow-up. However, significant improvement of Euro-Qol 5 (EQ-5D) and Chronic Venous Insufficiency Quality-of-Life Questionnaire Scores (CIVIQ) was demonstrated in all groups.[35]

Longer-term (5-8 years) follow-up for UGFS has been reported by Darvall et al.[36] with 351 patients (479 limbs) included; 285 patients (391 limbs) attended for review after at least 5 years. Disease specific QoL improved significantly at long-term follow-up (85.5% compared with baseline) as did generic QoL. 82% of patients were satisfied with their treatment, and 91% would recommend the treatment to their family. Retreatment for recurrence was required in 15.3% of limbs by 5 years.

Comparison of UGFS with conventional surgery has shown that UGFS is associated with less pain and lower analgesia requirement and a faster return to normal activity and work.[35-37]

The CLASS multicenter RCT compared UGFS, EVLA and surgery and used disease-specific and generic QoL at 6 months as the primary outcome measure. The secondary endpoints were clinical success, QoL, anatomical success at 6 months and cost-effectiveness. All groups showed similar improvement in disease-specific QoL score, but when comparing surgery with FS, patients receiving surgery had

significantly better improvement in their QoL scores. No difference was noted in the generic QoL scores between either surgery *vs* EVLA or surgery *vs* UGFS. At 6-weeks, there were no differences in both the physical or mental component of the SF-36 scores. At 6-months, however, the mental component scores of SF-36 in patients undergoing EVLA showed greater health gain compared with those receiving UGFS. UGFS was the cheapest treatment option. VCSS scores improved in all treatment options at 6 months. In term of effectiveness, UGFS was worse than both surgery and EVLA ($p < 0.001$).[38]

Siribumrungwong et al.[39] conducted a study comparing endovenous ablation (RFA and UGFS) with surgery in terms of QoL found no difference between groups but both had significant physical and mental QoL improvements.[39]

Devereux and colleagues[40] evaluated the occlusion rate using catheter-directed foam sclerotherapy (CDFS) in a prospective blinded RCT. Fifty patients were enrolled and randomized to receive CDFS with or without tumescence. The tumescence contained a saline solution (0.9% sodium chloride) without adrenaline due to guidelines of the German Federal Institute (BfArm). After 12 months, patients were evaluated by blinded investigators. The primary occlusion rate was 73.9% for the CDFS with tumescent group and 75% for the CDFS group without tumescence. The authors believe that this lack of difference could be explained by the absence of adrenaline in the solution. Both groups showed a significant decrease of the vein diameter post-treatment with patient tolerance and satisfaction was high in both groups.

Complications

A systematic review of 1023 studies, covering 10,819 patients reported 11 cases of venous thromboembolism (1.07%), 8 cases of migraines (0.78%), one episode of transient ischemic attack and 7 (0.68%) cases of visual disturbances. These neurological symptoms have been associated with a patent foramen ovale (PFO).[41] The authors argue that despite a relatively high estimate of PFO in the adult population (up to 25%), the rate of neurological complications following FS appear to be low.[42] Tissue necrosis, telangiectasia matting, and skin discoloration have also been observed after FS.[43]

Mechanochemical endovenous ablation (MOCA)

MOCA was introduced in 2010 using the ClariVein® device (Vascular Insights, Madison, CT, USA) (Figure 4). The principle of this method combines mechanical abrasion of the venous wall using a rotating wire (3500 rpm) with simultaneous injection of liquid sclerosant. Since no heat is applied, the use of tumescent anesthesia is not needed.[44] In 2016, National Institute For Health and Care Excellence (NICE) issued interventional procedural guidance permitting the use of the MOCA for the treatment of varicose vein in the UK as a standard treatment.[45]

In 2012, Elias et al.[46] reported 6-month follow-up on 30 patients treated with the ClariVein® device, obtaining an occlusion rate of 96.7%. One patient developed recanalization of the treated GSV, 3 had ecchymosis, with no other adverse events recorded. This study demonstrated initial safety of the MOCA device.

MOCA has been demonstrated to be less painful than RFA in a cohort study. Sixty-eight patients with unilateral GSV reflux were recruited and received either MOCA or RFA. Postoperative pain using a 100-mm VAS was significantly less for MOCA (4.8 ± 9.7 *vs* 18.6 ± 17.0 mm; p <0.001) during the first 14 days after treatment. Earlier return to normal activities was significantly shorter in those treated with MOCA. At 6 months, significant improvement in the QoL was demonstrated in both groups.[47]

A recent multi-center randomized study of MOCA *vs* RFA for truncal vein reflux (VVCVV) recruited 170 patients and randomized to either MOCA (ClariVein®) or RFA (Venefit). The primary study endpoint was pain level during the procedure. This was evaluated by a VAS, which demonstrated that MOCA was significantly less painful (median 15 mm (IQR 7-36 mm)) than RFA (median 34mm (IQR 16-53)) (p=0.003). Patients undergoing MOCA also reported less pain on a 0-10 number scale (median 3 (IQR 1-5)) than RFA (4 (IQR 3-6.5); p=0.002). There were no significant differences between the 2 groups for clinical severity scores, disease-specific or generic QoL scores, or time to return to normal activities. Occlusion rates were similar in both modalities. Adverse effects reported were 1 DVT in each group.[48]

Another prospective multicenter RCT (MARADONA trial) is due to report soon, comparing MOCA with RFA in the treatment of GSV incompetence. This trial is intended to examine the anatomical, clinical success and post-procedural pain between MOCA and RFA at 1 year in 460 patients with follow-up for 5 years.[49]

Complications

Complications of MOCA include superficial thrombophlebitis and mild bruising at the puncture site.[50] One case of DVT has been reported.[48]

Cyanoacrylate glue (CA)

Cyanoacrylate embolization (CAE) is another recently introduced NTNTs method for the treatment of incompetent truncal veins. There are currently 2 techniques of CAE in use, the VenaSeal™ Closure System (Medtronic, Minnesota, USA) (Figure 5) and the VariClose® vein sealing systems (Biolas, Ankara, Turkey) (Figures 6 and 7). In the former technique, which gained FDA approval in 2015, the

catheter used is pulled back segmentally, and the cyanoacrylate used has a slow polymerization rate,[51] whereas the latter catheter is pulled back continuously, and the cyanoacrylate utilized has a more rapid polymerization.[52]

Clinical result

Almeida et al.[53] reported on 38 patients treated with CAE using the VenaSeal™ Closure System. Occlusion rates were 92.1% at 12 months, 92% at 24 months and 94.7% at 36 months follow-up. No serious adverse events were noted.[51] All demonstrated improvement in VCSS from a mean of 6.1 at baseline to 2.4 at 36 months follow-up. One patient developed iliofemoral deep venous thrombosis at 31 months, which the authors suggested was not related to the technique.

The multicenter, prospective European Sapheon Closure System Observational ProspectiveE (eSCOPE) study was conducted in 4 European countries assessing the closure rate of incompetent GSVs; 70 patients were recruited and treated with VenaSeal CAE, without tumescent anesthesia or post-interventional compression stockings. Results obtained using a life-table method showed the occlusion rate was 94.3% and 92.9% at 6 and 12 months follow-up, respectively. Patients showed significant improvement in QoL from 16.3 (±7.99) at baseline to 6.7 (±6.40) ($p < 0.0001$) and in VCSS from 4.3 (±2.3) at baseline to 1.1 (±1.3) at 12 months. Eight cases of phlebitis (11.4%) were reported. One patient experienced a 6 mm thrombus extension beyond the saphenous femoral junction (SFJ) which was treated with low-molecular-weight heparin. The eSCOPE study showed that CAE is safe and effective in the treatment of GSV incompetence.[54]

The VeClose multicenter RCT has demonstrated that CAE is non-inferior to RFA. Among 222 patients with GSV reflux randomly assigned to receive either CAE with VenaSeal or RFA, occlusion rates were 99% for the CAE compared with RFA (96%) at 3 months follow-up. At day 3, patients in the CAE group experienced less postoperative ecchymosis compared with those in the RFA group ($p<0.01$). Pain experienced during the procedure for both groups was comparable.[55]

One-year data from a non-randomized study of cyanoacrylate CAE (VariClose®) compared with EVLA in 310 patients demonstrated an absence of GSV reflux in 95.8% of the groups treated with CAE compared with 92.2% for EVLA at 1-year follow-up. The CAE group was associated with a shorter operative time and less peri-procedural pain compared with the EVLA group. Patients treated with CAE had significantly less ecchymosis compared to those treated with EVLA ($p<0.001$). This suggests that VariClose treatment is safe and can be utilized for the treatment of saphenous incompetence.[52]

Complications

Complications following the use of CAE includes phlebitis and ecchymosis.[55] A thread-like thrombus extension has been reported with the VenaSeal system, which resolved spontaneously without additional adjunctive treatment after 6 months follow-up.[51]

Cost-effectiveness of Endovenous management

The cost of healthcare provision is a key issue in the management of varicose veins.[56] In 2015, Marsden et al.[57] conducted an economic analysis comparing surgery, endothermal ablation (ETA), UGFS and compression stockings (CS). Their analysis aimed to supplement the NICE clinical guidelines on varicose veins. Using a Markov decision model, ETA was found to be the most clinically effective treatment, and its incremental cost-effectiveness ratio was £3.767 per quality-adjusted life year (QALY) gained when compared to UGFS. Overall, all intervention modalities for varicose veins were cost-effective when compared with CS in the UK NHS.

Two recent systemic reviews have compared intervention modalities. In the first, Carroll et al.[58] conducted a systemic review and network-analysis of 31 RCTs comparing ETA (RFA and EVLA) and FS to traditional surgery for varicose veins, in terms of recurrence, VCSS, pain and QoL. They found that FS was the cheapest method and with a greater efficacy compared to surgery (+0.0015 QALYs). Both QALYs gained and incremental cost effectiveness were also higher with ETA. Thus, authors concluded that when the cost of ETA was equivalent to surgery, the former can be considered to be the more cost-effective option (Table 1).

The second systemic review performed looked at the comparative effectiveness and the cost-effectiveness of superficial venous interventions over 5-years. The methods investigated include conservative care (CONS), surgery (HL/S), UGFS, ETA, and the newer NTNTs techniques (MOCA and CAE). The studies included in this systemic review were RCTs for conventional treatment modalities and non-RCTs for the newer NTNTs. Results illustrated that CONS is associated with a lower overall cost and QoL. All other interventions seem to have similar cost and clinical effectiveness apart from CAE which was the most expensive. At the threshold of £20,000 per QALY gained in the National Health Service (NHS, UK), ETA was found to have the greatest QALY gain when compared with other interventions over 5 years (Table 2).[59]

Alternative method

Transillumination powered phlebectomy (TriVex)

TriVex is a less invasive surgical procedure for the removal of varicose veins. This was first described by Spitz et al.[27] in 2000.

Aremu and colleagues[28] compared conventional stab avulsions to TriVex. Their data showed that 21.2% patients in the TriVex group had recurrence at 52 weeks compared with 6.2% in the stab avulsions group. Patients who were treated with the TriVex had fewer incisions; however, both groups showed neither difference in operating time nor perceived cosmetic benefit. Longer-term results are still missing. Larger studies therefore are required to determine the real value of this method in the management of varicose vein disease.

Summary

- **Thermal treatment (TT) with RFA or EVLA is the mainstay of varicose vein treatment at present**
- **Both RFA and EVLA appear to have similar efficacies**
- **TT is associated with discomfort during tumescent infiltration and not ablation part of procedure itself.**
- **NTNTs do not require tumescent and do not use thermal energy – potentially more advantageous**
- **Foam sclerotherapy is cheap, but associated with higher recurrence rate**
- **So far, TT and NTNT seem to have similar efficacy, but longer term, comparative studies needed.**

Conclusions

The management of varicose veins has dramatically progressed since the advent of endovenous ablation. Thermal techniques have now superseded surgery as the gold-standard treatment method. So far, the non-thermal-non-tumescent options appear to be of similar efficacy without presenting the potential risk of nerve damage. However, further work is required to compare thermal against non-thermal ablation as well as non-thermal against non-thermal in high-quality prospective trials.

Author contribution

All authors contributed to: (1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and, (3) final approval of the version to be published.

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Figures:

Figure 1: A radiofrequency ablation generator and catheter

Figure 2: The Olympus-Celon RFiTT generator (radiofrequency induced thermotherapy)

Figure 3: (A) the Steam Vein Sclerosis device (B) the steam generator (C) the steam catheter[8]

Figure 4: ClariVein® Mechanochemical Ablation Device (40)

Figure 5: Figure 6: The VenaSeal™ Closure System

Figure 6: The VariClose® Vein Sealing System

Figure 7: Delivery tools of The VariClose® Vein Sealing System

Table 1: Results of the discounted probabilistic sensitivity analysis; an economic analysis of treatments for varicose veins.[58]

Table 2: Cost-effectiveness for each treatment option.[59]

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Figures:

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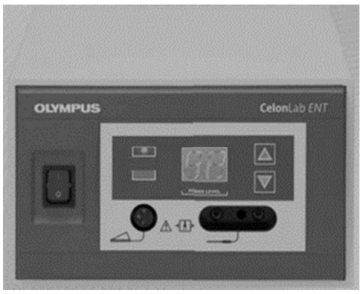

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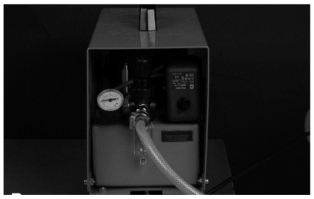
A



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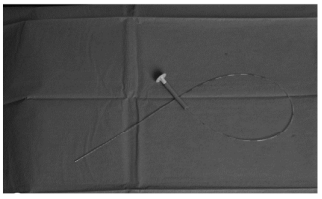


C

Figure 4: ClariVein® Mechanochemical Ablation Device.[40]

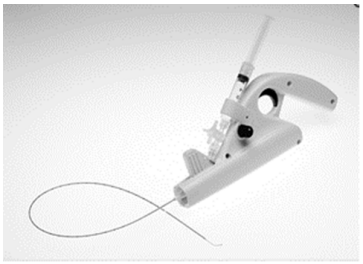


Figure 5: Figure 6: The VenaSeal™ Closure System

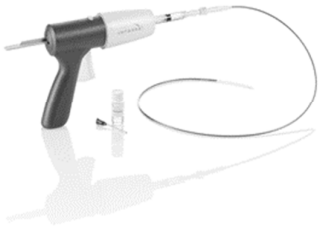
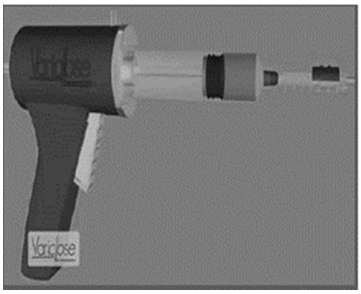


Figure 6: The VariClose® Vein Sealing System



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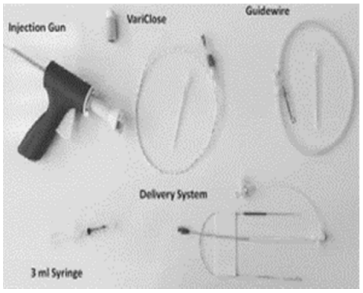

Running head: ENDOVENOUS MANAGEMENT OF VARICOSE VEINS
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Table 1: Results of the discounted probabilistic sensitivity analysis; an economic analysis of treatments for varicose veins.[58]

Discounted	**Incremental**				
Procedures	**Costs (£)**	**QALYs**	**Costs (£)**	**QALYs**	**ICER (£)**
Surgery	1334	8.0347	-	-	-
FS	804	8.0362	-530	0.0015	n. a
EVLA	2637	8.0372	1302	0.0025	518 462
RFA	2952	8.0359	1617	0.0012	1 352 992

(QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio; FS: foam sclerotherapy;

n.a: not applicable; EVLA: endovenous laser ablation; RFA: radiofrequency ablation)

Table 2: Cost-effectiveness for each treatment option.[59]

Procedures	**QALY**
CONS	0.170
HL	0.002
UGFS	0.136
EVLA	0. 316
RFA	0.265
MOCA	0.111
CAE	0.000

(CONS: conservative; HL: high ligation and stripping; UGFS: ultrasound-guided foam sclerotherapy;

EVLA: endovenous laser ablation; RFA; radiofrequency ablation; MOCA: mechanochemical ablation;

CAE: cyanoacrylate embolization; QALY: quality-adjusted life-year;)